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SECOND TASHKENT STATE MEDICAL INSTITUTE

YAKUBOVA NIGORA ABDUKHALIKOVNA

THE CONDITION OF AUDITORY AND VESTIBULAR ANALYZERS IN PATIENTS WITH BRUCELLOSIS INFECTION

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Yakubova N. A. The Condition of Auditory and Vestibular Analyzers in Patients with Brucellosis Infection

This monograph addresses pressing issues requiring resolution in the medical field today. It presents an analysis of the characteristics of hearing and balance disorders in acute and chronic forms of the disease, as well as the significance of diagnostic methods for auditory and vestibular impairments.

The research findings in this monograph facilitate early diagnosis of auditory and vestibular disorders in brucellosis patients, enabling timely treatment that contributes to positive treatment outcomes.

For otolaryngologists, infectious disease specialists, graduate students, doctoral candidates, and students in medical universities.

Editor-in-Chief: Kadyrova R. M. - PhD, Professor, Department of "General Pedagogy" at Nizami TSPU

Reviewers: Hakimov Z. Z. - Doctor of Medical Sciences, Professor, Department of Pharmacology, Tashkent Medical Academy

Khamrakulova M. A. - Doctor of Medical Sciences, Professor, Research Institute of Sanitation, Hygiene and Occupational Diseases of the Ministry of the Republic of Uzbekistan

CONTENTS

INTRODUCTION

The study of the current state and future spread of brucellosis does not allow for an optimistic forecast regarding the resolution of this issue, at least not in the coming decades. According to World Health Organization (WHO) statistics, brucellosis continues to be registered in countries across all geographic latitudes and climates. This problem is particularly relevant for Uzbekistan, where extensive livestock farming creates conditions favorable for the spread of *Brucella melitensis*, the most pathogenic strain for humans. The lack of a stable trend in reducing brucellosis morbidity rates, alongside the high occupational infection rate, is concerning. [54].

This issue is compounded by the widespread brucellosis infection in small livestock herds. The importance of studying this pathology is underscored by the fact that it predominantly affects young, working-age individuals, often leading to disability.

Despite the keen interest of scientists in the issue of systemic brucellosis, the study of ENT organ involvement in brucellosis infection remains underdeveloped. The literature contains some information on pharyngeal changes in brucellosis [44] and brief reports on certain clinical manifestations in the oropharyngeal mucosa in brucellosis and other infections [10, 37]. However, changes related to the nose, ear, hearing impairment, and vestibular analyzer involvement in brucellosis infection have not received adequate coverage in the literature. In practice, infectious disease specialists frequently seek consultations with otolaryngologists concerning ENT complications in patients recovering from brucellosis.

For otolaryngologists, there remains much that is unclear: only isolated clinical cases of this pathology are known, the pathogenesis is speculative, reliable diagnostic methods are lacking, and treatment approaches have not been developed. The majority of publications addressing these issues date back to the 1930s–1940s and 1960s–1970s. A study conducted with modern methodological approaches could

reveal early signs of hearing impairment and aid in developing preventive principles [1].

Numerous treatments for brucellosis have been proposed by researchers, including immunobiological, chemotherapeutic, physiotherapeutic, symptomatic, antibiotic, and other methods. The comprehensive therapy for brucellosis developed by domestic researchers yields positive results and often leads to full recovery. However, current brucellosis treatment protocols successfully employ ototoxic and vestibulotoxic drugs, which cause significant damage to the auditory and vestibular analyzers. Therefore, the trial of new, promising treatments for hearing impairments associated with this pathology may represent an important area for otorhinolaryngology research and practice.

CHAPTER 1. CURRENT STATE OF THE BRUCELLOSIS PROBLEM

1.1. CONDITION OF ENT ORGANS IN PATIENTS WITH BRUCELLOSIS

Currently, there is a trend towards an increase in the number of patients with various hearing impairments resulting from infectious diseases. This fact is associated with urbanization, unfavorable environmental conditions in many regions of our country, the lack of reliable preventive measures for most infectious diseases, particularly brucellosis, and impaired immunological reactivity in a significant part of the population.

In the systematic fight against many infectious diseases, aimed at sharply reducing brucellosis incidence and achieving the primary goal of complete eradication, healthcare workers and practicing physicians play a significant role.

According to views formed abroad, epidemic brucellosis is considered a disease of hot countries. However, in reality, epidemic brucellosis outbreaks periodically occur in any of the northern latitudes where small ruminants are infected.

There are two main routes of human infection with brucellosis: contact and alimentary (foodborne). In contact transmission, brucella bacteria enter the healthy body through mucous membranes and skin. Contact infection most often affects workers who care for brucellosis-infected livestock or handle the meat, wool, and hides of infected animals [22, 27, 43].

Alimentary infection primarily occurs through the consumption of dairy products—raw milk, cream, butter, cheese—or inadequately cooked meat from brucellosis-infected livestock. Additionally, water contaminated by secretions from infected animals can serve as a source of human infection [29, 30]. Thus, brucellosis spreads not only within infection hotspots but also far beyond their boundaries.

Brucellosis is characterized by a wide range of clinical manifestations that indicate systemic involvement, with a wave-like course featuring alternating periods of exacerbation and relative well-being, or even an absence of visible clinical signs of the disease.

The illness is accompanied by elevated body temperature and fever, which can present in four forms: undulant, irregular intermittent, remittent types, and prolonged low-grade fever [6, 12, 44].

According to most researchers, diagnosis plays a crucial role in the fight against brucellosis [25]. However, the clinical characteristics of contemporary brucellosis—with mild to moderate forms being predominant, a subdued clinical picture during the acute phase, and the polymorphism of somatic symptoms in subacute and chronic forms—significantly complicate primary clinical diagnosis. Literature sources [50] indicate that out of 624 patients with acute brucellosis, 256 were initially misdiagnosed. This is particularly common in cases where the nervous system is involved, resulting in a notably high rate of diagnostic errors. This reflects not so much a lack of knowledge among practicing physicians regarding brucellosis diagnosis, but rather the insufficient scientific development of clinical and instrumental criteria for diagnosing nervous system involvement in the current course of the disease.

Numerous clinical observations have shown that nervous system involvement occupies a central place in the clinical presentation of brucellosis [7, 12, 38].

A review of literature on the subject indicates that nervous system involvement in brucellosis occurs in 1.3% to 90.0% of cases [35, 38, 52, 57]. Researchers confirm that nervous system involvement remains one of the leading features in the clinical presentation of modern brucellosis, emphasizing the importance of neurovascular disorders [6, 36].

Literature sources reveal no consensus regarding the predominant involvement of the central or peripheral nervous system in modern cases of brucellosis. Some authors report a predominance of central nervous system involvement [15, 35], while others more frequently observed disorders affecting the peripheral nervous system [1, 25].

A comprehensive description of the clinical picture of contemporary brucellosis was provided by E. S. Belozerov (1985), who summarized years of observations conducted by the Infectious Diseases Department at the Semipalatinsk

Medical Institute. The author emphasizes the importance of nervous system involvement across all clinical forms of brucellosis.

Several authors [8, 41, 60] note that vascular lesions of the central nervous system are frequently seen in brucellosis, with several clinical variants identified. Vasomotor cerebral disorders are clinically characterized by transient, unilateral paresthesias of the limbs (more often in the arms than in the legs), with transient hemiparesis observed less frequently, sometimes accompanied by aphasia, localized or generalized seizures (petit mal), and migraine-type headaches. Spasms of the retinal and labyrinthine vessels (resulting in vertigo) have also been described.

Vasomotor cerebral disorders are more commonly observed in the later stages of brucellosis. Subarachnoid hemorrhages in brucellosis are marked by a significant temperature increase and a protracted course. These hemorrhages typically occur in the subacute or chronic stages of brucellosis, primarily during periods of exacerbation and relapse. They may appear independently or in combination with other forms of neurobrucellosis, such as brucellosis meningitis or meningoencephalitis. Consequently, the clinical presentation may include symptoms of meningeal irritation, involvement of various cranial nerves, spinal roots, and occasionally brain parenchyma. The development of subarachnoid hemorrhage is likely facilitated by the well-known diffuse vascular damage in brucellosis, particularly affecting the vessels of the pia mater. Hemorrhages into the brain parenchyma and thromboses of cerebral vessels predominantly occur in the course of brucellosis meningoencephalitis.

Researchers particularly emphasize the significance of widespread vascular involvement (allergic vasculitis) in the central nervous system in severe forms of neurobrucellosis [8, 15, 56].

A key element of the pathomorphological picture of brucellosis is widespread productive-destructive vasculitis of an allergic nature. In all forms of brucellosis, particularly with nervous system involvement, hyperergic vasculitis occurs, accompanied by pronounced mesenchymal and disseminated granulomatosis [7, 38, 53].

Brucellosis is associated with disturbances in vascular regulation, typically detected using plethysmography. Significant pathological lability in vascular tone, identified independently, indicates increased excitability of vasomotor centers, although some patients display inert vascular reactions.

Several studies [36, 6] demonstrate that the characteristics of plethysmograms are disease-form dependent: there is pronounced lability of plethysmograms in acute brucellosis, while an inert, primitive pattern, sometimes with a complete absence of responses, is observed in chronic cases.

A relationship has been established between the degree of allergic and vascular reactivity in brucellosis: hyperreactivity is associated with a wave-like background and strong responses, while hyporeactivity, on the contrary, is linked to an inert background and hyporeactive responses [12].

Productive-destructive vasculitis has been noted as a crucial element of the pathomorphological picture of brucellosis, often contributing to organ pathology in the disease [8, 36].

Studies of capillary condition using the Nesterov test in brucellosis also reveal abnormalities, characterized by an increase in pathological responses with a pronounced hemorrhagic effect. It has been found that capillary fragility, as shown in the Nesterov test, occurs 16 times more frequently in brucellosis patients than in healthy individuals, with fragility levels directly correlating with the severity of the condition.

Research on cerebral hemodynamics in brucellosis is limited. Pathological changes were identified in 85.7% of patients with brucellosis encephalitis using rheoencephalography. Peripheral blood circulation, assessed through rheovasography (RVG), was impaired in 92% of those examined. These findings suggest that brucellosis patients in the subacute or chronic stage consistently present with cardiovascular system involvement.

The considerable diversity of clinical manifestations in brucellosis is based on the effects of three factors: infectious, toxic, and allergic [130, 126]. In acute and

subacute forms of brucellosis, intoxication symptoms predominate, while in chronic forms, allergic changes in the vascular system appear alongside intoxication.

Disruption of the blood-brain barrier is considered the initial stage in the development of neurobrucellosis. There are two forms of neurobrucellosis: mesenchymal and parenchymal. The former is characterized by pronounced clinical and anatomical signs of allergic inflammation in the mesenchyme, while the latter shows marked nonspecific morphological changes in elements of the neural parenchyma. According to many authors, brucellosis infection affects the entire nervous system.

In the pathogenesis of neurological disorders in brucellosis, the penetration of the causative agents into the cerebrospinal fluid and their spread throughout various parts of the nervous system play a significant role. During the course of brucellosis infection, there is profound damage to the histostructural elements of the blood-brain barrier. The presence of brucella in the cerebrospinal fluid, subarachnoid spaces, choroid plexuses, ependyma, and brain tissue indicates that, in addition to lymphogenic and hematogenic routes, perineural spread of the pathogen also occurs. Anatomical changes in the brain membranes, the brain and spinal cord, peripheral nerve plexuses, and skeletal muscle nerve trunks serve as the morphological substrate for numerous clinical symptoms and forms of the disease.

According to the authors [26, 42], the peripheral nervous system is often involved much earlier than the central nervous system, being affected in 37-90% of cases, which is more frequent than other areas. In brucellosis, peripheral nervous system disorders—such as neuralgia, neuritis, plexitis, and radiculoneuritis—are almost constant findings.

