BMC Ophthalmology

CASE REPORT

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Eyelid abscess as an initial manifestation of whipple's disease: a case report and comprehensive literature review

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Abstract

Background Whipple's disease, caused by Tropheryma whipplei, is a rare chronic infection predominantly affecting the gastrointestinal tract. Ocular involvement is uncommon, and periorbital manifestations are exceedingly rare. This case report highlights a unique presentation of Whipple's disease as an eyelid abscess in a patient with type 1 diabetes mellitus.

Case presentation A 38-year-old male with poorly controlled type 1 diabetes mellitus presented with a two-weeks history of progressive swelling in the left upper eyelid. The swelling initially appeared three months prior and was associated with mild pain. Clinical examination revealed a large, erythematous, bluish, and non-tender swelling in the left upper eyelid, causing mechanical ptosis. Additional lesions were noted on the scalp and abdomen. Imaging showed a well-circumscribed fluid-filled lesion in the left upper eyelid. A tissue sample was taken for culture and biopsy during surgical drainage. The histopathology showed foamy macrophages with Diastase-resistant intracytoplasmic organisms that were further demonstrated by Gram stain confirming the diagnosis of Whipple's disease.

Conclusion This case illustrates a rare presentation of Whipple's disease manifesting as an eyelid abscess in a diabetic patient. The diagnosis was confirmed through histopathological examination, emphasizing the importance of considering Whipple's disease in the differential diagnosis of atypical ocular presentations.

Keywords Whipple's disease, Tropheryma whipplei, Eyelid abscess, Ocular, Diabetes mellitus

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Background

Whipple's disease (WD) is rare, with an incidence of fewer than 1 million cases per year [1]. It predominantly affects Caucasian males over 40 years age, with a male-to-female ratio of approximately 8:1 [2]. WD is caused by Tropheryma whipplei, a gram-positive bacillus related to Actinomycetes. Although an infectious cause was suspected as early as WD has been initially reported, successful antibiotic treatment was not documented until 1952 [3]. It typically affects the gastrointestinal (GI) system, but it can also involve the neurologic, hematopoietic, rheumatologic, cardiac, pulmonary, and ocular systems. Ocular involvement by WD may lead to inflammation, vitreous haemorrhage, or optic disc edema [4, 5]. In this report, we present a case of WD with an unusual presentation in the form of an eyelid abscess. The aim of this study is to enhance the understanding of WD by exploring the variety of ocular manifestations and the associated diagnostic challenges with summary of previously reported cases in the English-written literature.

