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The diagnostic challenge of orbital tuberculosis in an otherwise healthy individual: A case report

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Case Report

ABSTRACT

Ocular tuberculosis occurs in 1.5-18% of all extrapulmonary tuberculosis cases, with orbital tuberculosis being a very small proportion of all cases of ocular tuberculosis. High variability of manifestations of orbital tuberculosis may result in delayed diagnosis. Children are the populations most affected by this disease. This study aims to report a case of orbital tuberculosis in a patient without systemic tuberculosis symptoms. We present a 13-year-old girl who is reported protrusion of the right eye for four months. She complained diplopia and pain in the right eye radiating to the head. She reported no other systemic symptoms. Ophthalmological examination revealed that her best corrected visual acuity of the right eye was 0.25, and the left eye was 1.0. The movement of the right eye was limited to the superior, temporal, and nasal directions. Anterior segment examinations demonstrated proptosis of the right eye with 3 mm of lagophthalmos. The patient then underwent an orbitotomy and biopsy procedure. Histopathological analysis revealed chronic granulomatous inflammation with Langerhans cells, indicative of tuberculosis. The patient was diagnosed with proptosis of the right eye and multiple cranial nerve palsy due to orbital tuberculosis. The patient was subsequently prescribed an antituberculosis treatment and attended regular monthly follow-ups. Ten months after surgery and completed antituberculosis treatment, the proptosis improves and there is no further growth of the mass. Orbital tuberculosis is a rare condition and is often challenging to diagnose, particularly in healthy individuals. Thorough history taking, physical examination, and ancillary testing are essential to establish an accurate diagnosis. This case emphasizes the necessity for heightened suspicion of tuberculosis in atypical presentations, particularly in pediatric patients in endemic areas, to prevent morbidity and ensure timely treatment.

INTRODUCTION

Tuberculosis (TB) is an infectious condition primarily affecting the lungs. Nonetheless, this disease can also affect organs other than the lungs, a condition known as extrapulmonary TB. Extrapulmonary TB constitutes 16-27% of all cases in the United States, and within this category, ocular TB comprises 1.5-18% of cases. Ocular TB is a significant health concern in Indonesia, where it accounts for 11% of extrapulmonary TB cases. The country ranks second globally in TB prevalence, with a notable incidence of ocular manifestations that can lead to severe complications, including blindness. This rare form of extrapulmonary TB can affect various orbital structures, leading to complications such as proptosis, cellulitis, and even intracranial extension. Ocular TB can impact various structures of the eye, including the cornea, conjunctiva, sclera, eyelids, lacrimal glands, and orbital tissue. Orbital or periorbital TB is a particularly rare form, often occurring in conjunction with a systemic TB infection.[1–3] The challenges in diagnosing

orbital TB stem from its atypical presentation, often mimicking other inflammatory diseases, which can delay treatment.[4]

Orbital TB can arise from various factors, including hypersensitivity reactions, local enlargement of infected tissue surrounding the eyes, or hematogenous dissemination from the lungs as the primary sites of infection. Orbital TB often presents with proptosis or diplopia due to pressure exerted by a retrobulbar mass. These symptoms typically appear unilaterally and are more common in children. Diagnosing orbital TB can be challenging due to its atypical clinical presentation. Despite the challenges, the increasing awareness of orbital TB can lead to better outcomes in affected patients. However, the overlap with other conditions may still complicate timely diagnosis and treatment.[1,3,5] This case report aims to enhance the comprehension of the diagnosis and treatment of orbital TB, particularly in patients lacking systemic TB symptoms. This case report contributes to enhancing the understanding of atypical orbital tuberculosis in an endemic country such as Indonesia to prevent delayed diagnosis and treatment.

