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Case report

Isolated conjunctival granuloma as a first manifestation of Parinaud's oculoglandular syndrome: A case report

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ABSTRACT

Purpose: Parinaud's oculo-glandular syndrome (POGS) is the most frequent manifestation of ocular bartonellosis, and usually presents with local lymphadenopathies and systemic symptoms. We present a case of isolated conjunctival granuloma as the sole manifestation of ocular bartonellosis.

Observations: A 67-year-old female presented to the authors' eye clinic with complaints of a 2-week history of unilateral red eye and chemosis. Slit lamp examination revealed an isolated bulbar conjunctival granuloma. The remainder of the eye examination was unremarkable. Topical treatment with gatifloxacin and prednisolone acetate was started. Etiological work-up was performed. General laboratory tests revealed only a mild leukocytosis, and interferon gamma-release assay and chest computed tomography were normal. Serological testing for *Bartonella henselae* was positive at titers of 1:1024. Three weeks after initial symptoms, lymphadenopathies, malaise, and fever appeared. Systemic azithromycin was added, which resulted in complete regression of the disease.

Conclusion and importance: Conjunctival granulomas present a wide range of differential diagnoses to the practitioner. Ocular bartonellosis is a relevant cause of conjunctival granuloma. POGS should be suspected in cases of conjunctival granulomata non-responsive to local therapy. It is important to consider that other agents to treat POGS have been described and are available, and that appropriate serological tests should be performed.

1. Introduction

Conjunctival granulomata has a wide range of differential diagnoses, including local causes and systemic diseases. One relevant cause is ocular bartonellosis and its primary manifestation, Parinaud's oculo glandular syndrome (POGS), a self-limited unilateral conjunctivitis associated with preauricular suppurative adenopathies secondary to cat scratch disease (CSD), a zoonosis produced by *Bartonella henselae* (BH).[1] We report a case of POGS presenting as an isolated unilateral conjunctival granuloma. (see Figs. 1 and 2)

2. Case report

A 67-year-old, otherwise healthy woman presented to the authors' practice with a 2-week history of non-traumatic unilateral red eye and chemosis with no pain or any other symptoms. On slit lamp examination, a conjunctival granuloma, approximately 7 mm × 4 mm in size, was observed. It was attached to the sclera and exhibited central epithelial necrosis. Fundoscopy was normal. Ultrasound biomicroscopy (UBM) examination using a 50 MHz transducer revealed a high reflectivity echo source embedded deep in the conjunctiva, episclera and superficial sclera, surrounded by a low reflective mass (granuloma). Pseudocysts appeared as multiple linear echoes with low to medium reflectivity organized in such a manner that enclosed anechoic areas. Topical treatment with gatifloxacin and prednisolone acetate was initiated. Etiological work-up was performed. General laboratory tests revealed only a mild leukocytosis, interferon gamma-release assay (QuantiFERON- TB ®, Cellestis, Carnegie, Australia), chest computed tomography (CT), and treponemal and non-treponemal tests were normal. A BH serological test was positive at titers of 1:1024.

Three weeks after the first symptoms appeared, the patient developed fever, malaise and preauricular and submandibular ipsilateral adenopathies. Oral azithromycin (500 mg daily) was added to the topical treatment, which resulted in complete regression of systemic and ocular disease.

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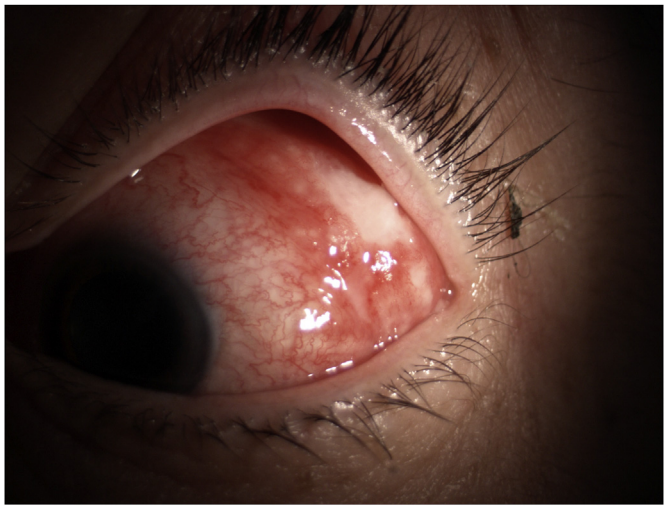

Fig. 1. Slit-lamp image demonstrating an elevated granulomatous lesion of the bulbar conjunctiva.

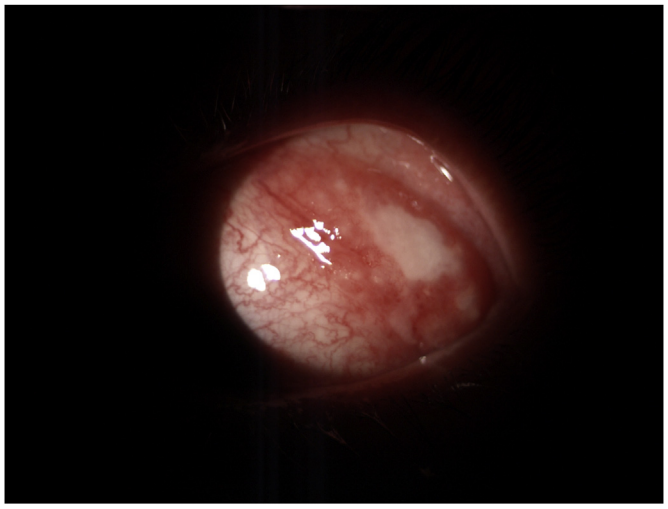

Fig. 2. Slit-lamp image of conjunctival granuloma with central epithelial necrosis.