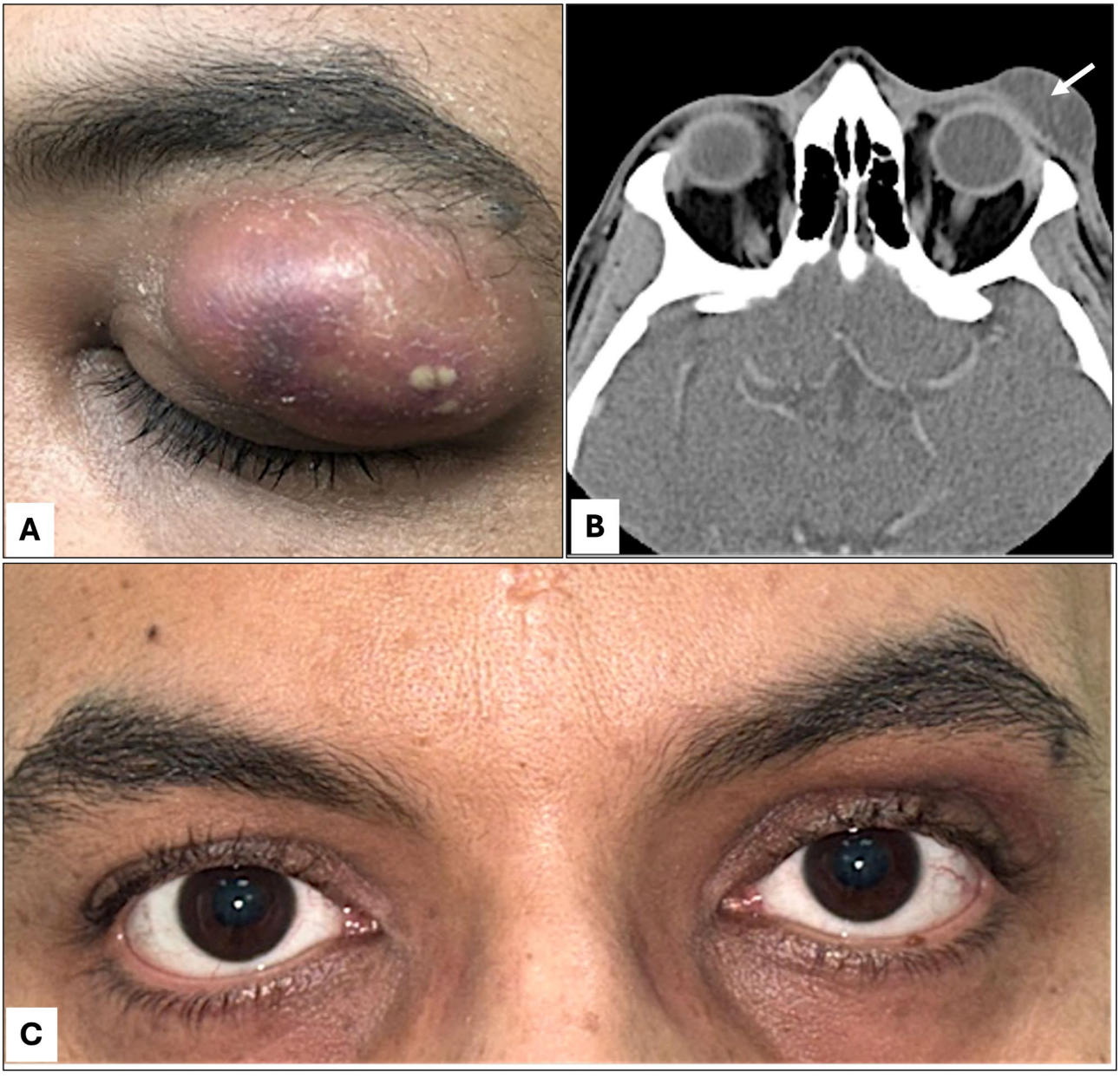

Fig. 1 **A**: Preoperative appearance of swelling of the large left upper eyelid. **B**: Computed tomography scan outlining the eyelid as a well-circumscribed, fluid-filled lesion (white arrow) without bone or lacrimal gland involvement. **C**: Postoperative appearance following excision with satisfactory cosmesis