CASE DESCRIPTION

A 13-year-old girl complained of a slowly progressive protruding of the right eye that began four months before the presentation during her visit to the Reconstruction, Oculoplasty, and Oncology outpatient clinic at National Eye Center Cicendo Eye Hospital. She experienced a persistent double vision that resolved when she closed one eye. Furthermore, the patient reported orbital pain and impaired vision in her right eye. She had a fever for three days in the previous month but no other symptoms, such as cough or vomiting. The patient denied any prior medical history of cancer in the family, trauma, recurrent red eyes, or bodily tumor. She had no history of persistent cough, night sweats, fever, or weight loss. She currently shares a room with students in a boarding school.

The patient underwent a head-orbital Computed Tomography (CT) scan at the local hospital. The CT scan revealed a right superolateral orbital mass, which was compressing the retrobulbar and lateral rectus muscles, causing the eye to protrude inferomedially. The patient received no treatment at the local hospital and was immediately referred to our institution for further examinations.

The ophthalmological examination revealed that her best corrected visual acuity of the right eye was 0.25, lower than her left eye, which was 1.0. An ocular alignment test revealed hypotropia in the right eye. The left eye had unremarkable eye movement in all directions, while the right eye exhibited limited movement to superior, temporal, and nasal directions. Figure 1 showed proptosis and ptosis of the right eye during the anterior segment examination, with margin-to-reflex distance (MRD) 1 measuring 1 mm, MRD 2 measuring 7 mm, and interpalpebral fissure (IPF) of 11 mm. Lagophthalmos of 3 mm and a negative Bell's phenomenon were observed in the right eye. The conjunctiva of the right eye's superior portion exhibited a mixed injection. The funduscopy showed normal bilateral optic nerve morphology.

The patient was diagnosed with proptosis and multiple cranial nerve palsy of the right eye, likely attributable to a retrobulbar mass. The patient was prescribed citicoline syrup, artificial tears, Vitamin A palmitate eye ointment, and eye tapping at night to prevent the exposure keratitis. A head-orbital CT scan with contrast was ordered, and a follow-up appointment was scheduled for seven days.

Figure 1. The patient exhibits right-sided proptosis and slight ptosis during the initial evaluation (white arrow).

A contrast-enhanced head-orbital CT scan observed a hyperdense mass in the right superolateral extraconal and intraconal region. The mass obliterated the right lacrimal gland and displaced the superior rectus muscle, the lateral rectus muscle, and the optic nerve to the medial side. The mass caused right-sided proptosis as shown in Figure 2A-C. Differential diagnoses included orbital cellulitis, lymphoma, and rhabdomyosarcoma. Anteroposterior and lateral views of chest X-rays were performed to investigate any lung lesions in this patient, as shown in Figure 2D-E. There were no active lung lesions shown in the chest X-ray.

