Case Report

Review of a Case: Neurobrucellosis with Occupational Exposure

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Review of a Case: Neurobrucellosis with Occupational Exposure

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Abstract: Neurobrucellosis is a rare but serious complication of brucellosis, a zoonotic disease caused by bacteria of the genus Brucella. The most common clinical manifestations of neurobrucellosis include meningitis, encephalitis, and seizures. The diagnosis of neurobrucellosis should be considered when patients present with undulant fever, lethargy, seizures, or other features of meningitis/encephalitis. Occupational exposure to Brucella bacteria, particularly through contact with infected animals or their products, is a significant risk factor for developing neurobrucellosis. Certain occupations, such as farmers, veterinarians, and slaughterhouse workers, are at a higher risk of exposure. Recent research has suggested a potential link between neurobrucellosis and Parkinson's disease, although further investigation is needed to fully understand this association. Prevention and control of neurobrucellosis involve measures such as occupational hygiene, vaccination of livestock, and public education campaigns.

Keywords: neurobrucellosis; Parkinson's disease; zoonotic disease; occupational exposure

Introduction

Neurobrucellosis is a rare but serious neurological condition caused by the Brucella bacteria. This nervous system disorder affects the central nervous system and leads to complications such as meningitis, encephalitis, and seizures [1]. The diagnosis of neurobrucellosis should be considered when patients present with symptoms such as undulant fever, lethargy, seizures, or other features of meningitis/encephalitis [2]. Although rare, neurobrucellosis can have serious consequences, so it is of great importance to understand its causes and possible risk factors.

The Brucella genus is classified in the group of gram-negative bacteria specifically as non-encapsulated aerobic coccobacilli with facultative intracellular capacity, which allows it to generate chronic infections transmissible mainly by the ingestion of unpasteurized milk from a variety of animals including cows, goats, etc. or contact with these same secretions. Brucellosis is a widely spread zoonotic bacterial disease that represents an occupational risk for personnel close to animals carrying the microorganism, them (caretakers, veterinarians, farmers) and/or those who have contact with animal secretions.

In the body, these bacteria are recognized by macrophages, which prevent intracellular damage by these microorganisms through a dysregulation of the immune response. However, these bacteria invade the phagocytic cells themselves and multiply intracellularly, which promotes their dissemination to the spleen, liver, lymph nodes and bone marrow. In Ecuador, despite the massive livestock activity, many cases are not identified in a timely manner at their different stages of presentation. Considering the biological risk associated with the group of workers with greater exposure to brucellosis, a recognized occupational disease, the statistical data of the General Insurance of Occupational Risks during the period 2017-2020 reveal only two cases classified as such. Neurobrucellosis (NB) is a rare presentation with an incidence of >2% of brucellosis cases, however, in most cases of the common disease, severe complications and characteristic predominant symptoms such as headache, fever, weight loss, hepatomegaly and low back pain are generated, while in NB,

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meningeal irritation, confusion and hypoesthesia stand out. Within the neurological process of NB, it can also include cranial nerve disorders, polyneuropathy/radiculopathy, paraplegia, abscess formation and even psychiatric components such as depression.

Zoonosis refers to infectious diseases that are naturally transmitted from wild or domestic animals to humans and vice versa. Brucellosis is a zoonotic disease which has a close correlation between animal and human disease [3]. People in certain occupations or environments may face greater exposure to Brucella bacteria such as slaughterhouse workers and employees of meat processing plants [4]. It is of utmost importance to take biosecurity measures to prevent the spread of brucellosis, including proper handling and disposal of animal products accompanied by good hygiene [5].

Occupational exposure to neurobrucellosis is also linked as a risk factor for developing Parkinson's disease so it is important for people in high-risk occupations to take the necessary precautions to minimize exposure to potential hazards [4]. Overall, understanding the risks associated with occupational exposure and zoonotic diseases such as neurobrucellosis can help people take and maintain biosafety standards.

Understanding Neurobrucellosis

Neurobrucellosis is a rare but severe form of brucellosis, a zoonotic disease caused by the bacterium Brucella. The bacterium is primarily transmitted to humans through contact with infected animals or consumption of unpasteurized dairy products [1]. Occupational exposure is also a common mode of transmission, particularly through inhalation of contaminated aerosols [7]. Patients with neurobrucellosis may present with a variety of neurological symptoms, including undulant fever, neuropsychiatric features, seizures, and meningitis/encephalitis [8][1][9]. Given the severity of the disease, it is important to understand its causes and transmission in order to prevent its spread.