According to available data, both domestic and foreign specialists noted nervous system involvement in brucellosis when describing its clinical manifestations even in the early stages of research. In many cases, these lesions determined the severity and outcome of the disease. Based on clinical observations, the authors concluded that both the central and peripheral nervous systems are

involved in the pathological process, with obligatory involvement of the meninges and vascular system.

Literature reports indicate that sensory organ damage occurs in brucellosis. For instance, cases of iritis, keratitis, neuritis, optic nerve atrophy, and other conditions have been described in brucellosis patients [29, 3, 52, 56].

Some cases of spinal cord lesions are documented, which may be combined with cranial nerve involvement, often affecting the optic nerves (“opticomyelitis”) or, more commonly, the auditory nerves (“acousticomyelitis”) [15]. Authors who describe the clinical manifestations of meninges lesions in the form of localized arachnoiditis also note involvement of the VII and VIII cranial nerve pairs [6, 36].

Researchers [8, 55] observed brucellosis meningitis with involvement of cranial nerves (oculomotor, facial, and auditory). One of the most severe forms of nervous system involvement in brucellosis—meningoencephalitis—almost always involves the auditory nerve [8, 15, 35, 38].

The clinical presentation of brucellosis may also include involvement of the upper respiratory tract and the auditory organ [44, 46].

Domestic scientists have made significant contributions to the study of brucellosis. They have thoroughly and extensively studied the symptoms, pathomorphology, therapy, epidemiology, and prevention of this disease [6, 26, 37, 51, 53].

Almost all studies addressing the clinical aspects of brucellosis emphasize the frequency and significance of nervous system involvement, highlighting the role of the vascular factor. Attention is drawn to the complexity of the pathogenesis and treatment of these disorders.

Brucellosis prevention became more successful following the introduction of a live brucellosis vaccine (a strain of cow-type brucella with reduced virulence but high immunogenic properties against all three types of brucella). Studies of this vaccine have demonstrated its complete safety and high epidemiological effectiveness; among vaccinated individuals, the incidence of brucellosis decreased by 3 to 25 times [15, 38].

Although numerous literary sources describe brucellosis, there is a lack of work specifically addressing ENT involvement in this disease.

Infectious diseases, including brucellosis, often affect the upper respiratory tract. The literature points to inflammatory and dystrophic changes in the upper respiratory tract mucosa observed in brucellosis. During the acute phase, hyperemia, infiltration, and swelling of the upper respiratory tract mucosa are noted [31, 32]; in chronic brucellosis, dystrophic changes (dryness, infiltration, subatrophy, etc.) are more commonly found.

One of the frequent symptoms of brucellosis is nosebleeds, caused by specific brucella-induced vascular damage: morphological and functional changes in precapillaries and capillaries [42]. Nosebleeds always indicate marked vascular system involvement and often coincide with severe cases of brucellosis, making them an important sign of the disease [14].

Regarding sinus diseases in brucellosis [56, 57], of seven brucellosis patients who reported pain in the nasal and sinus regions, three were clinically and radiologically diagnosed with sinus disease. The combination of vaccination and local radiotherapy led to recovery in all three patients, which, according to the author, confirms the brucella-related etiology of the sinusitis. The remaining four cases had pain caused by trigeminal neuralgia.

Some authors report dystrophic changes in the nasal mucosa in brucellosis. In the acute stage, these changes manifest as hyperemia, swelling, and infiltration of the nasal turbinates and septum; in the chronic form, varying degrees of atrophy and subatrophy of the mucosa are often observed. In 72% of cases, atrophic rhinitis and nasal mucosal changes are exacerbated by specific vaccine therapy and gradually subside after treatment completion, which further supports the brucella-related etiology of these changes [32].

Olfactory dysfunction is characteristic of brucellosis [47]. Olfactory disorders without visible organic changes in the nasal mucosa were detected in 9 out of 10 patients. The author attributes these issues to brucella-related olfactory nerve involvement.

Brucella-induced pharyngeal lesions have been documented [32, 33, 41, 47, 56]. Patients with brucellosis frequently show hyperemia and dryness in the posterior pharyngeal wall, along with changes in secretions. Symptoms include dryness, a scratching or constricting sensation, sometimes a foreign body sensation, and, in some cases, pain upon swallowing and thick mucus production.

The author notes, "…in some brucellosis patients, the pharyngeal region is in a state of acute inflammation. Acute pharyngitis symptoms persist stubbornly, and the process worsens during exacerbations of other brucellosis manifestations" [41].

Examinations of brucellosis patients [32] reveal hyperemia and vascular dilation in the palatine arches in 61% of cases; hyperemia and swelling of the uvula are seen in 50%.

Taste disorders in brucellosis are documented [47]. Taste disturbances (decreased, absent, or altered taste) were found in 7 out of 8 examined brucellosis patients. The author concludes that taste function is disrupted similarly to olfactory function in brucellosis.

Data from [32, 42, 59] and other authors suggest that the inflammatory process in brucellosis often involves the palatine tonsils, with a specific type of lesion. According to [57] and others, tonsillectomy shows positive effects in brucellosis patients with chronic tonsillitis, reducing joint and muscle pain, improving general health, extending fever-free periods, and making exacerbations milder. However, serological reactions to brucellosis remain positive.

Chronic tonsillitis in brucellosis, especially when frequently exacerbated, is thought to negatively impact the overall course of the disease [52].

Laryngeal involvement in brucellosis has been described by various authors, with three documented cases of laryngeal lesions in brucellosis patients. All cases were prolonged, with swelling, infiltration, and ulceration of the mucosa; laryngeal stenosis occurred in two patients. One patient improved with specific treatment, while another required a tracheotomy due to severe mucosal edema and infiltration; the third patient's breathing improved with specific treatment, but voice changes persisted. Due to the severe course of brucellosis, this patient ultimately died, and

autopsy findings included perichondritis and purulent melting of the cricoid cartilage. Histological examination of the larynx showed nonspecific chronic inflammation. The author attributes this condition to both intoxication and brucella infiltration of the laryngeal mucosa.

The author explains phonasthenia symptoms by general muscle weakness, characteristic of chronic and residual forms of brucellosis, and observed a case of hemorrhagic laryngitis with hemoptysis.

Histological examination of the upper respiratory tract mucosa in experimental brucellosis in guinea pigs [31, 32] revealed inflammatory changes in the nasal, pharyngeal, and laryngeal mucosa, resembling the brucellosis clinical picture.

Summarizing the data presented in the literature, it can be concluded that ENT organ involvement occurs in all stages of brucellosis. Many authors [14, 21, 32, 42, 48, 56, 60] suggest that ENT involvement in brucellosis is specific, i.e., brucella-related. Others question this specificity, as in most cases, brucella or related histological changes were not found in ENT lesions.

However, the results of pathological studies of ENT organs in individuals who died from brucellosis, as well as in experimentally infected animals, support the view of specific ENT diseases in brucellosis. The clinical presentation, indicating vascular and nervous system involvement in ENT organs, further strengthens this perspective.

The extent of ENT system involvement varies from mild to complete loss of organ function. These lesions may be the only manifestation of latent brucellosis.

1.2. DISORDERS OF THE AUDITORY AND VESTIBULAR ANALYZERS IN BRUCELLOSIS

The causes of sensorineural hearing loss are diverse, but it is most frequently associated with infectious diseases [2, 21, 61]. Sensorineural hearing loss of infectious origin accounts for about 30% of all cases of this condition [58]. Brucellosis is given considerable attention in the literature, as it often leads to various auditory and other ENT-related disorders.

In both domestic and foreign literature, there are brief reports on ear involvement in brucellosis [14, 21, 32, 33, 41, 47, 49, 52, 57, 61], indicating that brucellosis infection may cause ear pain, tinnitus, hearing loss, and balance disturbances. However, the type, nature, and extent of hearing impairment in relation to the form of the disease remain unclear.

Tartakovsky A. Y. [56, 57] wrote about the possibility of outer ear diseases in brucellosis. He documented a case of external auditory canal dermatitis that occurred simultaneously with vesicular skin eruptions; the tympanic membrane and hearing were unaffected. Improvement occurred after vaccine therapy and local ointment treatment.

It is noted that brucellosis can involve outer ear conditions (such as dermatitis, eczema, and furunculosis) and otalgia. According to the author's observations, external otitis and otalgia appear in all stages of the disease: acute, subacute, chronic, and during exacerbations of brucellosis. Anti-brucellosis treatment managed to resolve both the primary disease and the ear symptoms, although subsequent brucellosis exacerbations triggered recurrences in the auditory canal [48, 49].

Literature sources mention only isolated cases of middle ear disease in brucellosis. Complicated forms of purulent otitis media are more commonly reported in brucellosis patients. [56, 57] suggests that inflammatory processes in the middle ear developing in brucellosis patients should be considered manifestations of brucellosis infection, as otitis media occurred in patients following brucellosis infection and was resolved through specific anti-brucellosis treatment.

A patient with brucellosis and otitis media complicated by purulent mastoiditis was observed, with subsequent purulent meningitis. The brucellar etiology of the ear infection was confirmed by a biological method: Brucella melitensis was cultured from the ear discharge of the patient in a guinea pig model [54, 58].

Middle ear involvement in brucellosis patients, primarily affecting the sound-conducting apparatus, occurs in approximately 3% of cases. Based on his studies, the author concludes that brucellosis impacts the ligaments and muscles of the middle ear

in a manner similar to fibrositis and cellulitis, often leading to sclerosis, which is typical of brucellosis infection.

The literature provides a more detailed discussion on inner ear involvement in brucellosis. Like other chronic infectious diseases, brucellosis can cause atrophic-degenerative changes in the inner ear, sometimes bypassing the middle ear [44, 45], characterized by perceptual hearing loss with tinnitus. These changes may be localized either in the peripheral receptors of the auditory analyzer or its central pathways. Several authors [47, 48, 58] note that both the auditory and spatial analyzers are affected. Clinically, labyrinthitis presents with hearing loss, sometimes leading to total deafness, tinnitus, balance disorders, and autonomic reactions.

Many researchers studying ENT involvement in brucellosis report hearing loss. Initial reports of hearing impairment come from general practitioners, neurologists, infectious disease specialists, and other professionals. Inner ear involvement can occur in isolation or alongside brucella-related meningoencephalitis.

The literature includes a case of brucellar meningitis with auditory nerve involvement [54].

Three patients with neurobrucellosis involving the auditory analyzer have been documented [39, 40]. The author notes that hearing impairment is specific and may serve as a symptom of neurobrucellosis.

Auditory nerve damage is observed in 24% of brucellosis patients [35, 56, 57]. Hearing tests revealed various degrees of hearing impairment, from mild to severe hearing loss. Hearing loss developed gradually, was bilateral in most cases, and unilateral in only three cases; these patients reported persistent tinnitus.

During examinations, auditory nerve neuritis was detected in 25% of brucellosis patients [14]. Auditory nerve neuritis typically develops gradually in brucellosis, but deafness can occur suddenly during disease exacerbation in some cases.

The author attributes gradual auditory analyzer damage to degenerative-atrophic changes in the auditory nerve stem due to increased cerebrospinal fluid pressure, its alteration, and, consequently, the perilymph, as well as the toxic effects

of brucella on nerve fibers. Sudden deafness in brucellosis, according to the researcher [14], results from vascular spasms, leading to blood circulation disturbances in the inner ear and subsequent dysfunction of the cochlear and vestibular nerves. Persistent blood circulation issues cause irreversible degenerative-atrophic changes. The author describes a patient with severe brucellosis who experienced sudden hearing loss and was deaf for a month before hearing gradually returned. This type of deafness is likely due to hemorrhage in the organ of Corti, associated with vascular system damage in brucellosis.

