

Refractory Bilateral Blepharitis and Recurrent Chalazia in A Child with STAT1 Gain-of-Function-Associated Chronic Mucocutaneous Candidiasis

A. Hajjaji^{1*}, S. Sadiki², A. Bouzidi¹, A. El Ouaf¹

¹Department of Ophthalmology, Moulay Ismail Military Hospital, Meknes, Morocco

²Department of Ophthalmology, Military hospital Mohammed V, Rabat, Morocco

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*Corresponding author: A. Hajjaji

Department of Ophthalmology, Moulay Ismail Military Hospital, Meknes, Morocco

Abstract

Case Report

Background: Severe, bilateral, recurrent, and treatment-resistant blepharitis with multiple chalazia in childhood may occasionally be a clue to an underlying inborn error of immunity. STAT1 gain-of-function (GOF) variants are a recognized cause of chronic mucocutaneous candidiasis and can be associated with a broader infectious and inflammatory phenotype. **Case presentation:** We describe the ophthalmic phenotype of a 10-year-old boy with genetically confirmed STAT1 GOF-associated chronic mucocutaneous candidiasis. His systemic history included recurrent oral candidiasis, chronic nail candidiasis, recurrent herpetic gingivostomatitis, previous mycobacterial lymphadenitis, cutaneous infections, folliculitis, and multiple recurrent chalazia. Ophthalmic examination demonstrated severe bilateral anterior and posterior blepharitis, with irregularity of the lid margins, telangiectatic vessels, inflammatory changes and recurrent chalazia. There was no corneal ulceration, corneal abscess, or other documented corneal involvement. Conventional ophthalmic treatment included topical corticosteroid drops and ointment, eyelid hygiene, warm compresses with eyelid massage, and artificial tears, without satisfactory control of the recurrent inflammatory eyelid disease. **Conclusion:** Severe refractory bilateral blepharitis with recurrent chalazia may represent an under-recognized ophthalmic manifestation in children with STAT1 GOF-associated chronic mucocutaneous candidiasis. An atypical, recurrent, or treatment-resistant eyelid phenotype, particularly when accompanied by recurrent mucocutaneous infections, should prompt consideration of an underlying inborn error of immunity.

Keywords: Blepharitis; recurrent chalazion; STAT1 gain-of-function; chronic mucocutaneous candidiasis; inborn error of immunity; pediatric ophthalmology; meibomian gland dysfunction.

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1. INTRODUCTION

Blepharitis and chalazia are common pediatric eyelid disorders. Chronic inflammation of the anterior and posterior eyelid margins, meibomian gland dysfunction, and obstruction of meibomian glands may lead to recurrent chalazia. However, severe bilateral disease with repeated recurrence and poor response to conventional treatment should raise the possibility of an underlying systemic predisposition.

Chronic mucocutaneous candidiasis (CMC) is characterized by persistent or recurrent *Candida* infections involving mucous membranes, skin, and nails. Heterozygous gain-of-function variants in STAT1 are an established genetic cause of CMC and are associated with impaired IL-17-mediated mucocutaneous immunity. The clinical spectrum may extend beyond *Candida* infection to include viral, bacterial,

mycobacterial, inflammatory, and cutaneous manifestations.

Ocular manifestations have been described in association with STAT1 GOF. In particular, a published case reported chronic demodicosis presenting with facial papulopustular eruption, blepharitis, and chalazion in a patient with a STAT1 GOF mutation. This observation supports the possibility that severe eyelid disease may form part of the broader phenotype.

2. CASE PRESENTATION

A 10-year-old boy, born to non-consanguineous parents, had a history of recurrent mucocutaneous infections beginning in infancy. From approximately 8 months of age, he developed recurrent episodes of oral thrush and chronic nail candidiasis. At 7 months of age, he presented with left axillary lymphadenopathy, with histopathological findings reported as compatible with

tuberculosis; complete resolution was obtained after six months of antituberculous therapy. He subsequently experienced several hospitalizations for infectious complications.

His clinical phenotype also included recurrent herpetic gingivostomatitis, multiple intertriginous lesions, scalp lesions, facial folliculitis, and recurrent eyelid disease characterized by multiple chalazia and severe bilateral blepharitis.

3. Ophthalmic Findings

The ophthalmic presentation was characterized by severe bilateral anterior and posterior blepharitis with recurrent chalazia. Clinical examination demonstrated marked inflammatory changes of the eyelid margins, including irregularity of the lid margin, telangiectatic vessels, erythema, crusting and features consistent with

chronic meibomian gland dysfunction. The disease involved both the anterior and posterior eyelid surfaces.