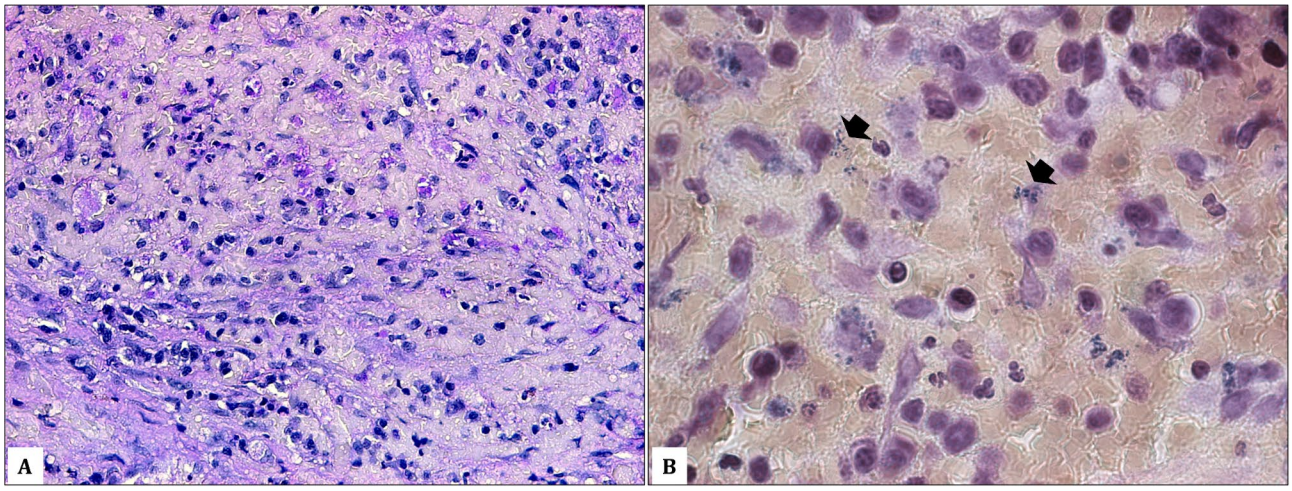

Fig. 2 **A**: Chronic inflammatory cells with Diastase-resistant intracytoplasmic organisms within foamy macrophages in the substantia propria of the excised eyelid nodule (Original magnification x 400 Periodic acid Schiff {PAS} with Diastase). **B**: Gram positive organisms (Black arrowheads) of Whipple's disease (Original magnification x 1000 {oil}Gram stain)

Case presentation

A 38-year-old male with poorly controlled type 1 diabetes mellitus on insulin therapy presented with a two-weeks history of progressive swelling in the upper left eyelid. Three months prior to his recent presentation, the swelling appeared as a small bulge accompanied by mild pain and feeling of pressure. He denied any vision changes, eye discharge, trauma, or previous ocular surgeries. He had positive history of multiple similar lesions on the scalp area and abdomen noticed within one month before the appearance of the eyelid lesion. There was no history of fever, weight loss, nocturnal sweats, or loss of appetite. There were no other affected family members with similar lesions. There was no history of recent travel or animal contact.

Upon examination, the patient had a large, erythematous, bluish firm swelling (measuring 23 × 16 mm) noted on the central part and extending to the temporal end of the left upper eyelid, causing mechanical ptosis. The lesion was warm, non-tender, non-translucent, and showed a pointing head indicating abscess formation. There were no signs of poliosis, madarosis, or ulceration (Fig. 1A). Other lesions were found on the scalp and abdomen with similar appearance and consistency as the eyelid lesion. The remaining eye examination was unremarkable. A brain and orbital computed tomography (CT) scan revealed a well-circumscribed, fluid-filled lesion in the left upper eyelid, with no bone or lacrimal gland involvement (Fig. 1B). Systemic workup, including tuberculin skin test, chest X-ray, rheumatoid factor, antineutrophil cytoplasmic antibodies, and angiotensin converting enzyme, were all negative. Human immune deficiency virus (HIV) and hepatitis tests were nonreactive. Glycosylated hemoglobin (HbA1c) level was 11%.

Treatment began on the first day of presentation, one day before the abscess draining operation. The clinical presentation indicated a preliminary diagnosis of preseptal cellulitis. The patient was prescribed oral Augmentin (875 mg amoxicillin/125 mg clavulanic acid), to be taken as one tablet every 12 h for a period of 10 days. Abscess drainage was performed for the patient the following day, and during surgical drainage, minimal purulent discharge with sanguineous dark material was observed. An incisional biopsy was taken from the lesion's base for culture and histopathological diagnosis. Following irrigation with povidone and gentamycin solution, the incision was allowed to heal by secondary intention. Two weeks later, the ptosis resolved, with a satisfactory cosmetic appearance for the patient (Fig. 1C). The culture results identified *staphylococcus epidermidis*, which was thought to represent contamination of normal skin flora. Histopathological examination showed significant infiltration of the dermal tissue by chronic inflammatory cells including foamy macrophages with Diastase-resistant intracytoplasmic organisms, which have proven to be positive with Gram stain confirming Tropheryma Whipplei infection consistent with WD (Fig. 2A and B).

After that, the decision to consult infectious disease and internal medicine specialists was made to initiate specific systemic antibiotic therapy and conduct a comprehensive evaluation, given the patient's multiple identical lesions on different parts of his body. While the patient had already finished his initial oral antibiotics course, the confirmed diagnosis of Whipple's disease was reached requiring a more targeted systemic approach. The patient was subsequently transferred to a general hospital for continued management; however, further

follow-up data was unavailable because the patient was lost to follow-up after that.