Pathohistological changes in the middle and inner ear of guinea pigs with experimental brucellosis are detailed in [44, 45]. The author notes that in the early stages post-infection (1-2 months), the morphological changes observed in the ear fall within the range of nonspecific inflammation. It is suggested that these changes may be reversible during this period, which could explain the relative rarity of brucellar otitis in the acute and subacute stages. In later stages (chronic brucellosis), the author observed marked vasodilation with blood engorgement. In some cases, vascular wall necrosis with subsequent hemorrhage was present. Typical brucellosis granulomas (brucellomas) were also noted, consisting of epithelioid, plasma cells, lymphocytes, eosinophils, and central giant cells. At five months post-infection, connective tissue proliferation and subsequent sclerosis were observed.

These findings suggest that the changes identified in the middle and inner ear of test animals 3-5 months post-infection are specific to brucellar lesions. Such data provide insights into the causes of persistent deafness in patients post-infection.

Regarding hearing disorders in brucellosis, [33] reports bone conduction shortening in 40% of cases. Auditory nerve neuritis was observed in 15.6% of patients, ranging from minor hearing loss detected only by tuning fork tests to complete unilateral or bilateral deafness.

Tinnitus of various kinds is a common symptom accompanying auditory nerve damage in brucellosis [6, 18, 19, 20]; the sensation of tinnitus is linked to vasomotor disorders affecting the auditory analyzer in brucellosis.

Managing tinnitus in various conditions poses significant challenges [48]. In brucellosis, anti-brucella treatment often alleviates bothersome tinnitus. However, for some patients, the treatment provides only partial relief.

Several authors [32, 37, 49, 47, 45] highlight vestibular apparatus involvement in brucellosis, noting that the spatial analyzer is affected less frequently than the auditory one. Vestibular dysfunction primarily manifests as suppression (up to complete non-excitability) rather than hyperexcitability. Vestibular analyzer involvement in brucellosis is found in 12.5% of cases [48, 49]. In 10% of cases, these changes coincide with auditory function impairment. Spatial analyzer dysfunction is often transient; only in chronic forms of brucellosis, with accompanying neurological and systemic disorders, are lasting vestibular dysfunctions observed.

Literature analysis indicates that the inner ear is more frequently affected by brucellosis than the outer or middle ear.

The prognosis for inner ear involvement in brucellosis patients is relatively unfavorable: inner ear function often does not recover, and despite general health improvements and recovery from brucellosis, persistent hearing loss and even deafness, as well as irreversible vestibular dysfunction, remain.

CHAPTER 2. GENERAL CHARACTERISTICS OF CLINICAL MATERIAL, RESEARCH METHODS, AND TREATMENT

2.1. RESEARCH MATERIAL

In accordance with the study’s objectives, 128 patients with various forms of brucellosis were examined (87 men and 41 women), all of whom were treated at the Clinical Infectious Diseases Hospital of the Scientific Research Institute of Epidemiology, Microbiology, and Infectious Diseases in the Republic of Uzbekistan.

The data indicate that the lowest incidence of brucellosis occurs in individuals under 20 years of age (9.4%), while the majority of cases occur in the 20 to 50 age group (81.2%). This prevalence is attributed to the fact that individuals in this age

group predominantly work in professions that involve contact with sources of brucellosis (such as animal care and processing various types of animal raw materials).

Most of the patients are agricultural and livestock industry workers. Among the patients, 53 (41.4%) contracted brucellosis through direct contact, 61 (47.6%) through the alimentary route, and in 14 cases (10.9%), the transmission route was unclear. Literature analysis shows that both contact and alimentary transmission occur with similar frequency.

Patients with brucellosis of less than six months' duration (acute and subacute forms) numbered 46 (36%), while 57 (44.5%) had suffered from brucellosis for over a year (chronic form); in 19.5%, the onset of the disease could not be determined (primary chronic form). For inclusion in the study and classification into groups, patients without comorbidities or without significant clinical manifestations of such were selected.

According to the classification by N. I. Ragoza (1941) and V. M. Madzhidov (1968), there are four forms of brucellosis infection: primary latent form, acute septic form, septic-metastatic (subacute) form, primary chronic, and secondary latent form.

Individuals residing in endemic areas or engaged in occupations with potential brucellosis exposure often exhibit positive seroallergic reactions without clinical manifestations of brucellosis. Such individuals are essentially healthy, and this condition is referred to as the primary latent or asymptomatic form of brucellosis.

The primary latent form of brucellosis corresponds to the phase of compensated infection, characterized by an absence of pronounced clinical symptoms. Typically, individuals with this form do not seek medical attention and are only identified during routine examinations.

Our observations indicate that brucellosis generally begins gradually, with nonspecific symptoms such as general malaise, fatigue, poor sleep, reduced appetite, decreased productivity, headaches, muscle and joint pain, and lower back pain. The prodromal period may last up to three weeks. The disease then gradually progresses

into an acute form with fever, chills, increased irritability, depression, euphoria, headaches, and dizziness.

In the acute phase, internal organ enlargement (liver, spleen, lymph nodes) is observed. This acute phase can last several days, accompanied by symptoms of autonomic nervous system involvement, including bradycardia, low blood pressure, and muffled heart sounds.

As intoxication symptoms gradually subside, allergic lesions of various organs and systems with fluctuating clinical symptoms emerge, characteristic of the subacute form of brucellosis.

If clinical manifestations persist for more than six months from the disease onset, the indolent or subacute form transitions to chronic brucellosis. This transition often occurs due to misdiagnosis. In cases where the pathological process does not resolve during the acute phase and takes a prolonged course, secondary chronic brucellosis develops.

Primary chronic brucellosis develops when the disease assumes a prolonged, chronic course from the beginning, without an acute septic phase. This form of brucellosis is relatively common today, with diagnoses often made long after disease onset.

Delayed diagnosis of primary chronic brucellosis can be attributed to its milder clinical presentation compared to secondary chronic brucellosis. This form has a more benign course.

In chronic brucellosis, musculoskeletal, nervous, and vascular system changes predominate, with a focus on peripheral vascular involvement. Severe localized joint damage occurs, including destructive arthritis and changes in major joints.

The secondary latent form of brucellosis involves process compensation and differs from the primary latent form in its development mechanism. Secondary latent brucellosis refers to individuals in a state of clinical recovery.

Nervous system involvement is quite common. The manifestations are highly variable since different parts of the peripheral and central nervous systems may be involved. Nervous system disturbances can occur in various phases and clinical

forms of brucellosis, significantly impacting the diversity and lability of symptoms. Cases where these manifestations dominate are classified as neurobrucellosis.

Among the patients observed, nervous system involvement was associated with mild symptoms, such as headaches, dizziness, and nausea (43%); severe manifestations included olfactory and visual disturbances, as well as pronounced vestibular disorders (67%). Numerous comorbid conditions involving other organs and systems were also identified.

Patients with atypical or mild forms of brucellosis (primary and secondary latent forms) were not found in the hospital and are therefore not included in this study.

2.2. BRUCELLOSIS DIAGNOSTIC METHODS

When diagnosing brucellosis infection, epidemiological history data (occupation, contact with infected animals), specific clinical features, and laboratory test results were considered.

In daily practice, specific serological tests are used to diagnose brucellosis, particularly the agglutination test, or Wright's test, and the Heddleston test (1928), as well as the intradermal allergic test with brucellin according to Burnet (Burnet's reaction). The classification of clinical forms of brucellosis by N. I. Ragoza, later supplemented by V. M. Madzhidov, remains in use for diagnosing brucellosis and is followed by infectious disease specialists working on brucellosis at the Clinical Infectious Diseases Hospital of the Scientific Research Institute of Epidemiology, Microbiology, and Infectious Diseases in Uzbekistan.

An analysis of development charts showed that laboratory test results for brucellosis, including the IHA, Heddleston, and Wright tests, were positive in all 128 of our patients.

2.3. OTOLARYNGOLOGICAL EXAMINATION

Patients treated for brucellosis at the infectious disease hospital underwent otolaryngological examination upon admission, at discharge, and were followed up in the long-term recovery period.

During a thorough medical history collection, attention was given to any prior ear diseases (such patients were excluded from the study). The otolaryngological examination focused on the condition of the nose, nasopharynx, and tympanic membrane (elasticity, retractions, perforation, scarring, adhesions). Hearing was assessed using whispered and spoken speech tests, and air-conduction tonal threshold audiometry was conducted at frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hz. In the acute and subacute phases of the disease, these assessments were performed in the initial days after hospitalization and exclusively on patients who had not previously received ototoxic antibiotics (such as streptomycin or gentamicin).

For comparison of hearing impairments identified in brucellosis patients who had taken ototoxic drugs (streptomycin, gentamicin), a group of patients with primary chronic brucellosis who had no history of ototoxic antibiotic use was included, as well as a group with secondary chronic brucellosis who had previously received ototoxic antibiotics.

Olfactometry

The function of the olfactory analyzer was evaluated using the V. I. Voyachek method. Test bottles contained a 0.5% acetic acid solution (weak odor), wine alcohol (moderate odor), and valerian tincture (strong odor). Testing was conducted in ascending order for each nostril separately.

Results were evaluated on a three-degree scale. If the patient could not detect the 0.5% acetic acid odor but identified the other solutions correctly, it was recorded as grade I olfactory impairment. If the patient could not recognize the odor of wine alcohol, it was classified as grade II impairment. If the patient could not differentiate

the valerian tincture odor, it was regarded as grade III impairment (severe reduction, equivalent to anosmia).

Hearing Examination

In addition to otolaryngological examination and preliminary hearing tests, a detailed functional assessment of the auditory and vestibular analyzers was performed on patients with acute, subacute, chronic, and primary chronic forms of brucellosis upon admission, at discharge, and in the long-term follow-up period.

Hearing assessment began with whispered and conversational speech perception, with the unaffected ear masked following Wegener's method. Tuning fork tests were conducted using C128 and C2048 forks according to standard protocols, including Weber's lateralization test, and the Rinne and Schwabach tests.

Tonal threshold audiometry was performed on an MA-31 audiometer by Klamann and Grachuert (Germany). Tone perception thresholds for air and bone conduction were measured across a frequency range of 125-8000 Hz. To prevent crossover hearing, the unaffected ear was masked with broadband noise at an intensity of 70 dB above the hearing threshold.

Among suprathreshold hearing assessment methods, the differential sound intensity perception threshold (DPT) was measured using Lucher's method (1948). Speech audiometry was conducted with a Rostov-2 tape recorder, delivering sound signals through MA-31 audiometer headphones. Standard tables of multisyllabic words in Russian (Grinberg G. I., Zindler L. G., 1957) and Uzbek (Agzamov S. A., 1952) were used.

The ultrasound hearing examination was conducted using the method of B. M. Sagalovich (1963) with a GZ-33 ultrasonic frequency generator. A generated signal at a frequency of 137 kHz, with a range of 0 to 30 V, was delivered through a piezoceramic emitter with the same resonant frequency to the mastoid area to determine ultrasonic hearing sensitivity, and to the forehead area to assess lateralization of ultrasound. Petroleum jelly was used as the contact medium. It was essential to ensure that the duration of contact between the ultrasonic emitter and the

skull surface did not exceed 1-2 seconds when measuring ultrasonic hearing sensitivity and assessing lateralization, as prolonged contact could lead to a disappearance or shift of the auditory effect.

An objective method—acoustic impedance audiometry (impedance audiometry)—was also used to assess hearing impairments in brucellosis. Testing was performed on a Zodiac 901 impedance meter by Madsen Electronix (Denmark), following the full protocol: tympanometry, measurement of static compliance (static ear impedance), and determination of the acoustic reflex threshold (acoustic reflexometry of middle ear muscles). Tympanometry was performed over a pressure range in the external auditory canal from +400 to -200 mm H_2O at a probe tone frequency of 275 Hz.

The acoustic reflex was measured with ipsilateral and contralateral stimulation using a pure tone at 1000 Hz.

Vestibulometry.

The study of the functional state of the vestibular analyzer included an assessment of spontaneous vestibular disorders and experimental vestibular tests. Vestibulometry was also conducted upon hospital admission and discharge.