Diagnosing neurobrucellosis can be challenging as symptoms can be nonspecific and may mimic other neurological conditions. However, a high degree of suspicion is required when patients present with undulant fever and neuropsychiatric features [8]. Diagnosis is usually confirmed by laboratory tests, including blood cultures and serological tests [3][10]. Early diagnosis and treatment are crucial to prevent the development of complications [1].

Treatment for neurobrucellosis typically involves a combination of antibiotics, including doxycycline, rifampicin, and ceftriaxone, for a period of 3 to 6 months [7]. Prevention of neurobrucellosis involves measures such as occupational hygiene, particularly for those at higher risk of exposure, such as farmers, veterinarians, and laboratory workers [3].

Public education campaigns can also help raise awareness about the disease and its prevention [11]. By understanding the causes, symptoms, diagnosis, and treatment of neurobrucellosis, we can work to prevent its spread and improve outcomes for people affected by the disease.

Understanding Zoonosis

As previously mentioned, zoonosis consists of the transmission of diseases transmitted from animals to humans. These diseases can be caused by all types of pathogens, including bacteria, viruses, fungi and parasites.

There are several types of zoonotic diseases, including viral, bacterial, fungal, and parasitic infections. Some of the most common zoonotic diseases include rabies, Lyme disease, salmonellosis, and toxoplasmosis [5]. These diseases can be transmitted through several modes, such as direct contact with infected animals, consumption of contaminated food or water, and insect bites [5]. Preventing and controlling zoonotic diseases requires a One Health approach, which involves collaboration between the human health, animal health, and environmental health sectors [11]. This approach aims to identify and mitigate risk factors associated with the transmission of zoonotic diseases and promote the health and well-being of humans and animals.

Preventing occupational exposure to zoonotic diseases requires the implementation of appropriate preventive measures, such as wearing personal protective equipment, practicing good

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hygiene, and following safe handling practices [12]. In addition, regular health checks and vaccination against zoonotic diseases can help reduce the risk of infection [13]. By adopting these preventive measures, individuals can protect themselves and others from the potential health risks associated with zoonotic diseases.

Occupational Exposure to Zoonotic Diseases

Occupational exposure to zoonotic diseases is a major concern for people who work with animals or animal products.

Occupations that involve direct contact with animals or their products are at the highest risk of exposure to zoonotic diseases. These may include slaughterhouse workers, veterinarians, farmers, and animal caretakers [4]. Aerosol transmission is also a major occupational risk for those who come into contact with infected material, such as the placenta, which can result in inhalation of the bacteria [7]. Other zoonotic diseases, such as leptospirosis, are also of concern to people who work with animals [14].

Prevention and control of occupational exposure to zoonotic diseases is critical to protecting the health of workers and the general public. Effective defensive measures, such as the use of personal protective equipment and proper sanitation practices, are necessary to prevent the spread of disease [12]. In addition, education and training of people who work with animals can help increase awareness of the risks associated with zoonotic diseases and promote appropriate prevention and control measures [11].

Case Description

CNS involvement is much less common (2%-10%). Most cases are acute or chronic meningoencephalitis. All types of neurological focality and sometimes hydrocephalus may be observed. Vascular involvement of the CNS is not rare and may cause transient ischemic attacks. Meningopolyradiculitis and mononeuritis are rare. Epiduritis or epidural abscess secondary to spondylitis sometimes occurs. Adenosine deaminase may be increased as in tuberculous meningitis. The microorganism is isolated from the CSF in half of the cases. Serological titers of the CSF are usually low but of great value; the ELISA method is especially useful.

Table 1. Patient demographics.

PATIENT DEMOGRAPHICS	
Age	51 years old
Sex	Male
Marital status	Married
Level of education	Third Level
Occupation	Veterinary Technician
Laterality	Right
Habitual residence	Nanegalito Km 61 Calacalí-La Independencia road
Pathological background	• Grade 3 obesity. • Hyperopic astigmatism, presbyopia, keratoconus. • Lumbar spondylodiscarthrosis.
Non-pathological background	Physical activity: volleyball and soccer once a week.

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Note: Patient description - Neurobrucellosis case.

Neurobrucellosis

Etiology. Brucella is a facultative intracellular aerobic gram-negative coccobacillus. The species mellitensis, abortus or suis can infect humans; the first is the one that most frequently causes neurobrucellosis. The reservoir of Brucella is animals (mainly goats and sheep). Man becomes infected through the gastrointestinal tract by ingesting insufficiently cooked milk or derivatives, or through eroded skin, conjunctiva and lungs when handling sick animals (this is the case of shepherds, veterinarians and slaughterers).