Discussion and conclusions

Whipple's disease typically affects the gastrointestinal

Table 1 Summary of all reported cases of Whipple's disease with ophthalmic manifestations

Case report	Gender	Age	Ocular/Orbital Manifestations	Systemic Manifestations (at Diagnosis)	Relapse	Treatment	Ocular Histopathology
Lieger et al. (2007) [9]	Male	61	Proptosis, periorbital edema, pain, limitation of ocular movements, Low visual acuity, chemosis, conjunctival hyperemia, RAPD	Arthralgia, constitutional symptoms	Positive	Oral Trimethoprim-sulfamethoxazole 160/800 mg BID (Co-Trimoxazole), I.V Ceftriaxone 2 g/day, I.V metronidazole 3 × 500/day, oral prednisolone, orbit surgical decompression performed)	Yes- Pas positive intracytoplasmic particles,
Huerva et al. (2008) [8]	Female	63	Proptosis, pain, limitation of ocular movements, conjunctival hyperemia, retinal hemorrhages	Chronic, Diarrhea, Arthralgias, constitutional symptoms.	Positive	I.V ceftriaxone, trimethoprim 160 mg-sulfamethoxazole 800 mg BID + Oral prednisolone	Yes - negative
Parkash et al. (2017) [14]	Female	38	Diplopia, Myositis	Arthralgias, rash, constitutional symptoms, abdominal pain, diarrhea, severe pneumonia and altered consciousness	Positive	I.V Ceftriaxone 2 g/day, Oral Co-Trimoxazole 960 mg BID, Oral Doxycycline 200 mg/day, hydroxychloroquine 300 mg/day, Oral prednisolone	Yes- Immunohistochemistry: positive staining of the macrophages with an antibody to T. whipplei
Testi et al. (2018) [13]	Patient 1: Male	35	Chronic bilateral keratoconjunctivitis	Abdominal pain, diarrhea, and progressive weight loss	Positive	Doxycycline 200 mg/day, hydroxychloroquine 200 mg TID/day, Oral	None
	Patient 2: Female	32	bilateral vitritis	Abdominal pain and swelling	None	cotrimoxazole 160/800 mg BID, ceftriaxone 2 g/day.	None
	Patient 3: Male	63	chronic bilateral panuveitis	Gait unbalance, mild dysarthria, and arthralgias	None	cotrimoxazole 160/800 mg BID, Doxycycline 200 mg/day, hydroxychloroquine 200 mg TID/day	Yes- diagnostic vitrectomy: positive PCR for T.whipplei DNA
Kanikunnel et al. (2020) [12]	Male	49	Unilateral optic nerve edema	None	Positive	Systemic antibiotic	None
Alsarhani et al. (2020) [11]	Patient 1: Male	60	Scleral nodule	none	none	Topical antibiotics, Prednisolone acetate drops	Yes- Intracytoplasmic organisms within foamy macrophages
	Patient 2: Male	53	Scleral nodules	None	None	Topical antibiotics, Prednisolone acetate drops	Yes- Intracytoplasmic organisms within foamy macrophages
Bosello et al. (2021) [10]	Male	53	Bilateral blurred vision, cystoid macular edema, optic disc edema, Roth spots.	None	None	Oral Prednisolone, Adalimumab, I.V ceftriaxone 2 g/day, doxycycline 100 mg BID. Pars plana Vitrectomy (PPV) + cataract surgery OU	None
Sampaio et al. (2022) [7]	Female	59	Proptosis, periorbital edema, limitation of ocular movements, conjunctival injection	Diarrhea, constitutional symptoms, adenopathy, pulmonary inflammation.	Positive	Doxycycline 100 mg bid, cotrimoxazole 160/800 mg BID, I.V ceftriaxone 2 g/day Oral prednisolone	None
Asiri et al. (current case)	Male	38	Swelling of the left upper eyelid	None	None	Evacuation	Yes- Intracytoplasmic organisms within foamy macrophages

(GI) system, but it can also affect other body systems [4, 5]. The histopathological evaluation of tissue biopsy samples with the support of immunohistochemistry and polymerase chain reaction (PCR) remains as the standard diagnostic tests for Tropheryma whipplei [6]. The hallmark of the histological diagnosis in Whipple's disease is the presence of foamy macrophages containing large amounts of Periodic acid Schiff (PAS)-positive, non-acid fast particles in the lamina propria of the GI mucosa [6].