Spontaneous nystagmus, static balance, and gait were visually observed, and coordination tests were performed. Experimental vestibular tests included a bilateral caloric test, conducted following the method of N. S. Blagoveshchenskaya (1984). Each ear was irrigated with 100 ml of water at temperatures of 25°C and 49°C, and the vestibular reaction components were visually evaluated. In analyzing results, attention was paid to the symmetry of responses when testing the right and left ears.

For objective registration of nystagmus and accurate quantitative and qualitative assessment of vestibular reactions, as well as to make an objective judgment on the dynamics of vestibular disorders, we used electronystagmography (ENG).

When processing the data, the following principle was applied: if the indicators of the vestibular analyzer’s functional state exceeded the range of values

obtained from the control group, this was considered a functional impairment—either hyperreflexia, hyporeflexia, or areflexia. The examination of patients with hearing impairments that developed during the clinical manifestations of brucellosis was conducted dynamically, following the principles and methods outlined in Chapter 3 of this work.

It is known that a common cause of various hearing disorders is a disruption of cerebral circulation. To clarify the mechanism of hearing changes that arose during brucellosis, we examined the functional state of the vessels in the carotid and vertebrobasilar vascular systems of the brain.

The examination was conducted at rest, in a specially equipped shielded cabin, using the URG-2M device and recorded on an 8-channel EEG "Medikor" (Hungary). Rheoencephalography was performed in the morning, following a five-minute adaptation period in a seated position in the cabin.

REG recording was conducted in the fronto-mastoid (FM) lead, reflecting hemodynamics in the carotid vascular system of the brain, and the occipito-mastoid (OM) lead, indicating cerebral blood flow in the vertebrobasilar vascular system (Eninya G. N., 1973; Yarulin Kh. Kh., 1983).

Visually evaluated parameters included vascular tone, presence of peripheral vascular resistance, tone lability, and venous congestion. Additionally, parameters such as anacrotic rise duration (α, sec), tonic tension index (H1, expressing the ratio of dicrotic notch height to wave maximum), rheographic index (N), and interhemispheric asymmetry coefficient (K) were calculated.

Mathematically calculated parameters included the rheographic index (RI), dicrotic index (DI), diastolic index (DSI), L/T ratio, and asymmetry coefficient (ASC).

Further studies focused on chronic hearing loss post-brucellosis and with ototoxic drug intake. This previously mentioned group included 25 patients with primary chronic brucellosis infection who did not report hearing reduction or impairment during illness onset. All patients with chronic hearing loss after

brucellosis were examined in the same manner as patients with acute and subacute forms.

Some patients with chronic hearing loss after primary chronic brucellosis infection were monitored dynamically during treatment.

Observation lasted two years, during which a total of 113 patients with acute, subacute, secondary chronic, and primary chronic brucellosis underwent three courses of comprehensive treatment for post-brucellosis hearing impairments. Each course lasted 10-12 days, with 3-4 month intervals.

For treatment, examined individuals were divided into four groups based on the form of brucellosis. The first group included 22 patients who had acute brucellosis; the second included 20 patients with the subacute form; the third included 46 patients with the chronic form (who had received ototoxic antibiotics for brucellosis); and the fourth included 25 patients with primary chronic brucellosis (a comparison group that had not received streptomycin).

According to study results, patients with acute and subacute brucellosis experienced conductive hearing loss. Therefore, treatment primarily aimed at eliminating residual inflammation or scar-induced obliteration of the tympanic cavity and restoring Eustachian tube function.

Forty-six patients aged 21 to 40 underwent catheterization of the Eustachian tubes using a metal probe. Suspensions of hydrocortisone, enzyme preparations (lidase, trypsin, chymotrypsin), combined with tragal pneumatic massage #10, were introduced into the Eustachian tube. The procedure was performed under topical anesthesia of the nasal mucosa using dicaine solution.

In parallel, helium-neon laser therapy was used to improve microcirculation, reduce mucosal edema of the Eustachian tube, and improve its patency. Treatment was performed with an LG-38 device (Russia), with a wavelength of 0.63 μm and output power of 10 mW. Radiation was delivered through a metal catheter inserted into the nasal cavity near the Eustachian tube’s pharyngeal opening via a flexible quartz light guide. Exposure duration was 5-7 minutes, with a course of 5-8 sessions.

Endaural electrophoresis with proserine was also applied, five sessions to each ear.

In patients with secondary chronic brucellosis, two types of hearing impairments were noted: mixed-type with a predominant perception component, and solely sensorineural. Therefore, these patients were divided into two subgroups.

In the first subgroup of 21 patients, treatment involved daily catheterization of the Eustachian tubes with the introduction of a Lidase solution, 10 sessions. Medications to improve blood supply to the auditory nerves and cochlea were prescribed, as well as drugs that enhance tissue metabolism and synaptic transmission of nerve impulses, taking into account general therapeutic contraindications. For this purpose, injections (a "cocktail") were administered in the postauricular area according to a specific protocol, consisting of the following solutions:

- Nicotinic acid 1% 0.2–1.0 ml in increasing dosage until a reaction occurs; it has a vasodilatory effect and improves carbohydrate metabolism.

- Aloe 1 ml, which has a stimulating effect and accelerates regeneration processes.

- Vitamin B1 5% 1.0 ml, which enhances tissue metabolism.

- Proserine 0.05% 1.0 ml, which improves peripheral mediator processes.

- Cavinton solution 2 ml in 200 ml of 0.9% saline solution, administered intravenously, 6 times, followed by oral administration of 1 tablet (15 mg) three times a day for 2 months.

Among physiotherapy procedures, electrophoresis with a 1% potassium iodide solution was applied to the mastoid process area, 6–8 sessions.

In the second subgroup of patients, where hearing impairment was observed only in terms of sound perception, treatment focused on restoring inner ear function. A cocktail was administered daily, 10 sessions, to the mastoid area (meatotympanically), consisting of: 1% nicotinic acid solution, 0.2–1.0 ml until a reaction occurred; 1.0 ml aloe solution; 5% vitamin B1 solution, 1.0 ml; 0.05% proserine solution, 1.0 ml; and 0.05% novocaine. Concurrently, the patients received

electrophoresis with 1% potassium iodide (KI) solution, 6–8 sessions, to the postauricular area.

It is known that tinnitus accompanies and exacerbates hearing loss, eventually causing nervous system disturbances (Veselago O.V., 2000). The pathogenic factor here involves impaired blood circulation in the cerebral and inner ear vessels. Changes in vascular regulation within the ear play a significant role in the complex mechanism of this pathological condition.

Numerous studies indicate that hyperbaric oxygenation (HBO) has a beneficial effect on the progression of pathological processes by increasing the amount of physically dissolved oxygen in the blood and tissues, promoting oxygen saturation of various tissues (Stewart R. J. et al., 1994).

Given that patients in the second subgroup with severe tinnitus showed no ventilation issues in the Eustachian tube, HBO was administered alongside medication therapy. HBO was performed in an OKA-MT single-patient therapeutic chamber. The HBO course consisted of 10 sessions. Individual selection of the optimal HBO regimen for each patient was conducted through titration with several adaptation sessions, monitored via acid-base balance (ABB) parameters. Oxygen pressure in the chamber averaged 1.5–2.5 atm, with exposure at target pressure lasting 40–60 minutes.

The results and rationale for the conducted treatment of hearing impairments in patients after brucellosis infection are detailed in Chapter 4 of this work.

Data obtained from the material analysis were processed using methods of variational statistics. Numerical data were analyzed using standard techniques on a Pentium III computer with Excel software. Statistical significance was calculated using the Student's t-test. Results were considered statistically significant when $P < 0.05$.

CHAPTER 3. STUDY RESULTS OF THE CONDITION OF ENT ORGANS, AUDITORY AND VESTIBULAR ANALYZERS DURING CLINICAL MANIFESTATIONS OF BRUCELLOSIS INFECTION

3.1. APPLICATION OF EARLY DIAGNOSTIC METHODS FOR HEARING DISORDERS IN PATIENTS WITH BRUCELLOSIS, CONSIDERING DISEASE FORM

Condition of ENT Organs in Patients with Brucellosis

According to scientific sources, during the acute phase of brucellosis, patients experience inflammatory and dystrophic changes in the mucous membranes of the upper respiratory tract. Based on this, we attempted to analyze the condition of the upper respiratory tract in the patients with brucellosis under our observation.

Condition of the Nose and Its Paranasal Sinuses

Among the 128 patients examined, no lesions of the external nose were detected, regardless of the form of brucellosis.

Most patients complained of nasal congestion and dryness, as well as reduced or, in some cases, loss of smell. Upon examination of the nasal cavity, changes in the mucous membrane were identified in 22 patients (22.7%).

In the acute and subacute stages of brucellosis, 15 patients (11.7%) exhibited hyperemia of the anterior sections of the nasal turbinates and nasal septum, with some patients showing mucosal infiltration of the anterior septum and crusts in the nasal passages.

In 12.3% of cases, patients presented with catarrhal and hypertrophic forms of rhinitis, characterized by whitish spots, most often in the anterior regions of the inferior nasal turbinates, and a narrowing of the nasal passages.

In 14 patients with chronic brucellosis, signs of atrophy or subatrophy of the nasal mucosa, including pallor, dryness, thinning, widening of the nasal passages, and the presence of crusts, were more or less pronounced. The atrophic changes

observed in the nasal mucosa were likely due to the disruption of trophic innervation caused by brucellosis intoxication.

Reduced olfactory function was recorded in 22 patients (17.2%) with the chronic form and in 1 patient (0.8%) with the subacute form of brucellosis. No olfactory disturbances were found in patients during the acute phase.

Seventeen of the 22 patients with olfactory function disorders had bilateral impairment, while the remaining 5 had unilateral impairment. In addition to changes in olfactory function, subatrophic mucosal processes were identified in 7 patients, and catarrhal rhinitis in 4 patients.

Thus, olfactory analyzer changes were more frequently observed in the chronic form of brucellosis among our patients. Reduced olfactory function can be explained by the presence of chronic nasal mucosal inflammation, damage to the olfactory epithelium, or impairment of the olfactory nerve stem due to brucellosis infection.

One of the common symptoms of brucellosis is nasal bleeding. It occurred in 11 patients (7.2%): 1 patient under 20 years old, 3 patients aged 21–30, 3 patients aged 31–40, and 5 patients over 41 years old. Among these patients, 2 had acute brucellosis, 2 had subacute brucellosis, and 7 had chronic brucellosis.

Our observations indicate that nasal bleeding in brucellosis is more common in elderly patients and in cases with a chronic course of the disease. The bleeding primarily originated from the anterior sections of the nasal septum in individuals with pronounced atrophy of the nasal mucosa.

It is worth noting that, in the patients observed, nasal bleeding was rare and minor in volume.

In addition to nasal bleeding, atrophic rhinitis was observed in 5 patients, catarrhal rhinitis in 5 patients, and olfactory disturbance in 1 patient during the clinical manifestations of brucellosis.

It should be noted that specific treatment for brucellosis in patients with frequent nasal bleeding yielded a positive effect: nasal bleeding ceased, and the general condition significantly improved.

Disease of the paranasal sinuses, confirmed by radiographic examination and maxillary sinus puncture, was detected in 16 patients (12.5%). Among them, 3 patients (2.3%) had acute catarrhal sinusitis, and 13 patients (10.1%) had chronic purulent sinusitis. Lesions of the paranasal sinuses were observed exclusively in patients with the chronic form of brucellosis.

These patients complained of pain in the area of the affected sinus, nasal congestion, abundant nasal discharge, headaches, joint pain, lower back pain, sweating, and other symptoms.

Bilateral sinus involvement was found in 12 patients (9.4%) and unilateral involvement in 4 patients (3.1%).

Changes in the paranasal sinuses among the patients studied were accompanied by nasal bleeding, olfactory disturbances, taste dysfunction, and auditory nerve neuritis.

As a result of therapeutic measures, improvement was observed in both nasal conditions and the general manifestations of brucellosis infection.

