Diplopia: A unique presenting symptom of neurobrucellosis: A case report

Yousef Mahmoud Nimer Habes^{1*}, Hassan Omar¹, Rabee Adwan², Anees Nasser³

Habes YMN, Omar H, Adwan R, et al. Diplopia: A unique presenting symptom of neurobrucellosis: A case report. J Neurol Clin Neurosci. 2024;8(1):1-3. ABSTRACT Brucellosis is the most frequent worldwide zoonotic disease. The disease is acquired through the ingestion of unpasteurized dairy products it may affect any organ or system in the body. Neurobrucellosis is a rare form of systemic brucellosis that may manifest as encephalitis, meningoencephalitis,	radiculitis, myelitis, stroke, and intracranial hemorrhage. We report a case diagnosed as neurobrucellosis who presented with unilateral diplopia along with right-sided body numbness. The diagnosis was confirmed by Cerebrospinal Fluid (CSF) culture and blood serology. Key Words: Neurobrucellosis; <i>Brucella</i> ; Diplopia Abbrevations: CSF: Cerebro-Spinal Fluids; Kg: Kilograms; MRI: Magnetic Resonance Imaging; MRV: Magnetic Resonance Venography; Mg: Milligram; TB: Tuberculosis; CT: Computed Tomography; IV: Intravenous
---	--

INTRODUCTION

 \mathbf{B} rucellosis, also called Malta fever, is a zoonotic infection caused by the bacterial genus *Brucella*. Its incidence across the world varies from less than 0.03 to 160 per 100,000, most commonly seen in the Mediterranean countries [1]. The disease is transmitted through ingestion of unpasteurized milk, contact with infected animals or their discharges, or rarely *via* sex or

The disease can be caused by four species: *Brucella melitensis* (from sheep, goats, and camels), *Brucella suis* (from pigs), *Brucella abortus* (from cattle), and *Brucella canis* (from dogs).

placenta to babies.

Neurologic involvement occurs in approximately 10% of cases and is a serious complication of brucellosis [2]. The patient may complain of headaches, fever, sweating, weight loss, and back pain. In addition, meningeal irritation, confusion, hepatomegaly, hypoesthesia, and splenomegaly are reported. Cranial nerve involvement, mostly affecting the sixth and eighth cranial nerves moreover, polyneuropathy and radiculopathy, depression, paraplegia, stroke, and abscess formation are reported. Walking difficulty and hearing loss are the predominant sequelae, followed by urinary incontinence, visual disturbances, and amnesia.

CASE PRESENTATION

A 32-year-old female from East Jerusalem, Palestine, was admitted due to diplopia for 20 days. The patient was in her usual state of health until May

2019, when she started to complain of numbness in the right side of her face, tongue, and upper limb. The numbness was episodic, occurring 2-4 times a week, once daily, and lasting for a few hours before resolving spontaneously. It was associated with a feverish sensation "not documented", lightheadedness that lasts for a few minutes, and vomiting. She also complained of a dull, aching headache in the frontal region. Those symptoms persisted and increased in frequency and severity over the following months, along with a weight loss of 22 kilograms (kg) within 4 months.

She denied chills, night sweating, neck pain, stiffness, confusion, photophobia, phonophobia, dysphasia, dysarthria, limb weakness, a history of falling down or loss of consciousness, a history of urine or stool incontinence, abnormal movement, hearing loss, or tinnitus.

After one month, she suddenly noticed a doubling of her vision, starting with far objects and progressing to near objects too. There was no history of eye pain or congestion. She sought medical advice at an ophthalmologist's clinic and was found to have bilateral papilledema. So, brain Magnetic Resonance Imaging (MRI) and Magnetic Resonance Venography (MRV) were done and showed bilateral optic disk flattening and an enlarged optic nerve sheath, otherwise unremarkable. So, she was diagnosed with pseudotumor cerebri and was prescribed acetazolamide (500 mg) twice daily.

After that, she was evaluated by a neurologist, and a lumbar puncture was done, with the results as follows (Table 1).

Table 1: Results of evaluation of lumbar puncture after administration of acetazolamide

Opening pressure	34 cm H ₂ O
White blood cells	171/µL
Protein	184 mg/dl
Red blood cells	89/µL
Gram stain	No bacteria seen
Tuberculosis (TB) test	negative
Blood glucose	-

¹Department of Medicine, Al-Quds University, Jerusalem, Palestine

²Departement of Infectious Diseases, Makassed Islamic Charitable Society, Jerusalem, Palestine

³Departement of Neurology, Makassed Islamic Charitable Society, Jerusalem, Palestine

Correspondence: Yousef Mahmoud Nimer Habes, Department of Medicine, Al-Quds University, Jerusalem, Palestine; E-mail: yousef.habis1996@hotmail.com

Received: 13-Sep-2023, Manuscript No. PULJNCN-23-6708; Editor assigned: 15-Sep-2023, PreQC No. PULJNCN-23-6708 (PQ); Reviewed: 29-Sep-2023, QC No. PULJNCN-23-6708; Revised: 20-Jan-2024, Manuscript No. PULJNCN-23-6708 (R); Published: 27-Jan-2024, DOI: 10.37532/puljncn.24.8(1).1-3

ACCESS This open-access article is distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC) (http:// creativecommons.org/licenses/by-nc/4.0/), which permits reuse, distribution and reproduction of the article, provided that the original work is properly cited and the reuse is restricted to noncommercial purposes. For commercial reuse, contact reprints@pulsus.com She reports no improvement in her symptoms and was referred to our hospital for further evaluation and management as an initial impression of TB meningitis.