Unlike GI symptoms, ocular manifestations of WD are uncommon and create considerable diagnostic challenges because of their unique characteristics. Few cases of this disease have been documented in the literature, especially as the first manifestation before the appearance of systemic signs and symptoms. Ocular manifestations varied significantly across the patients. Common complaints included proptosis, periorbital edema, and limitations in ocular movements, which were often accompanied by conjunctival injection or hyperemia, as observed in several cases [7–9]. Blurred vision, optic disc edema, and Roth spots were described by Bosello et al., while AlSarhani et al. (2020) reported two cases in which scleral nodules were initially mistaken for benign conjunctival cysts [10, 11]. Other ocular manifestations included chronic bilateral keratoconjunctivitis, panuveitis, diplopia, and myositis [12, 13]. Comparing these cases to our own case, several distinctions and similarities are evident. While our patient presented with a well-defined, abscess-like swelling of the eyelid, both our case and the reported ones in the literature (summarized in Table 1) experienced delays in diagnosis owing to the initial focus on ocular symptoms rather than a single manifestation of a systemic disease. In relation to the onset of the ocular symptoms in relation to the systemic involvement, our case featured early systemic symptoms in the form of multiple skin lesions, which provided additional diagnostic clues.

Different Treatment protocols were used among cases reported in the literature (Table 1). The treatment regimens vary depending on the specific ocular and systemic manifestations. Antibiotics, particularly doxycycline, ceftriaxone, and cotrimoxazole, are commonly used. Prednisolone is frequently administered to manage inflammation, in addition to advanced interventions such as pars plana vitrectomy and cataract surgery that might also be performed in complicated cases. For patients diagnosed with seronegative arthritis, immunosuppressants such as adalimumab and methotrexate were reported to be utilized before the diagnosis via PCR. Topical treatments, including ofloxacin and prednisolone acetate, were used for localized conditions, such as scleral nodules [7–14]. In our patient, evacuation was the treatment of choice for his localized of upper eyelid infectious swelling.

The literature identifies significant associations between Whipple's disease and various comorbidities and clinical manifestations, including arthritis, diarrhea, central nervous system (CNS) involvement, endocarditis, diabetes, malignancy, prior chemotherapy, weight loss, abdominal pain, lymphadenopathy, dementia, and iron deficiency [15]. Notably, among a cohort of patients diagnosed with Whipple's disease, 29% were found to have diabetes. These associations may assist clinicians in recognizing individuals at higher risk for Whipple's disease, thereby guiding the decision to pursue further diagnostic evaluation [15]. Our patient reported a 10-year history of poorly controlled diabetes, despite being on insulin therapy, which he acknowledged he had not consistently adhered to. We emphasized the importance of medication compliance and regular follow-up with his endocrinologist.

The cases presented here (Table 1), including our own, illustrate the diverse ways and complexity of WD manifestation, especially with ocular symptoms being the initial presentation. Understanding these variations is crucial for timely diagnosis and treatment. Clinicians should maintain a high index of suspicion for systemic diseases such as Whipple's when encountering persistent or atypical ocular lesions, especially in the absence of clear GI symptoms to ensure timely and effective treatment.

Abbreviations

WD	Whipple's disease
GI	Gastrointestinal
CT	Computed tomography
PCR	Polymerase chain reaction
HIV	Human immune deficiency virus

Acknowledgements

None.

Author contributions

AYA: Literature review and first draft of the manuscript; KAA and YAA: acquisition of data and shared in the drafting of the manuscript; HA: concept and design of the study and final approval of the submitted version; HMA: Histopathological diagnosis and critical review of the manuscript for submission as a corresponding author. All authors have read and approved the manuscript.

Funding

None.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

Competing interests
The authors declare no competing interests.

Received: 20 October 2024 / Accepted: 5 February 2025
Published online: 06 March 2025

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