Several factors indicate an etiological connection between diseases of the paranasal sinuses and brucellosis:

1) Bilateral involvement of the nasal sinuses;
2) Other nasal conditions (nasal bleeding, olfactory disturbance) frequently associated with brucellosis;
3) Involvement of other ENT organs (hearing impairment, vestibular analyzer dysfunction, taste disorder);
4) Sinus lesions occurred in all patients following brucellosis onset, with sinusitis developing simultaneously with exacerbation of the brucellosis process;
5) Specific anti-brucellosis treatment proved effective in addressing both general and local symptoms.

Similar results have been obtained by other researchers.

Condition of the Pharynx

Patients with brucellosis reported complaints of throat pain, tingling sensations, dryness, and scratchiness. Upon examination, varying degrees of pharyngeal mucosa and tonsil changes were detected in 44 patients (34.3%): pharyngitis in 18 cases (40.9%), tonsillitis in 17 cases (38.6%), and pharyngitis combined with tonsillitis in 9 cases (20.4%). Thus, 27 patients presented with acute or chronic pharyngitis, while 17 had toxic-allergic tonsillitis. Pharyngitis occurred against the background of chronic brucellosis in 13 patients and during the acute and subacute stages of the disease in 26 patients.

Among the 27 patients with pharyngitis, the catarrhal form was diagnosed in 19 cases (14.8%), while the atrophic and subatrophic forms were diagnosed in the remaining 8 cases (6.2%).

Changes in the pharyngeal mucosa, primarily in the form of atrophic pharyngitis, were more frequently observed in patients with chronic brucellosis. Additionally, among the 17 patients with tonsillitis, 11 (8.6%) had chronic tonsillitis of the toxic-allergic type I, and 5 (3.9%) had the toxic-allergic type II, which developed after contracting brucellosis. In 1 case (0.8%), simple chronic tonsillitis was detected, which presented subclinically. This suggests that tonsillitis in brucellosis patients may be more prevalent than indicated in the literature.

In the acute and subacute forms of brucellosis, tonsillitis was identified in 8 patients, while in the chronic form, it was identified in 19 patients, indicating that tonsillitis was more frequently associated with the chronic form of brucellosis.

Medical literature notes that, in some cases, brucellosis may initially present with symptoms of catarrhal angina, and that the palatine tonsils may serve as a portal or focal point of brucellosis infection. In our observations, three patients sought medical attention for pharyngeal complaints, and were subsequently diagnosed with brucellosis.

Condition of the Larynx

Laryngeal changes were observed in 32 patients (25.0%). Among them, 6 had acute brucellosis, 3 had subacute brucellosis, and 25 had chronic brucellosis. Laryngeal disorders were found in all forms of brucellosis, though they were more common in the chronic form.

Only 11 of the 34 patients (7.8%) exhibited subjective symptoms: hoarseness in 6 patients, throat pain, dryness, and rapid vocal fatigue in 5.

Upon examination, hyperemia of the mucosa was noted in 29 patients (85.2%); infiltration and swelling of the arytenoid and interarytenoid mucosal spaces, as well as the false vocal cords, were noted in 4 patients (11.7%); and mucosal atrophy was found in 2 patients (5.8%) (see Fig. 3.4).

We had reason to believe that in 11 patients (32.3%), laryngeal changes were of brucellosis origin (brucellosis laryngitis), as they also exhibited brucellosis-specific ENT symptoms: nasal bleeding, reduced olfactory function, and auditory nerve neuritis. In the remaining 23 patients (67.7%), laryngitis was a secondary condition (laryngitis in brucellosis).

Our findings suggest that laryngeal changes in brucellosis, as with changes in the nasal cavity and pharynx, often occur without subjective symptoms and are more frequently observed in the chronic form of the disease.

3.2. HEARING IMPAIRMENTS BASED ON THE FORM OF BRUCELLOSIS INFECTION

Nature of Hearing Impairment in Patients with Acute Brucellosis

A total of 24 patients (18.7%) with the acute form of brucellosis, who developed hearing impairment during the clinical phase of the disease, were examined. Of these, 15 patients were aged between 21 and 30 years, and 7 were aged between 31 and 40.

All patients reported ear pain, mild hearing loss, a sensation of ear fullness, and tinnitus. Five patients (21%) experienced tinnitus in both ears, one patient (4.2%)

reported tinnitus in the head, and one patient (4.2%) reported tinnitus only in the right ear.

On otoscopic examination, the tympanic membrane was markedly hyperemic, with light reflex, malleus handle, and folds barely discernible. Eustachian tube patency of grade III was noted in 15 patients, grade II in 5 patients, and two patients had complete Eustachian tube obstruction.

Of the patients examined, 14 (58.3%) could hear whispered speech from a distance of up to 2.5±0.9 meters, while the others could hear it from up to 4.2 meters. Ten patients (7.8%) could hear conversational speech from a distance of 3.8±0.7 meters, and in the remaining 8 patients (6.2%), conversational speech perception was within the normal range of 5.4±0.6 meters.

In tuning fork tests, the Rinne test was negative in 14 patients. Sound lateralization in Weber's test was symmetrical in both ears for 13 patients, while for 5 patients, the tuning fork sound was perceived on the crown of the head. No reduction in bone conduction was observed in Schwabach's test.

The lowest hearing loss in air conduction was at 1000 Hz, averaging 25.0±4.2 dB. Hearing loss increased at higher frequencies, reaching a maximum average of 37.2±3.8 dB at 8000 Hz. Bone conduction remained within normal limits across all frequencies, showing an air-bone gap with a maximum of 30.1 dB at 4000 Hz (Table 3.1).

In suprathreshold audiometry, none of the patients demonstrated the phenomenon of rapid loudness growth. The average threshold adaptation was 0.72±0.7 dB.

Bone perception of ultrasound remained within normal limits. The bone conduction threshold for ultrasound did not exceed 3 V, with an average threshold for all patients in this group of 1.3±0.5 V. When the sensor was applied to the forehead, sound lateralization was centered on the forehead in 17 patients, and directed toward the left ear in 1 patient. All patients in this group demonstrated 100% speech discrimination with a speech signal intensity between 35 and 50 dB.

As previously noted, patients with acute brucellosis reported a sensation of ear fullness. To clarify the nature of their auditory function impairment, acoustic impedance testing was conducted.

The results revealed a type B tympanogram. Acoustic reflexes were present in all 18 patients at a stimulus intensity of 1000 Hz, with ipsilateral stimulation at 82 dB and contralateral stimulation at 87 dB, indicating the presence of middle ear inflammation.

Nature of Hearing Impairment in Patients with the Subacute Form of Brucellosis

The second group consisted of 22 patients (17.1%) with the subacute form of brucellosis, including 17 patients aged 21 to 30 years and 5 patients aged 31 to 40 years.

Hearing loss in both ears was reported by 16 patients (72.7%), while all 22 patients reported a sensation of ear fullness and tinnitus. Otoscopic examination revealed that the tympanic membrane was pale pink, opaque, with poorly defined contours and slightly bulging, particularly in the lower quadrants.

Eustachian tube dysfunction of grade III was observed in all patients.

In hearing function tests, whispered speech was heard up to 2.5±1.2 meters, and conversational speech up to 3.5±0.7 meters.

In tuning fork tests, Rinne’s test was negative in all 15 (68.1%) examined patients. Weber’s test showed symmetrical lateralization of sound to both ears in 12 patients (54.5%), while the remaining 3 patients (13.6%) perceived the tuning fork sound in the head. Schwabach’s test revealed no shortening of bone conduction.

Pure-tone audiometry across frequencies from 125 to 8000 Hz revealed hearing loss of a conductive nature. Air and bone conduction curves showed a small gap averaging 15-20 dB across the frequency range. The lowest hearing threshold for air conduction was at 125 Hz (30.8±1.8 dB), with the highest at 4000 Hz (44.2±3.6 dB). For bone conduction, the minimum threshold was 4.6±1.2 dB at 250 Hz and the

maximum was 8.5±2.1 dB at 4000 Hz (Table 3.2). The audiometric curve was of the horizontal type (Fig. 3.7).

Impedance audiometry in 4 patients showed a type C tympanogram, with acoustic reflexes at 70-80 dB for both ipsilateral and contralateral stimulation. Eleven patients exhibited a type B tympanogram, with contralateral stimulation at 76.2 dB and ipsilateral stimulation at 82.1 dB.

Bone conduction of ultrasound was perceived in the head, with an average threshold of 2.3±0.2 V.

Patients in this group did not show any decrease in differential thresholds for sound intensity perception, with an average threshold of 0.89 dB.

Speech discrimination did not exceed 90%, averaging 88.2% with a speech signal intensity of 60 dB.

The results indicate that hearing impairments in patients with acute and subacute forms of brucellosis infection are predominantly conductive in nature. This is supported by findings from tuning fork tests, pure-tone threshold audiometry, suprathreshold audiometry, speech audiometry, ultrasonic audiometry, and impedance audiometry.

Nature of Hearing Impairment in Patients with Chronic Brucellosis

Hearing status was assessed in 57 patients (44.5%) with chronic brucellosis. Among them, 3 patients were under 20 years old, 12 were aged 21 to 30 years, 29 were 31 to 40 years, 11 were 41 to 50 years, and 2 were over 50 years old.

Based on the nature of hearing impairment, these patients were divided into two subgroups: the first subgroup consisted of 33 individuals (57.8%) with mixed hearing loss, while the second subgroup comprised 26 individuals (45.6%) with sensorineural hearing loss only.

The main complaints of the patients in the first subgroup were hearing loss, a sense of fullness or heaviness, and tinnitus. Persistent tinnitus in both ears was reported by 28 individuals (82.3%), and 3 individuals (8.8%) reported tinnitus in the head.

Otoscopic examination showed that the tympanic membrane was gray, opaque, slightly retracted, and with blurred contour margins. Pneumatic otoscopy with Siegle's funnel revealed immobility of the tympanic membrane. Eustachian tube patency was grade II in 15 patients and grade III in 19 patients.

Hearing loss was more pronounced in these patients than in those with acute or subacute brucellosis. Thirteen patients could detect whispered speech only at the auricle and conversational speech from a distance of up to 3.5±0.3 meters. The remaining 18 patients detected whispered speech from an average distance of 1.8±0.4 meters and conversational speech from 4.0±0.7 meters. In tuning fork tests, Rinne’s test was negative in 27 patients, with minor results on the right side in 1 patient and on the left side in another.

In Weber’s test, 17 patients perceived the tuning fork sound in the head, while 6 heard it in both ears; the remaining patients did not perceive it at all.

Audiometric studies (pure-tone audiometry) indicated a higher degree of hearing loss in this group than in the control group. Significant hearing loss was noted in both air and bone conduction across all frequencies. The air conduction threshold at 125 Hz was 39.1±3.2 dB, with the minimum hearing loss level at 500 Hz (34.2±0.8 dB) and the maximum at 8000 Hz (58.4±2.1 dB).

The bone conduction curve showed a similar decline, with the smallest loss at 500 Hz (14.4±1.9 dB) and the largest at 8000 Hz (25.2±2.8 dB).

Hearing loss in these patients was of the mixed type, predominantly conductive in nature.

Impedance audiometry in 17 patients showed a type As tympanogram, suggesting scar formation in the middle ear, while 14 patients had a type C tympanogram, indicating impaired ventilation of the middle ear with negative pressure development.

The differential threshold of sound intensity perception was measurable in 30 patients (88.2%). Among them, 17 patients (50%) showed no change in this threshold, while 13 patients (38.2%) exhibited loudness recruitment (mean sound intensity threshold 0.78±1.7 dB).

The average bone conduction threshold for ultrasound perception in this group was 4.5±0.7 V.

Speech discrimination was impaired in nearly all cases, with elevated thresholds. None of the patients reached 100% speech intelligibility, with an average intelligibility score of 72.6% at a sound intensity of 75 dB.