On physical examination, the patient looked well, conscious, oriented, and alert with stable vital signs. The respiratory, cardiovascular, gastrointestinal, and extremity examinations were normal. The neurological examination was normal except for horizontal diplopia.

Table 2: Testing results of tumor markers

In hospital investigations, including a complete blood count, kidney function tests, C-reactive protein, C3, and C4, all were within the normal range. We also tested tumor markers: Anti-nuclear antibody, rheumatoid factor, B-human chorionic gonadotropin, and purified protein derivatives, all of which were negative. Lumbar puncture was done again and showed (Table 2).

Total cell	520
WBCs	375
Lymphocytes	89%
Glucose	34
Protein	223
CSF culture	No growth
CSF cytology	No malignant cells
CSF cryptococcal antigen test,	Negative
CSF acid fast bacilli	Negative

Further investigations include the chest, abdomen, and pelvis. On a Computed Tomography (CT) scan with and without contrast, it was normal. A whole-spine MRI without contrast showed only a slightly prominent and slightly enhanced pia mater of the spinal cord.

A brain MRI with IV contrast was suspicious for an intra-orbital mass (suspicious for lymphoma), otherwise unremarkable.

LP was repeated in our hospital and showed findings in Table 2. CSF culture and broth culture were sent.

Orbital MRI and CT with Intravenous (IV) contrast were done, and no abnormalities could be seen. The patient was then diagnosed as having an autoimmune disease and discharged on methylprednisone for follow-up after one week.

Over the next week, CSF broth, blood culture, and serology were positive for Brucella. Now, she is diagnosed as having neurobrucellosis and treated with oral rifampicin 600 mg once daily, oral doxycycline 100 mg twice daily, IM streptomycin 1 g twice daily for one week, then once daily for another week, IV ceftriaxone 2 g twice daily and oral prednisolone 20 mg twice daily.

On discharge after 2 weeks after treatment, lumbar puncture was done again and showed: Total cells 250, WBC 162, lymphocytes 98%, neutrophils 2%, protein 67.5, glucose 50, and discharged on oral Rifampicin 600 mg once daily, oral doxycycline 100 mg twice daily, IV ceftriaxone 2 mg once daily, and oral prednisolone 10 mg once daily.

DISCUSSION

Brucellosis is a common zoonotic infection in many parts of the world, including the Mediterranean and Middle Eastern countries, including Palestine. There are two subtypes of bacteremic brucellosis: *Brucella melitensis* genus and *Brucella abortus* genus, with predominance for melitensis in prevalence (83% vs. 17%) [3]. Due to its zoonotic nature, this disease has a major impact on Palestinian health and the economic system. In 1998, Hebron had the highest incidence rate (139.9/100,000), followed by Jericho and Bethlehem [4]. A total of 837 cases were reported to the ministry's health surveillance system, with 546 of those coming from Hebron district [5]. The economic burden of brucellosis is grave. In 1994, the direct loss suffered by livestock was estimated to be in excess of \$10 million.

To our knowledge, neurobrucellosis is still considered a rare disease. The differential diagnoses considered included meningitis, tuberculosis, lymphoma, and autoimmune disease. Our patient was young and had no past history of migraines or risk factors for cerebrovascular or neurological

disease. She tested negative for tuberculosis (purified protein derivative PPD), tumor markers, antinuclear antibodies, rheumatoid factor, C3, C4, and beta HCG. Lumber puncture was done and showed: Total cell 520, WBC 375, lymphocyte 89%, glucose 34, protein 223, and cerebrospinal fluid cytology showed no malignant cells; the cryptococcal antigen test was negative.

In reviewing our case, we found some case reports and case series of neurobrucellosis. in the report by al-Deeb et al. [6]. It categorizes the neurological involvement in brucellosis into 5 groups: acute meningoencephalitis, meningovascular involvement, central nervous system demyelination, peripheral neuropathy, papilledema, and increased intracranial pressure. Sometimes neurological symptoms may be the only presentation in the course of the disease. The criteria for a definite diagnosis of neurobrullosis are:

- Neurological disability not explained by other neurological diseases.
- Abnormal CSF indicating lymphocytic pleocytosis and increased protein.
- Positive CSF culture for brucella organisms or positive brucella IgG agglutination titer in the blood and.
- CSF response to specific chemotherapy with a significant drop in lymphocyte count and protein concentration.

