Infectious Medicine 3 (2024) 100132

Contents lists available at ScienceDirect

Infectious Medicine

journal homepage: www.elsevier.com/locate/imj

Case Report

Ocular tuberculosis associated with Epstein-Barr virus myelitis: A case report

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ARTICLE INFO

Keywords:
Epstein-Barr virus
Mycobacterial infection
Myelitis
Ocular tuberculosis

ABSTRACT

Ocular tuberculosis (OTB) is a chronic eye infection caused by *Mycobacterium tuberculosis*. Some cases of myelitis are associated with *Epstein-Barr virus* (EBV), with 1-5% of EBV infections leading to neurologic complications. We describe a 34-year-old Iranian woman with OTB and EBV coinfection. Despite initial success with anti-TB agents, the disease progressed, necessitating enucleation. *Mycobacterium tuberculosis* was detected by a tuberculin coagulation test, and EBV was confirmed via polymerase chain reaction. MRI showed plaques in the spinal cord and brain. The patient was treated with anti-TB and antiretroviral agents. Recognizing TB in the differential diagnosis of EBV myelitis is crucial.

1. Introduction

Ocular tuberculosis (OTB) is an uncommon extrapulmonary infection caused by *Mycobacterium tuberculosis* that has variable manifestations. Affected patients may develop headaches, flashes, floaters, red eyes, reduced visual acuity, and light sensitivity. Ocular lesions can result from direct (primary) invasion by *M. tuberculosis* as an active infection. OTB can also develop indirectly (secondary) by hematogenous spread or occur independently of the infectious agent following an immune reaction [1]. Corneal involvement is generally infrequent. The differential diagnoses of ocular lesions include infectious diseases such as Epstein-Barr virus (EBV), varicella-zoster virus, herpes simplex virus, and Lyme disease and noninfectious conditions such as multiple sclerosis, rheumatoid arthritis, Behcet's disease, and sarcoidosis [2]. Rapid OTB diagnosis is crucial because it facilitates early anti-TB therapy and prevents disease exacerbation. Vision loss may occur if OTB is not diagnosed and treated promptly. Because immediate OTB diagnosis is often unavailable, various diagnostic and treatment approaches must be revised [3]. The treatment for OTB is similar to that for pulmonary TB. Four-drug therapy (rifampin, isoniazid, pyrazinamide, and ethambutol) may be required for up to 2 months, followed by two-drug therapy (rifampin and isoniazid) for an additional 4 to 7 months [4,5].

Traditionally, acid-fast bacilli and bacterial cultures were examined under a microscope to diagnose TB. However, a more precise diagnosis can be made through mycobacterial nucleic acid amplification using molecular methods [6]. EBV, a double-stranded DNA virus from the herpes family, is a common virus that infects humans. EBV infections vary from asymptomatic conditions to a spectrum of diseases. Most EBV infections (>99%) are self-limiting and rarely can lead to diverse central nervous system complications, including encephalitis, myelitis, encephalomyelitis, meningitis, and peripheral

Abbreviations: EBV, Epstein-Barr virus; MBT, *Mycobacterium tuberculosis*; TB, tuberculosis; OTB, ocular tuberculosis; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

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https://doi.org/10.1016/j.imj.2024.100132
Received 2 December 2023; Received in revised form 23 January 2024; Accepted 6 April 2024

Table 1
Laboratory test.

Index		Results	Units	Flag
Blood	Blood Urea Nitrogen	8.0	mg/dL	
	Creatinine	0.9	mg/dL	
	Prothrombin	13.6	Sec	
	PT.INR	1.0	Sec	
	PTT. Patient Time	28.8	Sec	Low
	Tuberculin Coagulation test (PPD 5 units)	25	mm	Positive
CSF	Bacteria	Not seen	Number	
	Glucose	63	mg/dL	Normal
	Protein	45.2	mg/dL	Normal
	WBC	65	Per Cu/mm	
	RBC	0	Per Cu/mm	
	Lymph	95	–	
	MTB (PCR)	Negative	–	Negative

neuropathies [7]. Acute EBV myelitis can present as neurologic dysfunction due to involvement of the white matter [8]. The symptoms of EBV myelitis can include sensory alteration, weakness, and autonomic dysfunction. Myelitis caused by EBV is successfully treated with steroids plus acyclovir [9]. We herein present a unique case study of a patient with concurrent OTB and EBV.

2. Case presentation

A 34-year-old woman was diagnosed with OTB after experiencing vision problems. She was prescribed a 6-month course of isoniazid (5 mg/kg) and rifampin (10 mg/kg) as part of her anti-TB therapy. However, the disease continued to progress, leading to further complications. Methotrexate (12 mg/week) and prednisolone (2 drops every 3 h) were administered, and further investigations were conducted to determine the underlying cause of the disease progression.

Based on the examination and evidence of upper motor neuron disease, the patient was diagnosed with weakness of the lower limbs and paresthesia. Further diagnostic tests were performed, including brain and spinal cord magnetic resonance imaging (MRI), complete blood cell count and cerebrospinal fluid (CSF) analysis. The patient's symptoms and MRI findings confirmed myelitis, and the presence of EBV in the CSF confirmed the diagnosis.