3. Discussion

Conjunctival granulomata (or granulomatous conjunctivitis) often poses a challenge to ophthalmologists because of the wide variety of possible etiologies. Main causes include inflammatory, infectious and neoplastic diseases, allergies, foreign bodies, and topical medication (brimonidine-timolol fixed combination).

When encountering a conjunctival granuloma, a useful approach is to determine whether necrosis is present. If necrosis is present, the most frequent causes are tuberculosis (especially in the upper lid tarsal conjunctiva), POGS, and granulomatosis with poliangiitis (Wegener's vasculitis). Non-necrotizing granulomas have a wider differential diagnosis, which include local causes, such as foreign bodies (caterpillar hair, suture remnants, glove talcum), and a diverse group of systemic diseases including sarcoidosis, Crohn disease and lymphoma, among others.

Another useful discriminating factor is the presence or absence of systemic involvement. The presence of fever, lung nodules, adenopathies and tumors, for example, suggest systemic disease, whereas the lack of systemic symptoms may be more suggestive of local diseases involving a foreign body. In this scenario, anterior segment imaging, such as UBM, may be useful in non-obvious cases. When diagnostic tests do not reveal the cause of granuloma, a biopsy is useful to determine its nature.[2] In the present case, there were no factors, neither in the patient's history nor in the physical examination, that could explain local causes of conjunctival granuloma, and UBM only revealed signs of inflammation. Therefore, although no signs or symptoms of systemic disease were present, diagnostic tests, such as thoracic CT and blood tests for infectious agents, were needed. At first, the isolated conjunctival granuloma, together with the high titers of anti-BH immunoglobulin (Ig)G antibodies was a peculiar manifestation of ocular bartonellosis. However, the later appearance of adenopathies and systemic involvement provided important clues that contributed to the correct diagnosis.

BH is a Gram-negative intracellular fastidious bacillus, responsible for CSD. It is widely distributed among cats, with prevalence ranging from 18.1% to 41.7% in local studies.[3,4] BH can also multiply in the digestive system of cat fleas, and survive for several days in cat feces.[5] The contagion is produced by inoculation of infected cat flea feces from the cat's scratch.

CSD produces local lymphatic disease, usually with suppurative adenopathies; however, extra lymphatic manifestations can also occur. Among the ocular manifestations of CSD, POGS is the most common (approximately 5% of patients).[6] Other ophthalmological manifestations of CSD include neuroretinitis (up to 1–2% of CSD patients) and, less frequently, choroiditis, retinal branch artery occlusion, retinal vein occlusion, serous retinal detachment, and macular hole.[7]

POGS usually presents as a unilateral conjunctivitis with or without conjunctival granulomata (which may be bulbar or tarsal), ulceration or necrosis, and ipsilateral preauricular or submandibular adenopathies, which may be suppurative. Additionally, mild fever and malaise may be evident. The present case is interesting because the lymphatic disease (i.e., adenopathies) and the systemic symptoms developed three weeks after the local disease.

Although BH is the agent mainly responsible for POGS, other infrequent infectious agents have been reported, including *Yersinia enterocolitica*, Herpes simplex virus I, Epstein Barr virus and members of the *Rickettsia* genus, among others.[8–12]

The gold standard test for the diagnosis of BH infection is the serological indirect immunofluorescence assay (IFA) to detect anti-BH IgG antibody. The high rate of seroprevalence in the normal population makes the specificity of the IgG IFA valuable. A titer > 1:64 strongly suggests *Bartonella* infection, with a sensitivity and specificity of approximately 70% and 95%, respectively.[13,14] Cross reactivity with other *Bartonella* genus members and other bacteria have been reported in BH serology.[15] IgM assays alone have high specificity, but lack diagnostic value due to their low sensitivity.[16] Molecular studies using specific polymerase chain reaction primers may be useful, especially to avoid cross reactivity; however, they lack sensitivity compared with IgG serology.[14]

The main difficulty for diagnosis of POGS is the lack of suspicion due to its low incidence. POGS should always be suspected in cases of isolated conjunctival granuloma, or in granulomatous conjunctivitis, especially if adenopathies are present and there is a history of cat petting or contact.

Although usually self-limited, antibiotic therapy is usually administered to reduce symptom duration. Oral azithromycin for 5 days is the first-line antibiotic choice (500 mg orally daily the first day, and 250 mg orally daily on days 2–5).[17] For more severe cases (i.e., neuroretinitis), combined treatment with doxiciline and rifampicin is preferred.

4. Conclusion

POGS should be suspected in patients presenting with unilateral conjunctivitis that persists despite topical medication(s), especially if accompanied by regional adenopathies. The main difficulty for diagnosis is the lack of suspicion. When encountering a conjunctival

granuloma, ocular bartonellosis should be always considered because, although it is a usually self-limited disease, systemic therapy may be needed, and in the other eye, more severe manifestations may develop. Finally, it is important to consider that other agents for POGS have been described and are available and, moreover, that appropriate serological tests should be performed.

Patient consent

Consent to publish this case report was not obtained. However, this report does not contain any personal information that could lead to the identification of the patient.

Authorship

All authors attest that they meet the current ICJME criteria for Authorship.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2019.02.007.

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