In a pulled analysis of 187 cases of neurobrucellosis done by Gul HC and Erdem H et al. in turkey [7]. Headache, fever, sweating, weight loss, and back pain were the predominant symptoms, while meningeal irritation, confusion, hepatomegaly, hypoesthesia, and splenomegaly were the most frequent findings. The major complications in patients were cranial nerve involvement, polyneuropathy/radiculopathy, depression, paraplegia, stroke, and abscess formation. Antibiotics were used in different combinations and at different intervals. The duration of antibiotic therapy reported ranged from 2 to 15 months (median 5 months). The mortality rate was 0.5% with suitable antibiotics. They concluded that neurobrucellosis may mimic various pathologies, so a thorough evaluation of the patient with probable disease is crucial for an accurate diagnosis and proper management of the disease.

In one study, three cases of neurobrucellosis were reported by Deniz Tuncel, Hasan Uçmak, et al., [8]. In Turkey, one patient had diffuse cerebral white matter lesions as leukoencephalopathy and presented with gait disturbances, behavior changes, and seizures. Another patient had bilateral progressive motor weakness for four months and a headache for one year. The third patient had brachiocephalic transient numbness attacks and headaches for twenty days. He also had signs of meningitis. A single case was reported by Ghosh D, Gupta P, and Prabhakar S from Chandigarh [9]. A young adult presenting with an 11-month history of fever, headache, and vomiting was found to have CSF lymphocytic pleocytosis with increased protein. His serum tested strongly positive for *Brucella* (standard tube agglutination titer 1:320), whereas his CSF was weakly positive. He became asymptomatic on treatment with tetracycline, rifampicin, and streptomycin, with a significant CSF response.

Neurobrucellosis treatment must include antibiotics that cross the bloodbrain barrier. Combination therapy must include: Ceftriaxone 2 mg IV twice daily for at least 1 month; Doxycycline 100 mg PO twice daily for 4-5 months; and rifampin 600–900 mg (15 mg/kg) PO once daily for 4-5 months. The alternative regimen consists of: Trimethoprim-sulfamethoxazole 160/800 mg PO twice daily for 5-6 months; doxycycline 100 mg PO twice daily for 5-6 months; and rifampin 600–900 mg (15 mg/kg) PO once daily for 5-6 months. Sometimes corticosteroid is added and used to be useful in patients with raised intracranial pressure, papilledema, or polyneuropathy, and our patient has one of these symptoms.

CONCLUSION

In summary, this case of neurobrucellosis underscores the diagnostic challenges and complexities associated with this rare manifestation of a globally prevalent zoonotic disease. The patient's journey from initial misdiagnoses to the eventual identification of neurobrucellosis highlights the importance of considering uncommon presentations in regions where brucellosis is endemic. Neurobrucellosis, although rare, can manifest with diverse neurological symptoms, necessitating a high index of suspicion and thorough evaluation. A timely diagnosis, confirmed through cerebrospinal fluid culture and serology, is crucial for effective management and improved patient outcomes. This case serves as a reminder for healthcare providers in endemic areas to remain vigilant, especially when confronted with atypical neurological presentations. Early recognition and appropriate treatment are essential to preventing complications and ensuring a successful outcome for patients with neurobrucellosis.

REFERENCES

- Principles and practice of infectious diseases of worldwide Incidence of brucellosis. 9th Edition. Douglas RG, Bennett JE, Mandell GL, Editors. 2020.
- Principles and practice of infectious diseases of Percent of neurobrucellosis of Brucella patients. 9th Edition. Douglas RG, Bennett JE, Mandell GL, Editors. 2020.
- 3. Dokuzoguz B, Ergonul O, Baykam N, et al. Characteristics of *B. melitensis* versus *B. abortus bacteraemias*. J Inf. 2005;50(1):41-5.
- Husseini A, Ramlawi AA. Brucellosis in the west bank, Palestine. Saudi Med J. 2004;25(11):1640-43.
- Amro A, Mansoor B, Hamarsheh O, et al. Recent trends in human brucellosis in the West Bank, Palestine. Int J Infect Dis. 2021;106:308-13.
- Al Deeb SM, Yaqub BA, Sharif HS, et al. Neurobrucellosis: Clinical characteristics, diagnosis, and outcome. Neurology. 1989;39(4):498-501.
- Gul HC, Erdem H, Bek S. Overview of neurobrucellosis: A pooled analysis of 187 cases. Int J Infect Dis. 2009;13(6):e339-43.
- Tuncel D, Ucmak H, Gokce M, et al. Neurobrucellosis. European J General Med. 2008;5(4):245-48.
- Patil S, Narkhede MG. Neurobrucellosis: A case report. Int J Res Med Sci. 2014;1:353-57.