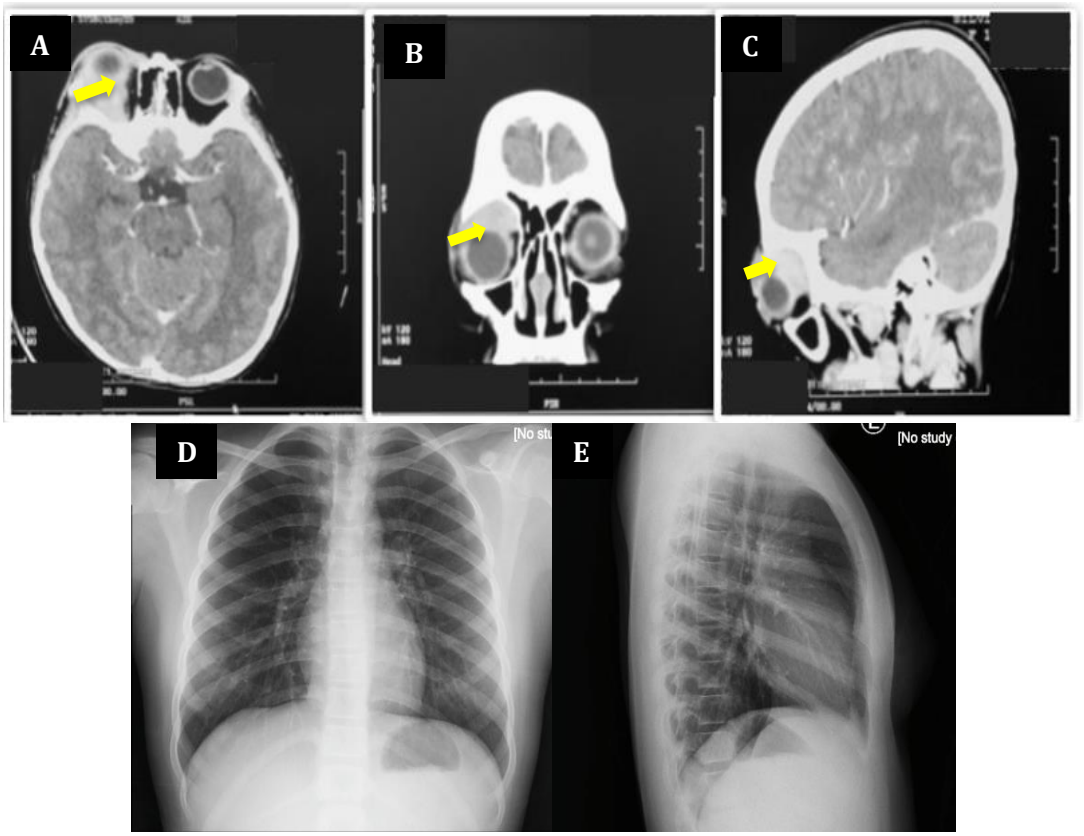

Figure 2. Contrast-enhanced Computed Tomography (CT) of the head and orbit one month prior to the presentation (upper panel) and preliminary chest X-ray (lower panel). Axial (A), coronal (B), and sagittal planes showed right-sided proptosis and enhancement lesions (yellow arrows) without bony involvement. Both anteroposterior (D) and lateral views of the chest X-ray reveal no lesions suggesting any active lung infection.

The patient underwent a lateral orbitotomy with biopsy, bone marrow puncture, and lumbar puncture for staging under general anesthesia. The surgical approach involved a lateral orbitotomy through the upper eyelid crease. The mass, located superiorly and extending to the orbital equator, was accessible by widening the incision, as shown in Figure 3A. The initial periorbital skin dissection was performed along the superior orbital margin until the orbital septum was reached. The preaponeurotic fat pad and levator aponeurosis served as anatomical landmarks during the procedure.

The mass sample was brownish white with a dense, springy texture and sized 2 x 1.6 x 1 cm3. The specimens were then sent to the anatomic pathology laboratory for microscopic examination. A 4-0 polyglactin suture for the internal layer and a 6-0 nylon for the skin were used to close the surgical wound. The patient was discharged for three days postoperatively and instructed to return for a follow-up visit in seven days.

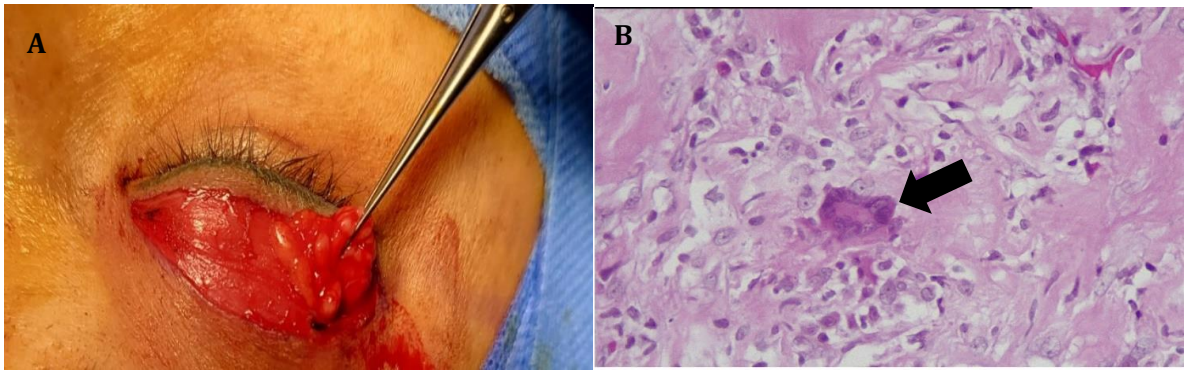

Figure 3. The lateral orbitotomy with incision in the upper eyelid crease (A) and histopathological analysis of the orbital tissue (B) identifies the presence of Langerhans cells (black arrow) consistent with granulomatous inflammation and suggestive of tuberculosis