Patients in the second subgroup (26 individuals) complained of hearing loss and persistent tinnitus. No pathological changes were observed on otoscopy; the tympanic membrane was gray with preserved light reflex, and the handle of the malleus and folds were visible. Tympanic membrane mobility was within normal limits.

Eustachian tube patency was normal in 22 patients, with grade II patency observed in 4 patients.

Conversational speech was perceived at a distance of 3.3±1.1 meters, and whispered speech at 1.9±0.7 meters.

Tuning fork tests revealed a mild Rinne's test in this group. Shortening of bone conduction in Schwabach's test was noted, averaging 7.1±1.3 seconds in all patients. Audiograms showed bilateral hearing loss of the sensorineural type (Fig. 3.11), with minimal hearing change at 125-1000 Hz and a steep parallel decline in air and bone conduction starting at 2000 Hz. The highest hearing loss at 8000 Hz was 66.3±2.4 dB for bone conduction and 39.4±1.3 dB for air conduction.

The bone conduction threshold for ultrasound perception in the second subgroup exceeded normal values, averaging 5.2±1.1 V.

Speech discrimination thresholds were impaired in almost all patients in this subgroup, with a maximum discrimination score of 82.4%.

Impedance audiometry in all patients in this subgroup revealed a type A tympanogram.

Nature of Hearing Impairment in Patients with Primary Chronic Brucellosis

This group was included to assess hearing conditions in brucellosis, particularly considering the impact of ototoxic antibiotics (streptomycin, gentamicin), commonly used by infectious disease specialists to treat chronic forms of brucellosis. The group consisted of 25 individuals (19.5%).

All 25 patients exhibited bilateral hearing impairment. Otoscopy revealed no abnormalities, with the tympanic membrane appearing gray, a well-defined light reflex, and clear contours. Tympanic membrane mobility was maintained during pneumatic otoscopy.

Evaluation of Eustachian tube function showed normal tube patency in these patients.

The average detection range for whispered speech was 1.8±0.4 meters, and for conversational speech, 3.1±0.8 meters. In tuning fork tests, Rinne's test results were minimal for all patients. In Weber's test, 5 patients noted the sound in their head, while 9 patients did not perceive it anywhere. In Schwabach's test, bone conduction time was shortened in all patients, averaging 6.4±1.3 seconds.

As shown in the table, air and bone conduction thresholds decreased in parallel across the frequency spectrum. Hearing loss in air conduction was noticeable from the lower frequencies (125, 250, and 500 Hz) with thresholds of 23.0±1.4, 28.3±4.0, and 38.8±3.2 dB, respectively. The hearing loss was more pronounced at higher frequencies, especially at 8000 Hz (64.5±3.7 dB).

In bone conduction, there was also a noticeable decrease at low frequencies (125-500 Hz), averaging 33.8±4.0 dB, while the highest frequency loss reached 52.3±1.3 dB.

Speech discrimination thresholds were impaired in 5 patients. With sufficient amplification, 100% speech intelligibility was achieved in 10 patients. The maximum speech discrimination rate was 74.6%.

Impedance audiometry showed no deviations in parameters reflecting auditory function, as all patients presented with a type A tympanogram.

The bone conduction threshold for ultrasound perception in this group exceeded 3 V, averaging 5.2±0.9 V.

The acoustic reflex threshold was higher than normal, averaging 102 dB for contralateral stimulation and 80 dB for ipsilateral stimulation, with an average of 85 dB. These findings indicate conductive hearing impairment of varying severity in patients with acute and subacute brucellosis.

The research also suggests that patients with chronic brucellosis show two forms of hearing pathology:

Some patients exhibited mixed-type hearing loss with a predominance of sensorineural impairment.

In others, the hearing loss was primarily due to sensorineural impairment (sensorineural hearing loss).

Hearing, vestibular function, olfactory, and taste impairments observed in these brucellosis patients often coincided with other neurological symptoms (e.g., neuralgia, meningoencephalitis, radiculitis). Therefore, these should be considered manifestations of neurobrucellosis.

3.3. EVALUATION OF VESTIBULAR FUNCTION IN PATIENTS WITH BRUCELLOSIS

Out of 128 patients with acute, subacute, and chronic forms of brucellosis, 19 exhibited significant vestibular function impairments of varying degrees. Isolated vestibular analyzer impairments were not observed; these typically coincided with auditory analyzer impairments.

Virtually all patients in this group reported headaches. Many experienced various types of dizziness: rotational dizziness was observed in 7 patients, non-rotational dizziness in 10, and a combination of both in 2. Vestibular disorders, such as spontaneous nystagmus, were present in 11 patients, arm deviation in 9, static balance disturbances in 2, gait disturbances in 2, and autonomic reactions in 14. True positional nystagmus occurred in 3 patients.

Spontaneous nystagmus appeared as clonic, horizontal-rotational, small-amplitude (Grade I) in 4 patients, and as tonic-clonic, horizontal, large-amplitude (Grades II-III) in 7.

After conducting the caloric test, we identified the spontaneous nystagmus as excitatory. By analyzing the frequency and characteristics of spontaneous and experimental vestibular symptoms among the patients, we identified vestibular hyperreflexia, hyporeflexia, and areflexia syndromes.

Vestibular Hyperreflexia Syndrome was observed in 35 patients (27.3%), including 18 (81.8%) with acute brucellosis, 15 (62.5%) with subacute, and 12 (21%) with chronic forms. Among 13 patients (37.1%), spontaneous vestibular disturbances were noted, though not always uniform. In 4 patients (11.4%), these disturbances presented with all components of vestibular response in a harmonious manner. In 9 cases (25.7%), spontaneous vestibular disturbances, consistent with hyperreflexia, exhibited disharmonious patterns. Symptoms included non-rotational dizziness, tonic-clonic, horizontal, large-amplitude (Grade I) nystagmus, outward or downward arm deviation toward the fast phase of the nystagmus, non-systematic swaying in Romberg's stance, or dissociation; nystagmus presence without arm deviation, static or gait disturbances, or autonomic reactions.

Significantly more often, the syndrome of increased vestibular excitability was detected only after performing the caloric test (27 patients, 77.1%). In some of the examined patients (16 patients, 45.7%), the syndrome of vestibular hyperreflexia was characterized by an increase in both the duration and intensity of all vestibular reaction components, while in 11 cases (31.4%) there was disharmony and dissociation in the vestibular reactions after calorization.

The syndrome of vestibular hyporeflexia, observed after the experimental test in 50 (39%) patients, also manifested in various forms. In 38 (76%) of the examined patients, it was characterized by a harmonious decrease in duration and intensity of all vestibular reaction components. Less frequently (7 patients, 14%), vestibular hyporeflexia presented as a pronounced shortening of duration and decrease in

intensity only in nystagmus; sensory and vegetative reactions were markedly expressed, while tonic reactions were either moderately intense or absent.

The syndrome of vestibular areflexia, identified after the caloric test in 22 (17.1%) patients, was characterized by different manifestations. In some cases (3 patients), it presented as a complete absence of all vestibular reaction components. In another 6 patients, areflexia was limited to nystagmus, while sensory and vegetative reactions were enhanced, and tonic reactions occurred normally.

In 3 (13.6%) of the examined patients, there was a complete absence of all vestibular reaction components following the caloric test.

In most patients, disturbances in the vestibular analyzer were short-term, manifesting only as subjective sensations: spontaneous dizziness was brief and mild in intensity. The spontaneous nystagmus was characterized by being fine-amplitude, quick, rhythmic, horizontal-rotational, of 1st degree, and intensified when looking in the direction of the fast component. However, a distinctive feature was its rapid disappearance.

Similar findings were obtained from the analysis of caloric nystagmus parameters recorded using electronystagmography. Electronystagmography (ENG) was performed on 106 patients with brucellosis. Based on the caloric nystagmus parameters, the patients were divided into three groups; the obtained data were compared with those in the control group (Fig. 3.16).

In 22 (20.7%) patients of the first group with the acute form of brucellosis, there was a shortening of the latent period (6.4±0.1 s), an increase in frequency (2.8±0.2 Hz), prolongation of nystagmus duration (115.2±0.3 s), an increase in its amplitude (13.5±0.1 degrees), and in the speed of the slow component (70.5±0.9 degrees/s).

In 24 (22.6%) patients of the second group with a subacute course of brucellosis, there was an elongation of the nystagmus latency period (12.7±0.4 s), a decrease in frequency (1.4±0.02 Hz), nystagmus duration (51.8±0.5 s), and a smaller amplitude than in patients of the first group (8.2±0.1 degrees). The slow component speed tended to decrease compared to the control group (49.1±0.5 degrees/s).

In 60 (56.6%) patients of the third group, with pronounced toxic effects of brucellosis infection on the body, the latency period was prolonged (29.7±0.7 s), the frequency was reduced (1.5±0.03 Hz), the duration decreased (49.2±1.7 s), and there was a tendency toward a decrease in the amplitude and slow component speed of nystagmus.

Average ENG indicators in experimental tests among patients with chronic brucellosis

An analysis of nystagmograms in three patients with central nervous system disorders revealed asymmetry in vestibular reactions: on one side, vestibular excitability was absent or severely reduced, while on the other, it was normal or increased, indicating a high degree of discrepancy.

Quantitative and qualitative analysis of electronystagmograms conducted over time showed that the nature of vestibular disturbances changed depending on the disease phase: hyperreflexia in the acute period of the disease shifted to hyporeflexia and areflexia as the infection generalized.

Thus, our observations indicate that vestibular analyzer impairments occur in all forms of brucellosis infection—acute, subacute, and chronic—but are more frequent in chronic cases. Vestibular analyzer impairment occurs less often than auditory analyzer impairment, is often short-term, and manifests as subjective symptoms. Vestibular dysfunction in brucellosis is more often expressed as suppression of function.

The observations in patients who had brucellosis support findings in the medical literature, according to which vestibular analyzer disturbances in brucellosis are less common than auditory analyzer impairment. It appears that, being phylogenetically older, the spatial analyzer is more resistant to brucellosis infection.

3.4. RESULTS OF RHEOENCEPHALOGRAPHIC EXAMINATION IN PATIENTS WITH CHRONIC BRUCELLOSIS

Brucellosis represents a specific lesion of the nervous system in general brucellosis infection, manifested by a complex set of functional and structural disturbances in the body. There is a close pathogenetic association between changes in the nervous and vascular systems.

To study the relationship between intracranial hemodynamics and perceptual auditory impairment in patients with chronic brucellosis, we applied rheoencephalography (REG), which provides insight into the tone of vessels and blood filling in the basins of the internal carotid and basilar arteries, thus allowing assessment of the functional state of cerebral hemodynamics.

In addition to REG indicators, data from audiometry, vestibulometry, and results from therapeutic and neurological examinations were studied in patients with chronic brucellosis of both sexes, aged 21 to 60, suffering from varying degrees of auditory nerve neuritis, with disease duration from several weeks to several years.

In examining 57 (44.5%) patients with chronic brucellosis, particular attention was paid to their complaints. Patients reported throbbing, shooting headaches, dizziness, tinnitus and various types and intensities of head noises, hearing loss, palpitations, chest pain, memory loss, irritability, and fatigue.

After consultation with a neurologist, it was found that the clinical form of chronic brucellosis was characterized by polymorphic neurological symptoms. The most frequently identified neurological syndromes were: autonomic-vascular (100%), including arterial hypertension (20.6%), vestibular (27.5%), hypertensive (17.2%), asthenic (37.2%), astheno-organic (22.4%), astheno-adynamic, and astheno-neurotic (5.1%).

A coefficient exceeding 25% was considered a significant difference in interhemispheric REG amplitudes. To identify the functional features of intracranial blood circulation, alongside baseline REG, pharmacological testing with nitroglycerin (1/2 tablet sublingually) was recorded in 2/3 (63.1%) of the patients.

Analysis of these REGs showed various degrees of vascular tone changes in the brain in 54 patients, or the majority. Moderate decreases in vessel wall elasticity were observed in 43 patients and severe decreases in 11 patients. In the first subgroup of patients, the REG peak was slightly rounded, the dicrotic notch and incisura were slightly smoothed and positioned at the upper part of the descending REG limb (α = 0.17±0.02 s; H1 = 0.8±0.03; H = 1.1±0.2).