In developed countries, brucellosis has been almost eradicated, but there are still many endemic areas where the incidence is high, such as in North African countries and Turkey. Only 5% of patients with brucellosis have neurological complications.

Pathological anatomy. Brucella infection of the CNS produces a subacute-chronic lymphomonocytic inflammation that can affect the brain, spinal cord and spinal roots, either diffusely or by forming granulomas and abscesses. It also produces vasculitis with cerebral or spinal cord infarcts.

Clinic. Neurological symptoms may appear without a history of systemic disease, or when the disease has been so mild that it has not been diagnosed. Neurobrucellosis is usually accompanied by other symptoms of systemic disease when it occurs in the early phase of bacteremia (fever, general wasting syndrome, lymphadenopathy, hepatosplenomegaly, orchitis, muscle pain), or neurological symptoms may appear as a delayed complication months or years after the general infection.

Neurobrucellosis causes a subacute meningitis indistinguishable from tuberculous meningitis. In the more chronic forms of meningoencephalitis, patients present with symptoms of mental deterioration, sometimes with very few focal signs or symptoms, but frequently associated with epileptic seizures.

Vasculitis may lead to subcortical lacunar stroke, non-stroke encephalopathy with diffuse hemispheric white matter signal disturbance, and, more rarely, to subarachnoid hemorrhage or transverse myelopathy due to spinal cord infarction. The spinal cord may also be affected secondarily by spondylodiscitis with epidural abscess.

The involvement of multiple sacral and lumbar roots or cranial nerves by arachnoiditis is characteristic and sometimes the main symptom of the clinical syndrome. Sensorineural deafness is very common. Other rarer manifestations include optic neuritis, dural sinus thrombosis and hydrocephalus.

Diagnosis. Given the highly varied clinical presentation of neurobrucellosis, its diagnosis requires laboratory support. The CSF pattern includes lymphocytic pleocytosis, elevated protein and decreased glucose. Gamma globulin is highly elevated with oligoclonal bands, unlike in tuberculous meningitis.

Diagnosis is based on the isolation of Brucella from blood or CSF (<50% of cases) or on serological techniques. The sensitivity of the culture is improved if it is performed directly from the LP needle under anaerobic conditions. The rose bengal test in CSF and blood has a low percentage of false negatives. The ELISA method detects IgG antibodies against antigens of the microorganism, both in blood and CSF.

MRI is more sensitive than CT for detecting lesions in both the brain and the spinal cord. Several changes can be seen: a) hypersignal and diffuse uptake of the meninges with or without granulomas and hydrocephalus; b) intracerebral or intramedullary abscesses; c) lacunar infarcts; d) diffuse hypersignal of the hemispheric white matter (suggestive of vasculitis), and e) contrast uptake by inflamed spinal roots (sometimes only the anterior ones).

Treatment. In neurobrucellosis, three drugs are recommended together (doxycycline, 100 mg/12 h; gentamicin, 240 mg/day im; and rifampicin, 600 mg/24 h) for at least 12 weeks. In other regimens, the aminoglycoside is replaced by ceftriaxone or cotrimoxazole. The goal of treatment should be to

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normalize the cells in the CSF. Therapeutic failures are frequent, requiring repeating and changing treatment courses.

Link Between Neurobrucellosis and Parkinson's Disease

Recent research has suggested a potential link between neurobrucellosis, a rare complication of brucellosis, and Parkinson's disease. Neurobrucellosis is diagnosed in only 1.7% and 0.8% of cases in adult and pediatric populations, respectively [1]. When a patient presents with undulant fever and neuropsychiatric features, neurobrucellosis should be considered as a differential diagnosis [8]. Brucellosis is a common zoonosis affecting half a million people annually, with the most common mode of infection being consumption of unpasteurized dairy products [7]. The potential link between neurobrucellosis and Parkinson's disease warrants further investigation as it could have significant implications for the prevention and treatment of Parkinson's disease.

The mechanisms by which neurobrucellosis may cause Parkinson's disease are still not fully understood. A study by Soares et al. in 2022 noted that neurobrucellosis can be insidious and is often underreported, further complicating the understanding of its potential link to Parkinson's disease [18]. Furthermore, lipopolysaccharide, a component of the Brucella bacteria, has been proposed to be the main mechanism for the bacteria's intracellular survival [3]. Further research is needed to fully elucidate the mechanisms by which neurobrucellosis may lead to Parkinson's disease.