The follow-up histopathological examination of the orbital tissue revealed orbital caseating granuloma with suspicion of mycobacterial infection. As shown in Figure 3B, the tissue showed mild caseous necrosis within the connective tissue stroma and soft and hard tubercles composed of epithelioid cells. Multinucleated giant Langerhans cells were also observed in the analysis. Despite the negative tuberculin test, the histopathological findings were highly suggestive of chronic granulomatous inflammation due to TB infection. The patient received six months of antituberculosis treatment from the primary healthcare service. The patient was administered a fixed-dose combination of rifampicin, isoniazid, pyrazinamide, and ethambutol, to which she adhered well. There were no adverse effects of the TB treatment. Ten months post-surgery and after complete antituberculosis treatment, a follow-up orbital CT scan indicated no presence of a new mass in the extraconal or intraconal region, as presented in Figure 4. The patient reported significant improvement in her right eye protrusion and ocular discomfort in the ten-month follow-up post-surgery and antituberculosis treatment, as shown in Figure 5.

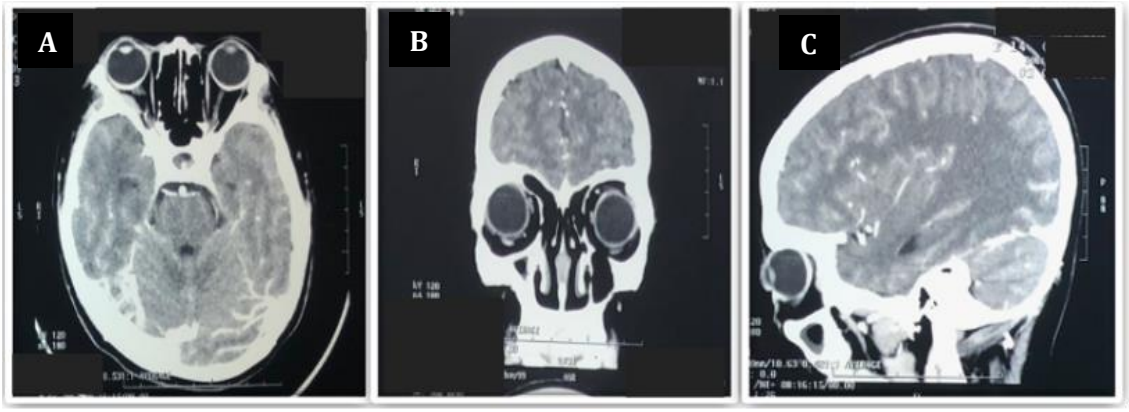

Figure 4. Head orbital CT scan with contrast ten months post-surgery and complete antituberculosis treatment. (A) Axial, (B) coronal, and (C) sagittal plane shows no evidence of retroorbital mass of the right eye.

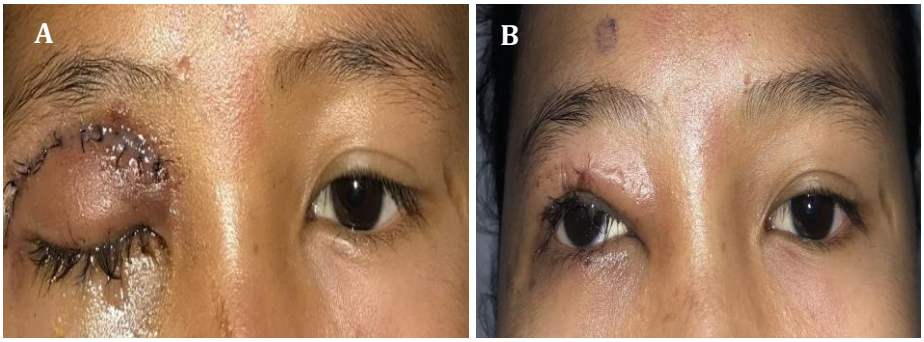

Figure 5. Post-operative evaluation at (A) one day and (B) ten months after antituberculosis therapy and surgery demonstrates improved proptosis of the right eye