In the second subgroup of patients, the wave peak was dome-shaped, with a smoothed dicrotic notch and incisura located at the peak of the REG or absent (α = 0.22±0.02 s; H = 1.0±0.03). In 4 patients, the REG was within the normal range. REG forms showed a consistent pattern of individual components, a sharp peak, and a well-defined dicrotic notch and incisura located in the middle of the descending wave limb (α = 0.11±0.01 s; H1 = 0.65±0.01; H = 1.25±0.02).

The response to nitroglycerin in these patients was the same as in practically healthy individuals. It is worth noting that nitroglycerin administration generally led to slight improvements in primary REG parameters in cases of baseline REG changes; however, normalization was practically absent, with only a temporary improvement in waveform. All of this indicated reduced compensatory-adaptive mechanisms in the brain's vascular system.

The studies showed that changes in intracranial vessel wall elasticity were not accompanied by decreased pulse blood filling (the rheoencephalographic index was within or near the normal range). Apparently, the increase in cerebral vascular tone at certain stages of this disease occurs earlier than intracranial blood filling decreases. Only when compensatory mechanisms are severely lacking (absence of collateral blood flow, etc.) do these changes occur in parallel. Increased resistance to brain blood flow was generally observed in both vascular basins. Only in three patients who had meningoencephalitis was increased cerebral vascular tone noted (mainly in the internal carotid artery system); three other patients exhibited interhemispheric asymmetry in pulse blood filling.

Thus, signs of increased cerebral vascular tone with reduced intracranial blood flow functionality were observed in 54 of 58 patients in the chronic stage of

brucellosis. The nature of the changes in cerebral vascular tone, inadequate response to pharmacological influence, and interhemispheric blood filling asymmetry indicate neuro-reflex disturbances in the vascular system.

The vasculitis characteristic of brucellosis, due to the underlying structural changes, affects the initial afferent pathways' receptors and the terminal links of vasomotor innervation, as confirmed by literature data.

CHAPTER 4. RESULTS OF COMPREHENSIVE TREATMENT FOR HEARING IMPAIRMENTS AND VESTIBULAR DISORDERS IN PATIENTS WITH BRUCELLOSIS INFECTION, BASED ON DISEASE FORM

4.1. RESULTS OF HEARING IMPAIRMENT TREATMENT IN PATIENTS WITH ACUTE BRUCELLOSIS

Patients who had recovered from brucellosis infection experienced various types of hearing impairment. During the acute and subacute stages of brucellosis, conductive hearing issues were prevalent. Medical literature suggests that in the acute and subacute forms of brucellosis, processes in the outer and middle ear follow a pattern of nonspecific inflammation. When the infection enters the middle ear, it likely induces mucous swelling, small-cell infiltration, and arterial hyperemia within the mucous membrane of the tympanic cavity and Eustachian tube. Over time, the epithelial layer thickens significantly, with swelling of the submucosal endosteal connective tissue, increased hyperemia, and intensified small-cell infiltration. Exudate accumulates, and the thickened mucous membrane and exudate fill all the middle ear cavities, rendering the ossicles almost immobile.

Sensorineural hearing loss more commonly develops in patients who have experienced chronic forms of brucellosis. The toxic effects of the infection lead to damage in the inner (sound-receiving) part of the auditory analyzer. The toxic factor initially provokes an inflammatory response, resulting in serofibrinous or hemorrhagic exudate surrounding nerve cells and fibers, within the peri- and

endolymphatic spaces, and around the cochlear root sheath. This is followed by the breakdown of nerve elements and their replacement with connective tissue.

This chapter presents an analysis of the treatment results for 113 patients with various forms of brucellosis and hearing impairments resulting from the primary disease, assessing the effectiveness of the treatment.

In selecting medications to treat hearing impairments in patients who had recovered from the acute form of brucellosis, we based our choices on data from medical literature and our own observations of the pathogenesis of auditory changes in brucellosis infection. Initially (in the acute and subacute forms), the observed morphological changes in the ear fall within the scope of a nonspecific inflammatory process. After recovery from brucellosis, amidst an overall improvement in health, the acute inflammation in the middle ear may transition to a chronic form, leading, as mentioned previously, to adhesions and scarring within the middle ear cavities.

Patients underwent three treatment courses to address the hearing impairments that had developed. Before treatment, patients reported a feeling of fullness and tinnitus, mild hearing loss, and, in some cases, autophony—a strong resonance of their own voice.

Upon otoscopic examination, the tympanic membrane appeared retracted and dull, with shortening of the malleus handle and light reflex. Due to the retraction of the tympanic membrane, its shiny appearance became duller. Limited mobility of the tympanic membrane was detected using Siegle’s funnel.

The evaluation of Eustachian tube function in all patients showed impaired patency: 19 patients had Grade III impairment, and 3 had Grade II. During acoumetry, whispered speech was perceived at a distance of 3.3±1.0 m, while conversational speech was close to normal at 5.4±0.8 m.

The Rinne test was negative for all patients, and the Weber test indicated lateralization of tuning fork sound in both ears. Audiometry results revealed conductive hearing loss, with an air-bone gap, decreased air conduction, and preserved bone conduction.

Impedance audiometry displayed a Type C tympanogram, indicating impaired middle ear ventilation and the presence of negative pressure. Ultrasonic bone conduction thresholds were within normal ranges for these patients.

To assess treatment effectiveness in restoring hearing function, specific acoumetry and audiometry parameters were evaluated before and after treatment.

The treatment proved to be quite effective. Twelve patients experienced hearing improvement and a reduction in tinnitus intensity directly after the completion of the first full treatment course. One patient discontinued the course early, leaving treatment results inconclusive. For three patients, improvement manifested as reduced tinnitus intensity and relief from ear fullness.

In the initial days after the first course, hearing returned to baseline for four patients, while significant improvement was only seen in others after the second course.

Post-treatment results showed an average whispered speech perception distance of 4.1±0.6 m ($p>0.05$). The threshold for air conduction improved from 32.1 dB before treatment to 28.1 dB after the first course, and 22.1 dB following the second course. These findings indicate significant treatment efficacy, as seen by an average 11 dB increase in hearing thresholds across all frequencies. Bone conduction remained stable.

Following treatment, tympanogram results also improved in cases of hearing impairment post-brucellosis. Acoustic impedance curves showed a Type A tympanogram for 11 patients after the first course and for an additional two patients after the second course, indicating restored middle ear function.

There were no functional impairments in the vestibular analyzer. Only eight patients exhibited transient mild hyperreflexia after experimental tests, while heightened vestibular analyzer excitability resolved in the remaining patients.

4.2. RESULTS OF HEARING IMPAIRMENT TREATMENT IN PATIENTS WITH SUBACUTE BRUCELLOSIS

A total of 20 patients were examined, of which 18 were aged 21 to 30 years and 2 were aged 31 to 40 years. Bilateral hearing impairment with conductive hearing system defects was identified in these patients. Otoscopy revealed that all patients had tympanic membranes that were gray, opaque, retracted, and had indistinct landmarks.

Twelve patients showed Grade II Eustachian tube obstruction, while eight exhibited Grade III. Pneumatic otoscopy showed an almost immobile tympanic membrane.

The average distance at which whispered speech was perceived was 2.6 ± 0.8 meters, and conversational speech was understood up to 3.5 meters. All 20 patients had a negative Rinne test result. The Weber test showed localization in the head for 6 patients, and the Schwabach test indicated no shortening.

During pure-tone threshold audiometry, most patients displayed an air-bone gap averaging 13-18 dB across all frequencies, with the greatest hearing loss in air conduction noted at 8000 Hz, averaging 42.6 dB.

Seventeen patients had Type C tympanograms, with 80 dB contralateral and ipsilateral stimulation, and 3 had Type B tympanograms.

This group received a treatment protocol for hearing loss associated with acute brucellosis. Observations indicated that this treatment was effective for patients who had experienced subacute brucellosis, albeit over a relatively longer period than for those with the acute form of the disease.

After one treatment course, slight improvements in hearing function were noted in only 3 of the 20 patients, with reductions in ear congestion and tinnitus. These patients could understand conversational speech from up to 4.3 meters and whispered speech from up to 3.2 meters.

Overall, the most significant differences in hearing function before and after treatment were observed in the low and mid-frequency ranges. Post-treatment, an

average improvement in air conduction of 4-7 dB across the frequency range was observed.

Following a second course of treatment, 4 more patients reported hearing improvement, with cessation of tinnitus and reduced ear congestion. The remaining 13 patients experienced minimal improvement in hearing.

No complaints or visible dysfunction of the vestibular analyzer were detected.

In summary, our observations indicate that patients recovering from acute and subacute brucellosis develop varying degrees of conductive hearing loss that responds well to treatment. For patients presenting with conductive hearing loss following brucellosis infection, timely treatment yields positive results.

4.3. RESULTS OF HEARING IMPAIRMENT TREATMENT IN PATIENTS WITH CHRONIC BRUCELLOSIS

Medical literature contains extensive research on the treatment of chronic sensorineural hearing loss, including cases following various infectious and viral diseases. Patients in this group complained of reduced hearing, a feeling of ear congestion, and tinnitus. Otoscopy showed gray, opaque tympanic membranes with areas of petrifaction, primarily in the lower quadrants. Eustachian tube function was impaired, with seven patients exhibiting Grade III and four exhibiting Grade II obstruction. Pneumatic otoscopy indicated an immobile tympanic membrane.

Before treatment, whisper speech was perceived at an average distance of 1.6 ± 0.4 m, and conversational speech at 3.7 ± 0.4 m. In tuning fork tests, all 11 patients had a negative Rinne test, and the Schwabach test was shortened, with an average value of 7.1 seconds.

Following the first course of treatment, patients experienced satisfactory results. Four reported reduced ear congestion, seven noted a decrease in tinnitus intensity, and six experienced improved hearing, with whisper speech distance increasing to an average of 2.0 ± 0.3 m and conversational speech to 4.3 ± 0.5 m.

After completing two full courses of comprehensive treatment, eight patients showed significant hearing improvement, with complete relief from tinnitus and congestion. In the remaining four, tinnitus occurred periodically with decreased intensity, and hearing improved slightly. One patient showed some improvement after the first course, but their hearing remained unchanged after the second course.

Audiometry results confirmed positive outcomes. Hearing levels for both air and bone conduction improved across all tested frequencies. Air conduction thresholds at low frequencies (125-250-500 Hz) improved by an average of 2-3 dB post-treatment. At higher frequencies (1000-8000 Hz), hearing levels improved by 4-8 dB, with a minimum loss of 31.8 ± 1.2 dB at 500 Hz and a maximum of 54.0 ± 1.1 dB at 8000 Hz.

Bone conduction levels improved by an average of 2-5 dB across the frequency spectrum, with a maximum of 31.3 ± 2.4 dB at 8000 Hz and a minimum of 15.4 ± 1.7 dB at 125 Hz. The second subgroup, comprising 25 patients, primarily reported hearing loss and constant tinnitus of varying nature and intensity.

Otoscopy revealed gray tympanic membranes with clearly visible malleus handle, umbo, light reflex, and folds. The tympanic membrane was highly mobile during pneumatic otoscopy.

Eustachian tube function was normal. Patients could distinguish whispered speech at an average distance of 0.9 ± 0.7 m and conversational speech up to 3.0 ± 1.1 m.

In tuning fork tests, the Rinne test was mild, and the Schwabach test was shortened, with an average of 4.8 seconds.

All patients showed positive outcomes, with improved hearing and overall well-being.

Air conduction levels showed similar improvements but with better results. Hearing levels increased across all frequencies from 125 to 8000 Hz almost uniformly. The most effective frequency for treatment was 8000 Hz, with an increase of 8.1 dB. Low-frequency (125-500 Hz) improvements ranged from 2-4 dB.