The potential link between neurobrucellosis and Parkinson's disease has important implications for prevention and treatment.

Furthermore, determining baseline levels of infection and disease in both humans and animals could aid in prevention and early detection efforts [20]. Long-term use of dopaminergic therapy in Parkinson's disease is associated with reduced efficacy and disabling dyskinesias [16].

Prevention and Control of Neurobrucellosis and Parkinson's Disease

Parkinson's disease is a neurodegenerative disorder that affects millions of people worldwide. While the exact cause of Parkinson's disease is not known, there are several strategies that can help prevent or manage the disease. These include regular exercise, a healthy diet, and avoiding exposure to environmental toxins such as pesticides and herbicides [21]. Furthermore, recent research has suggested a link between occupational exposure to certain chemicals and an increased risk of Parkinson's disease [22]. Therefore, implementing measures to reduce exposure to these chemicals and promoting healthy lifestyle practices is critical to preventing or managing Parkinson's disease.

The One Health approach is crucial to prevent and control zoonotic diseases such as neurobrucellosis and Parkinson's disease. This approach recognizes the interconnectedness of human, animal and environmental health and emphasizes the importance of collaboration across different sectors to address zoonotic diseases [23]. By adopting the One Health approach, governments can prioritize zoonotic diseases and implement surveillance, prevention and control strategies [24]. This approach can also help address the economic impact of zoonotic diseases by reducing disruption to daily activities and decreasing livestock losses [25]. Therefore, adopting a One Health approach is essential to prevent and control zoonotic diseases, including neurobrucellosis and Parkinson's disease.

Table 2. Chronology of clinical manifestations of neurobrucellosis.

CHRONOLOGY OF CLINICAL MANIFESTATIONS	
Clinical manifestations	***Date of appearance***
• Fine tremor in right upper limb	April 2018
• Parkinson	January 2019

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• Thermal rise • Hyporexia • Arthralgia of large joints • Weight loss 12 kg • Headaches • Nausea • Shivers • Right testicular edema	February 2019
• Secondary right hemiparkinsonism	November 2019
• Hyperintensity focused on the anterior aspect of the right inferior cerebellar peduncle. Discrete post- contrast enhancement of the pial cover to be correlated with uroclinical findings as a possible	January 9, 2020
sequel to an infectious inflammatory process. • Thickening of the mucosa of the maxillary antrum, sphenoid sinus, ethmoid cells and left frontal sinus, in relation to pansinusitis.	
• Diagnosis of neurobrucellosis, consequence of right hemiparkinsonism with functional impairment for writing and walking.	January 16, 2020
• Anxiety • Nausea • Insomnia • Gait with distal tremor • Fine distal tremor in the right side of the body.	January 17, 2020
• Mild hemiparesis, full range of motion for all four limbs, fine distal tremor for the right side of the body. Deep tendon reflexes II/V for the left and right sides of the body. Hand tremor with loss of muscle strength that interferes with writing and fine manipulative activities. • Range of motion preserved for 4 extremities, presence of predominantly distal tremor for upper limbs in the right lower limb.	February 27, 2020

Note: Chronology of clinical manifestations according to appearance.

Conclusions

In conclusion, neurobrucellosis is a zoonotic disease that should be considered as a differential diagnosis in patients presenting with undulant fever and neuropsychiatric features [8]. Brucellosis is a common zoonotic disease affecting half a million people annually, with the most common mode of infection being consumption of unpasteurized dairy products [7]. Occupational exposure to zoonotic

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diseases, including brucellosis, is a major concern for certain groups of workers, such as farmers, veterinarians, and slaughterhouse workers [4]. The epidemiology of brucellosis as an occupational disease has been best understood through systematic reviews [11,12].

In the future, further research is needed to explore the links between neurobrucellosis and Parkinson's disease. Recent studies have suggested that occupational exposure to manganese may be a risk factor for developing Parkinson's disease [16]. As brucellosis is a zoonotic disease that can cause neurological symptoms, it is important to investigate whether there is a potential association between neurobrucellosis and Parkinson's disease.

Action is also needed to address occupational exposure to zoonotic diseases and Parkinson's disease. This includes implementing measures to prevent and control brucellosis in livestock, such as vaccination programs and improved hygiene practices [3]. In addition, workers in high-risk occupations should receive appropriate training and protective equipment to reduce the risk of exposure to zoonotic diseases [23]. Finally, more attention should be paid to recognizing and reporting neurobrucellosis as a potential occupational disease [18]. By taking these steps, we can work to reduce the burden of zoonotic diseases and occupational diseases in our communities.

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