DISCUSSION

This case report on orbital TB presents a rare and clinically challenging manifestation of TB, highlighting the difficulties in diagnosing this condition due to its atypical presentation, especially in healthy individuals. Orbital TB is one of the uncommon manifestations of extrapulmonary TB infection. *Mycobacterium tuberculosis* infiltrates the orbital space via the hematogenous route or through direct extension from the adjacent paranasal sinuses.[1] There are five recognized forms of orbital TB: lacrimal gland TB, classic periostitis, orbital soft tissue tuberculoma or cold abscess, secondary infection to paranasal sinus expansion, and tuberculosis dacryoadenitis.[5,6] Classic periostitis typically presents as a persistent or recurrent sinusitis characterized by nasal discharge. In cases of chronic sinusitis, the overlying skin may appear darkened, puffy, or blistered.[5] Imaging studies often reveal mild soft tissue inflammation and abnormalities in the underlying orbital bones, including irregularity, sclerosis, or destruction.[7–9]

Proptosis is the principal symptom in individuals with orbital tuberculoma or cold abscess. These conditions are often accompanied by edema, palpable soft tissue induration (mass-like), and sometimes a cold abscess.[7] Decreased vision and diplopia are also common symptoms. Orbital tuberculoma can spread to nearby tissues, including the sinuses, temporal fossa, and extradural space. Delayed diagnosis may result in the onset of orbital apex syndrome.[9–11]

Lacrimal gland TB is an uncommon type of orbital TB. Typical clinical manifestations include non-axial proptosis accompanied due to a lacrimal gland mass, ptosis, and eye movement disorders. Involvement of the lacrimal gland frequently coincides with periostitis of the lateral orbital wall.1,9 Orbital TB can also result from an expansion of infected paranasal sinuses, with the maxillary sinus being the most affected site. Complimentary clinical signs may include proptosis, sinus-related fluid-filled fistulas, masses, and epistaxis.[12,13] Patients with tuberculous dacryoadenitis often present with persistent lacrimal gland inflammation that does not respond to antibiotics or anti-inflammatory medications. These cases require systemic evaluation to identify the primary site of infection.[2,9,12]

The patient in this report exhibited right-sided proptosis and diplopia. The anterior segment examination and chest X-ray were unremarkable. A contrast-enhanced head-orbital CT scan identified a hyperdense mass in the right superolateral extraconal and intraconal region.[2] The identified mass was found obliterating the lacrimal gland and displacing the superior and lateral rectus muscles and optic nerve medially. These appearances suggested lacrimal gland involvement of orbital tuberculosis. A head-orbital CT scan is an effective instrument to pinpoint the infection's site of the orbital tuberculosis.[14]

A comprehensive and systematic patient history is essential to identify clinical symptoms in TB cases. Classic TB symptoms include persistent cough and fever lasting over two weeks, despite adequate treatment. Additional systemic symptoms may include weight loss, lack of improvement in the past two months, or failure to gain weight despite nutritional efforts.[15] The lack of systemic symptoms consistent with TB was a challenge in this case report. This condition leads to the importance of exploring organ-specific symptoms, such as swelling, watery eyes, or blurred vision.[16,17]

Bacteriological examination is a crucial diagnostic test for TB. Specimens for examination can be obtained through sputum induction, gastric lavage, or sputum collection.[8] The specimens are further examined microscopically with Ziehl-Neelsen staining to identify acid-fast bacilli (AFB). Moreover, rapid tuberculosis polymerase chain reaction (RT-PCR) and Lowenstein-Jensen media for culture can be used for further testing in this patient.[17,18]