Multiple chalazia occurred repeatedly despite conservative and topical treatment. The ophthalmic treatment regimen included topical corticosteroid eye drops and ointment, regular eyelid hygiene, warm compresses associated with eyelid massage, and artificial tears. Despite these measures, there was no satisfactory sustained improvement, with persistent or recurrent eyelid inflammation.

No corneal involvement was documented. In particular, there was no corneal ulcer, corneal abscess, or other evidence of infectious keratitis.

4. Clinical Photographic Documentation



Figure 1: Severe bilateral eyelid inflammation in a child with STAT1 gain-of-function-associated chronic mucocutaneous candidiasis. Marked bilateral eyelid erythema and edema with inflammatory changes of the eyelid margins and periocular skin

5. Immunological and Genetic Assessment

Complete blood count showed hemoglobin 12 g/dL and a total leukocyte count of 8,500/mm³, including 2,810 lymphocytes/mm³ and 4,200 neutrophils/mm³. Quantitative immunoglobulins were reported as IgA 7.2 g/L, IgG 18.1 g/L and IgM 3.9 g/L. Lymphocyte subset analysis showed CD3+ 2,002/mm³, CD4+ 923/mm³, CD8+ 768/mm³, CD19+ 753/mm³ and CD16+ 206/mm³. Total IgE was elevated at 649.12 IU/mL. The dihydrorhodamine test was normal.

Mycological samples obtained from the intertriginous lesions, scalp and nails identified *Candida albicans*. Genetic analysis confirmed a heterozygous gain-of-function mutation in STAT1, establishing the diagnosis of STAT1 GOF-associated chronic mucocutaneous candidiasis. The exact nucleotide and

amino-acid change should be inserted from the original genetic report before submission.

6. Treatment and Follow-up

Systemic fluconazole was initially administered without sufficient efficacy. Antifungal susceptibility testing demonstrated resistance of the isolated *Candida albicans* strain to fluconazole, and treatment was subsequently changed to voriconazole with favorable clinical evolution. The patient also received intravenous immunoglobulin every four weeks and trimethoprim-sulfamethoxazole prophylaxis.

During follow-up, episodes of oral candidiasis became less frequent and responded to voriconazole. The previously reported ocular infectious manifestations

subsequently improved, and no corneal complication was documented.

7. DISCUSSION

The present case highlights a severe and refractory ocular phenotype occurring in the context of genetically confirmed STAT1 GOF-associated chronic mucocutaneous candidiasis. The combination of bilateral anterior and posterior blepharitis, lid-margin irregularity, telangiectasia, meibomian gland dysfunction and recurrent chalazia is compatible with a severe chronic inflammatory eyelid disorder.

Although recurrent chalazia are common in children, their repeated occurrence in association with severe bilateral blepharitis and poor response to standard local treatment should prompt consideration of predisposing systemic conditions. In the present patient, the ocular findings occurred within a broader phenotype characterized by chronic mucocutaneous candidiasis and recurrent infections.

The precise mechanism linking STAT1 GOF to severe eyelid disease remains uncertain. STAT1 GOF mutations cause dysregulated cytokine signaling and impaired IL-17-mediated mucocutaneous immunity. This may alter host-microorganism interactions at mucosal and cutaneous surfaces. In addition, previously reported STAT1 GOF-associated demodicosis has been associated with facial papulopustular disease, blepharitis and chalazion, suggesting that altered cutaneous microbial homeostasis may contribute to the ophthalmic phenotype.

The absence of corneal ulceration, abscess or keratitis in this patient is clinically relevant. The disease was predominantly confined to the eyelid and ocular surface structures, despite the striking severity of the external inflammatory phenotype.

From an ophthalmological perspective, recurrent bilateral chalazia should therefore be

interpreted in the context of the entire clinical history. When eyelid disease is unusually severe, recurrent, bilateral or refractory to conventional management and is accompanied by recurrent fungal, viral, bacterial or mycobacterial infections, an immunological evaluation should be considered.

8. CONCLUSION

Severe bilateral blepharitis with recurrent chalazia may be an important ophthalmic manifestation in children with STAT1 gain-of-function-associated chronic mucocutaneous candidiasis. An unusually severe or treatment-resistant eyelid phenotype, particularly when associated with recurrent mucocutaneous infections, should prompt clinicians to consider an underlying inborn error of immunity and multidisciplinary evaluation.

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