Ultrasound bone conduction measurements registered 4.8 ± 0.3 V in seven patients and 3-5 V in five others.

Impedance testing showed a Type A tympanogram. Speech discrimination scores averaged 85.2% at a 70 dB signal intensity.

In patients with chronic brucellosis who did not report vestibular issues, functional testing revealed decreased vestibular excitability. These impairments often coincided with hearing loss, though they occasionally appeared in isolation.

Overall, certain vestibular function impairments tended to normalize with recovery from brucellosis infection and ongoing therapy.

4.4. RESULTS OF HEARING IMPAIRMENT TREATMENT IN PATIENTS WITH PRIMARY CHRONIC BRUCELLOSIS

Patients in this group exhibited hearing loss resulting from primary chronic brucellosis. This latent, slowly progressing form of infection was marked by a blurred clinical picture. Patients who visited clinics and outpatient facilities struggled to receive a correct diagnosis for an extended period. Symptomatic treatment did not improve their overall condition; instead, hearing loss gradually developed against the background of symptomatic therapy.

Patients reported reduced hearing and persistent tinnitus. The hearing impairment was sensorineural, affecting results in speech testing, tuning fork tests, audiometry, and ultrasound examinations. Examination of the tympanic membrane showed no visible pathological changes, and it was mobile upon inspection with a pneumatic otoscope. Eustachian tube function was unimpaired.

During acoustic tests, patients perceived whispered speech from a distance of 1.8 ± 0.4 m and conversational speech from 3.1 ± 0.8 m. Tuning fork tests showed a mild Rinne test and a shortened Schwabach test of 4.7 seconds.

Treatment involved the administration of a cocktail (nicotinic acid 1%, aloe, vitamin B1, proserin 0.05%, novocaine 0.5%) injected in the postauricular area, ten

sessions of electrophoresis with 1% potassium iodide to the mastoid region, and ten sessions of hyperbaric oxygenation (HBO).

After two full treatment courses, noticeable improvement occurred in 7 of the 15 patients, while 2 interrupted their treatment and were therefore excluded from the study. Two patients showed hearing improvement after one treatment course, and by the end, hearing remained unchanged in three patients.

After treatment, the average distance for perceiving whispered speech increased to 2.2 ± 0.5 m, and for conversational speech, 3.8 ± 0.3 m. Audiometric testing showed clear improvement in hearing across many tested frequencies. Significant and reliable improvement in bone conduction was observed at high frequencies (1000-8000 Hz), with a rise in hearing levels up to 7 dB at 2000 Hz. Bone conduction loss at 8000 Hz, initially absent, registered at 76.4 ± 1.9 dB after treatment.

At low frequencies, hearing also improved by an average of 2-5 dB, with values of 28.2 ± 0.4, 28.0 ± 1.2, and 34.1 ± 1.9 dB at 125, 250, and 500 Hz, respectively. Treatment was also effective for air conduction at all frequencies. At 125 Hz, air conduction levels improved from a pre-treatment 23.0 ± 1.4 dB to 19.3 ± 1.7 dB post-treatment. At 8000 Hz, average hearing levels improved from 64.5 ± 3.7 dB to 58.1 ± 1.5 dB post-treatment.

The average ultrasound bone conduction level post-treatment was 4.4 ± 0.3 V. Improvements in speech discrimination were noted across all levels, with hearing discrimination reaching 90% at 75 dB in seven patients.

Two patients experienced sudden deafness, likely due to hemorrhage in the auditory center resulting from cerebrovascular impairment caused by brucellosis infection.

In conclusion, modern knowledge suggests that comprehensive treatment for sensorineural hearing loss is the most effective. Treatment should be initiated promptly to enhance synaptic transmission across all levels of the auditory analyzer and improve the trophism of the damaged neural elements. Treatment should be intensive and prolonged.

Based on the treatment outcomes for patients with hearing impairment following brucellosis, we conclude that hearing loss following acute and subacute brucellosis occurs due to conductive impairment, where acute nonspecific inflammation in the middle ear eventually transitions into a chronic form.

After chronic brucellosis, two types of hearing pathology are observed: mixed-type hearing loss with predominant sensory impairment (subgroup 1), likely related to brucellosis-induced connective tissue proliferation in the tympanic cavity; and more commonly, sensorineural hearing loss due to vascular damage in the cochlea and direct brucella-induced injury to its neuroepithelium (subgroup 2 and patients with primary chronic form).

The results of the study allow the following **conclusions:**

1. Hearing impairment in the acute and subacute forms of brucellosis is characterized by lesions in the conductive system (35.9%). Chronic brucellosis leads to impairment in the sensory system (64%), with predominant damage to the receptor apparatus and auditory nerve.

2. In the primary chronic form of brucellosis, hearing impairments are observed in the sensorineural type, predominantly affecting the receptor apparatus and auditory nerve. The secondary chronic form of brucellosis, whether independently or in the context of ototoxic antibiotic use, manifests as mixed-type hearing loss.

3. Vestibular disturbances in brucellosis patients appear as hyporeflexia in 22.6%, hyperreflexia in 20.7%, and areflexia in 56.6% of cases. These disturbances are functional and result from the toxic impact of brucellosis infection on the vestibular analyzer.

4. Pure-tone threshold audiometry and impedance audiometry offer the highest diagnostic value for detecting hearing impairments in patients with acute and subacute brucellosis. In chronic brucellosis, pure-tone audiometry, suprathreshold tests, impedance audiometry, and ultrasound examination are most diagnostically valuable.

5. Comprehensive treatment of the initial manifestations of conductive system impairment in the middle ear—through procedures aimed at scar resorption in the tympanic cavity and restoration of the mobility of the conductive system components in the middle ear—has proven to be most effective in 57% of cases. Improved microcirculation and nourishment of the inner ear yield positive results in 22% of cases.

Practical Recommendations for the Prevention and Treatment of Auditory and Vestibular Analyzers in Patients with Brucellosis Infection:

1. Early diagnosis of hearing impairments in patients with brucellosis infection, within the first 3 months, is essential to prevent the initial manifestations of hearing loss from progressing to more severe degrees of impairment and, ultimately, to deafness.

2. To accurately determine the type of hearing impairment, regardless of the form of brucellosis, a comprehensive examination of the auditory analyzer is necessary. This examination should include tonal threshold audiometry, speech audiometry, impedance audiometry, and ultrasound testing of hearing.

3. Alongside assessing the vestibular analyzer in brucellosis patients, vestibulometry using experimental tests and ENG (electronystagmography) is also advisable. This approach aids in identifying complicated forms of the disease, such as neurobrucellosis.

4. For patients with impairments in the sound-perception system of the auditory analyzer, treatment aimed at improving microcirculation and restoring the trophic function of the inner ear should ideally be combined with sessions of HBOT (hyperbaric oxygen therapy), totaling six sessions per treatment course.

5. It is advisable to classify individuals with brucellosis infection as a high-risk group for hearing loss. Monitoring of their auditory function should be conducted both during the clinical manifestations of brucellosis and in the long term after recovery.

6. To facilitate the early detection of toxic effects of brucellosis infection on the auditory and vestibular analyzers, and to diagnose hearing impairments, implement timely preventive and therapeutic measures, assess work capacity, and assist with job placement, the involvement of an otolaryngologist is essential. This should be part of the medical examinations conducted by control commissions within occupational health services during both initial and periodic check-ups.

CONCLUSION

Brucellosis, especially in its chronic form with frequent exacerbations, is known to affect various organs and systems, including the ENT system. Otolaryngologists need to be well-informed about brucellosis diagnosis, as its clinical presentation often mimics other ENT conditions, such as labyrinthitis, chronic tonsillitis, sinusitis, and others. Our observations indicate that patients with brucellosis, presenting with ENT complications or brucellosis-specific involvement of the ear and upper respiratory tract, often undergo prolonged ENT treatments before receiving an accurate diagnosis.

Nasal bleeding is more frequently observed in elderly patients with chronic brucellosis, often originating from the anterior part of the nasal septum in individuals with pronounced nasal mucosa atrophy. Specific treatment in these cases leads to cessation of nasal bleeding and noticeable improvement in general health.

An objective examination of the pharynx revealed mucosal changes in 44 (34.3%) patients, including pharyngitis (40.9%), tonsillitis (38.6%), and combined pharyngitis and tonsillitis (20.4%). Atrophic pharyngitis was more common among patients with chronic brucellosis.

During brucellosis, especially in subacute and chronic cases, patients frequently experience bilateral hearing impairment. Studies confirm that the auditory analyzer is often involved in the disease process. Hearing impairments due to brucellosis are more common in young, working-age individuals, typically employed in livestock and animal husbandry.

The state of the auditory and vestibular systems in brucellosis patients has not been well-documented in the literature. Reliable diagnostic methods and specific treatments for hearing impairments and their prevention are still lacking.

The frequency of hearing impairments in brucellosis patients depends on the form and course of the disease. Detailed studies of the functional state of the auditory and vestibular analyzers in acute brucellosis patients using a combination of methods—acumetry, audiometry (tonal threshold, suprathreshold, speech, bone

conduction of ultrasound), acoustic impedance measurements, and vestibulometry—show that hearing loss in these cases is often conductive.

The degree of auditory impairment in acute and subacute brucellosis is minor, often accompanied by middle ear dysfunction, as indicated by a Type B tympanogram. Hearing loss in the acute form of brucellosis is associated with the intense development of non-specific middle ear inflammation, which leads to conductive hearing loss.

Vestibular disturbances typically present as hyporeflexia during experimental tests. In more advanced cases (primary chronic forms of brucellosis), hearing impairments are of a sensorineural nature, as shown by audiometry. Speech discrimination was compromised in nearly all cases, with none of the patients achieving 100% clarity. Changes in the auditory and vestibular systems in brucellosis were associated with impaired cerebral blood flow, with more pronounced changes in the vertebrobasilar vascular system, with no observed asymmetry coefficient, indicating bilateral cerebral blood flow abnormalities.

Patients whose hearing impairments stemmed from inflammatory middle ear processes responded well to timely therapy. Treatment focused on restoring Eustachian tube function through catheterization and administration of the proteolytic enzyme lidase, as well as physiotherapy with a helium-neon laser. Post-treatment audiograms and impedance measurements indicated favorable outcomes.

Vestibular disturbances vary with the disease phase: hyperreflexia during the acute phase transitions to hyporeflexia and areflexia as brucellosis progresses. Vestibular analyzer involvement occurs across all forms of brucellosis—acute, subacute, and chronic—but is more common in chronic cases. Vestibular disturbances are generally transient, presenting as subjective symptoms, and resolve with recovery from the primary infection following pathogenetic therapy.

Patients with sensorineural hearing loss after brucellosis benefit from parenteral administration of Cavinton or Trental. The majority report improved hearing acuity, reduced tinnitus, and better overall well-being.

The study indicates that hearing impairments associated with brucellosis infection change over time. For patients with hearing deficits lasting from six months to a year, two patterns emerge: mixed-type hearing loss in some cases and pronounced bilateral sensorineural hearing loss in others.

If hearing loss developed after recovery from brucellosis and was linked to progressive connective tissue proliferation in the tympanic cavity, the hearing impairment evolves into adhesive otitis with a sensorineural component in the later stages. Such patients require treatment focused on scar tissue resorption in the tympanic cavity, restoration of middle ear sound-conducting system mobility, and improved microcirculation and nourishment of inner ear structures.

Ultimately, any hearing impairment from brucellosis, regardless of its origin, progresses to bilateral sensorineural hearing loss characterized by profound hearing loss in the long term. One of the causes of bilateral hearing loss after brucellosis is the ototoxic effect of medications like streptomycin and gentamicin. Our main objective was to promptly identify patients receiving ototoxic drugs and implement preventive measures to mitigate the toxic effects of both brucellosis and ototoxic antibiotics.

Patients who have recovered from brucellosis are at high risk of developing hearing loss.

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