Viral and bacterial panels for myelitis were conducted in the CSF. The tuberculin coagulation test revealed the presence of *M. tuberculosis* with a purified protein derivative measurement of 25 mm. The CSF analysis results showed a normal protein level of 45.2 mg/dL (reference range, <150 mg/dL) and slightly elevated glucose level of 63 mg/dL (reference range, 40–90 mg/dL) (Table 1). MRI revealed a large plaque in the spinal cord and several small plaques in the brain; however, they were not distinct or striking (Fig. 1). The virus panel showed evidence of EBV in the CSF (Table 2).

Based on this comprehensive diagnostic evaluation, the patient was diagnosed with OTB and EBV coinfection.

Table 2
Panel of pathogens in CSF. PCR reports.

Index Pathogens causing viral Meningitis	Results
HSV-1 *(Herpes Simplex Virus-1)*	Negative
HSV-2 *(Herpes Simplex Virus-2)*	Negative
CMV (*Cytomegalovirus)*	Negative
EBV (*Epstein Barr Virus)*	Positive (35 copies)
VZV *(Varicela-Zoster Virus)*	Negative
EV *(Entrovirus)*	Negative
HpeV *(Pareachovirus)*	Negative
Pathogens causing bacterial Meningitis	
MTBc *(Mycobacterium tuberculosis complex)*	Negative
SPNEU *(Streptococcus pneumonia)*	Negative
Leptospira (*Leptospira interrogans)*	Negative
HINF (*Haemophylus inflenzae)*	Negative
LEIS *(Listeria monocytogenes)*	Negative
N. meningitidis (Nisseria meningitidis (ctrA))	Negative
N. meningitidis (sod) (Nisseria meningitidis (sod))	Negative
CRYPT *(Cryptococcus neoformans (fungus))*	Negative

Treatment involved the administration of anti-TB and antiretroviral (acyclovir) agents. The patient underwent regular follow-up visits, laboratory tests, and imaging studies to assess treatment response and effectiveness, resulting in significant improvement and her discharge in good general condition.

3. Discussion

TB is the second most lethal infectious disease after COVID-19 and the 13th leading cause of death globally. It affects one-third of the global population and causes over 10.6 million new cases annually. Ocular TB, a rare manifestation, accounts for 1% to 2% of all TB cases [10]. To our knowledge, this is the first report of concurrent OTB and EBV myelitis. However, one report described ocular symptoms of EBV in the form of optic neuritis [11]. In another case study in 1986, EBV infection was described in a patient with active pulmonary TB [12].

In this case report, a 34-year-old woman with OTB developed weakness in her lower limbs, paresthesia, and upper motor neuron disease. Her unique epidemiology, clinical symptoms, and imaging results underscore the impor-