Histopathological analysis of tissue specimens, chest X-rays, and tuberculin testing are valuable supportive tests for tuberculosis. In children, especially those with uncertain exposure history, the tuberculin test can be a useful diagnostic tool.[12,19] A negative result of the tuberculin test does not exclude the possibility of tuberculosis. The additional test with interferon-gamma release assay (IGRA) can identify TB infection, but it cannot differentiate between latent and active infections.[16,18]

Histopathological examination of tissue suspected of containing *Mycobacterium tuberculosis* is a definitive diagnostic test for TB.[18] This examination can be performed

independently or in conjunction with other supportive tests. A characteristic feature that is highly suggestive of TB is the presence of granulomatous inflammation with caseous necrosis and Langerhans cells, often containing *Mycobacterium tuberculosis* bacteria. There are other potential etiologies of necrotizing granuloma that can be considered, such as non-tuberculous mycobacterial infection and granulomatous polyangitis. That differential diagnosis can mimic the clinical and radiological findings of orbital TB.[4,7]

Chest X-rays serve as a valuable diagnostic tool for TB, although the findings can be non-specific, except in cases of miliary TB. Common radiographic features associated with TB include hilar gland enlargement, segmental consolidation, pleural effusion, miliary, atelectasis, cavities, calcifications and infiltrates, and tuberculomas.[14,17] The patient exhibited no systemic signs or symptoms suggestive of tuberculosis, which could have resulted in a delayed diagnosis and treatment of similar atypical cases.[15] Chest X-ray was within normal limitation and the tuberculin test showed no induration. This case report is highly suggestive of the diagnosis of orbital TB through histopathological analysis of the biopsy specimen, revealing soft and hard tubercles composed of epithelioid cells, multinucleated giant Langerhans cells, and mild caseous necrosis within the connective tissue stroma. These findings are consistent with the characteristic histopathological features of TB.[15,18,20]

The treatment of TB in children necessitates antituberculosis therapy. During the intensive phase (two months), children with positive acid-fast bacilli, severe TB, or adult-type TB receive a combination of pyrazinamide, ethambutol, rifampicin, and isoniazid.[6] In the continuation phase (four months), the regimen is reduced to rifampicin and isoniazid. Fixed-dose combinations are used to enhance patient adherence, and parental involvement is essential for effective treatment. A combination of antituberculosis treatment and surgical removal of the orbital mass is the recommended treatment of orbital TB.[21,22] In this case, the patient received the recommended drug regimen of the intensive phase for two months, followed by the continuation phase for four months. Ten months after surgical mass removal and treatment of TB, the CT scan shows no evidence of new mass growth. The patient also feels that there is an improvement in the clinical symptoms. Complete removal of the mass and appropriate administration of antituberculosis drugs are essential factors in the patient's successful treatment.[1,4,20] The limitation of this current case report is the definitive confirmation of TB, which can be performed by the AFB staining and other molecular tests are not performed since they are not available in our institution.

CONCLUSION

The challenges in diagnosing orbital tuberculosis stem from its atypical presentation, particularly in patients without systemic involvement. It often mimics other inflammatory diseases, which can delay treatment. Comprehensive local and systemic examinations and appropriate diagnostic testing are essential for establishing a diagnosis and providing appropriate treatment.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare. The patient provided written informed assent, and her parents gave written informed consent for the publication of this case report and its associated images.

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AUTHORS CONTRIBUTION

RAA conceived the main conceptual idea and had the role of the operator in the report. FME

and GS wrote the manuscript in consultation with RAA. NPD, SFB, and MRD contributed to the analysis of the results and the final version of the manuscript.

LIST OF ABBREVIATIONS

TB: tuberculosis; CDC: Centers for Disease Control and Prevention; CT: Computed Tomography; MRD: margin-to-reflex distance; IPF: interpalpebral fissure; AFB: acid-fast bacilli; RT-PCR: rapid tuberculosis polymerase chain reaction; IGRA: interferron-gamma release assay

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