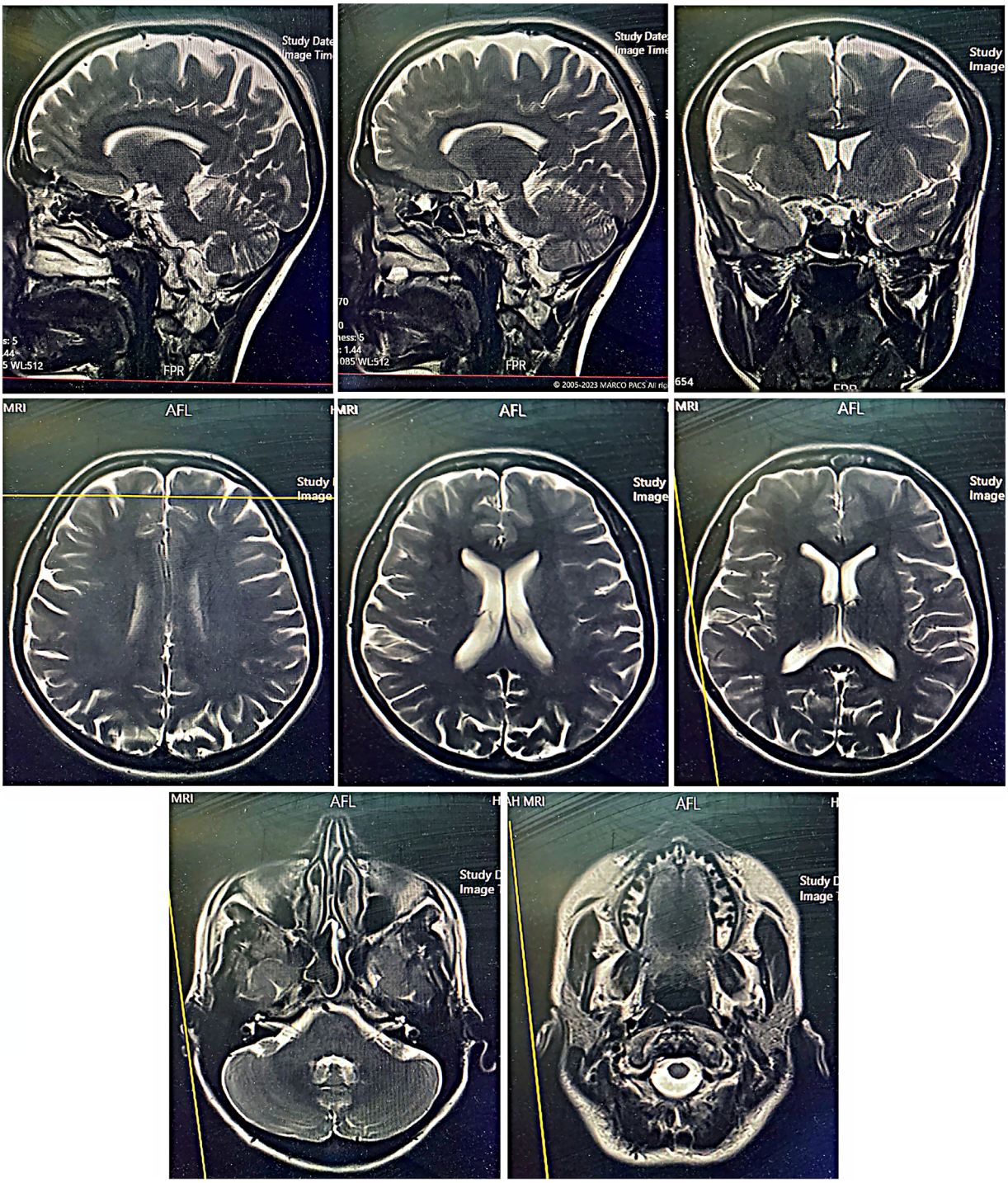

Fig. 1. Magnetic resonance imaging showed no pathological lesions.

tance of early detection and treatment. Laboratory tests such as a complete blood cell count, the tuberculin coagulation test, and CSF analysis can help diagnose TB and other infections, and showed normal protein and glucose levels. The diagnosis of meningitis was made through PCR and a combination of DNA probes. A positive tuberculin coagulation test and brain and spinal cord MRI revealed a large plaque in the spinal cord and several small plaques in the brain.

Mycobacterium tuberculosis infection can occur directly or indirectly in organs like eyes, skin, and joints [13], with OTB manifestations resulting from active infection or immune response [14]. The diagnosis of OTB through a prolonged histopathological examination can be challenging. PCR is a quick diagnostic method with high specificity for pulmonary TB (98.0%) [15] and extrapulmonary TB (95.7%) [16]. However, culture method remains the gold standard for laboratory diagnosis of *M. tuberculosis*, with

enzyme-linked immunosorbent assay being the standard technique for diagnosing OTB [13]. According to some investigations, the low bacterial load in ocular fluids and the thick cell wall of *M. tuberculosis* may account for the low sensitivity of PCR for diagnosis of TB [17,18]. In this case, we did not find *M. tuberculosis* by PCR; it was detected by the tuberculin coagulation test.

Chronic active EBV infection is a systemic dysfunction characterized by recurrent inflammation, fever, liver dysfunction, and vasculitis, which can progress to malignant lymphoma, multiple organ deficiency, or hemophagocytic lymphohistiocytosis [19]. An immediate diagnosis is crucial for better care, and considering viral infections like EBV is essential. In our case, EBV virus was detected in the CSF by a PCR viral panel. When the viral panel was reassessed, EBV was again present within the CSF. EBV myelitis was finally diagnosed in this patient with OTB, and acyclovir was administered. The patient was discharged in satisfactory condition after completing the treatment.

The clinicall significance of the case was a 34-year-old woman with ocular lesions was diagnosed with OTB and also found to have EBV myelitis. This unique case of concurrent OTB and EBV was successfully treated with steroids and acyclovir. The coexistence of these infections in one patient is uncommon, and the treatment represents a tailored, multidisciplinary approach to address the specific challenges of this coinfection. The findings prompt consideration of whether, in certain communities, OTB and viruses causing cellular immunosuppression are related.

4. Conclusions

Despite financial and technical challenges in Iran, this unique case demonstrates limited clinical data consistent with primary EBV. The report shows that during anti-TB treatment, *M. tuberculosis* can trigger a delayed immune response in ocular tissue. It is essential to consider OTB when diagnosing chronic, atypical ulcerative, or interstitial keratitis. Despite the severe nature of the infection, the desired result was achieved due to the prompt diagnosis using a tuberculin coagulation test, appropriate treatment with steroids and antibiotics, and accurate post-treatment monitoring.

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

Javad Hosseini Nejad: Supervision, Conceptualization, Software, Validation. **Fakhri Alahyari:** Data curation, Writing- Original draft preparation, Visualization, Investigation. **Raheleh Halabian:** Writing and Edited manuscript, Methodology. All authors read and approved the final manuscript.

Acknowledgments

The authors would like to thank all clinical staff for their contribution to this research. Email Address r.halabian@bmsu.ac.ir

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data available statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics statement

Not applicable.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review on request.

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