SKIN

BRIEF ARTICLE

An Initial Presentation of Facial Impetigo in IgG4-related Disease: A Case Report

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ABSTRACT

Background: Immunoglobulin G4-related disease (IgG4-RD) is a rare multi-organ, immune-mediated, fibro-inflammatory condition presenting with tumefactive lesions. Although this condition has characteristic clinical and histopathological features, the phenotypic variability of IgG4-RD provides a diagnostic challenge. Here, we describe a case of facial impetigo presenting as a manifestation of IgG4-RD.
Case Presentation: An 18-year-old female presented to the emergency department with acute facial impetigo in the setting of chronic dacryoadenitis, sialadenitis, parotitis, and lymphadenopathy which had been clinically diagnosed as IgG4-RD. The impetiginized facial rash resolved with oral doxycycline, and the steroid-recalcitrant IgG4-RD symptoms responded to rituximab infusions.
Conclusions: Due to the rarity of IgG4-RD, secondary manifestations and associations of the disease are continuously emerging. Immune-mediated conditions with cutaneous involvement, such as in IgG4-RD, may prime the skin for the inoculation of bacteria and lead to skin infection(s) such as impetigo. Rituximab may be used for steroid-resistant cases of IgG4-RDs without concurrent corticosteroid therapy.

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is an uncommon immune-mediated disorder which presents with IgG4 plasma cell infiltration and fibrosis in nearly any organ.[1] Common features of IgG4-RD include sialadenitis, dacryoadenitis, retroperitoneal fibrosis, and autoimmune pancreatitis.[2] Histologically, IgG4-RD can present with 1) lymphoplasmacytic infiltrate; 2) evidence of fibrosis; and 3) obliterative phlebitis.[1,2] Although the disease has common clinical and histological features, the phenotypic variability of IgG4-RD provides a diagnostic challenge.[3] Furthermore, secondary manifestations of the disease remain poorly understood.[3] We describe a case of an 18-year-old female who developed impetigo in the setting of IgG4-RD.

CASE PRESENTATION

An 18-year-old female with a history of clinically diagnosed IgG4-RD presented to the emergency room with a one-week history of a bilateral non-pruritic facial rash that originated from the epicanthal folds and spread inferiorly. At the time of presentation,

she was not taking any medications. Her vital signs were within normal limits. Examination revealed bilateral honey-yellow to white-brown crusts on an erythematous base localized to the periorbital area and nasolabial folds (**Figure 1**). Chronic left-sided orbital swelling and lymphadenopathy were also noted and unchanged from previous examinations. A review of systems was positive for a posterior headache, nausea, and unsteady gait. She did not have any known sick contacts and was not sexually active.

Initial imaging in the emergency department included Computerized Tomography scan of the head (CT head) and Magnetic Resonance Imaging of the brain (MRI brain). There were no acute changes noted in any of the imaging. CT head showed ongoing left lacrimal gland enlargement (**Figure 2A**), a left-sided parotid mass (**Figure 2B**), and several prominent lymph nodes bilaterally, unchanged from previous imaging. The patient had previously been worked up by ophthalmology and rheumatology for a one-year history of left-sided orbital swelling (**Figure 3**), left-sided parotid gland mass, and bilateral lymphadenopathy and was diagnosed with IgG4-RD based on clinical presentation. Prior pathology reports for biopsies of her left lacrimal gland and cervical lymph node showed atypical reactive lymphoid infiltrate and scant IgG4 cells (7/hpf) on the immunohistochemical stain. An IgG panel was also conducted during her emergency visit for her facial rash, but all values were within normal limits.

Due to her facial rash's acuity and clinical presentation, the diagnosis was declared as impetigo secondary to her underlying IgG4-RD. She was started on empiric oral doxycycline 100 mg twice daily with plans for a dermatology follow-up in a week for reassessment and consideration for a skin biopsy. The patient tolerated antibiotic treatment well, and the facial rash cleared by the one-week follow-up appointment. No further intervention was necessary for the facial rash.

The patient was discharged from with plans for ophthalmology and rheumatology follow-up. Her left-sided orbital swelling and lymphadenopathy persisted despite treatment with corticosteroids, and a few months later, her right orbit became swollen as well (**Figure 4**). Rheumatology continued to work up her IgG4-RD with an additional left-sided parotid mass biopsy which showed a reactive lymph node without a significant increase in IgG4 plasma cells, like previous biopsies. Due to an insufficient response to systemic steroids for her chronic symptoms, she was started on non-steroidal treatment with Rituximab infusions (1,000 mg in NaCl 0.9% 900 mL IV) and finally noticed an improvement in her condition. Her symptoms have remained well-controlled with this regimen.

DISCUSSION

IgG4-RD is a rare fibro-inflammatory disorder commonly seen in glandular tissue, such as in this individual with sialadenitis, dacryoadenitis, parotitis, and lymphadenopathy. Other commonly affected organs include the meninges, thyroid glands, lungs, major blood vessels, and pancreas.[4] Although the disease mostly affects middle-aged adults, it can rarely be seen in young adults and children.[3] The diagnosis of IgG4-RD was historically based on 1) clinical features; 2) serum IgG4 >135 mg/dL; and 3) histopathological features.[4] Other antibodies such as antinuclear antibodies (ANAs) may also provide some information but are not usually included in the diagnostic criteria for IgG-related diseases.[4] However, the 2019

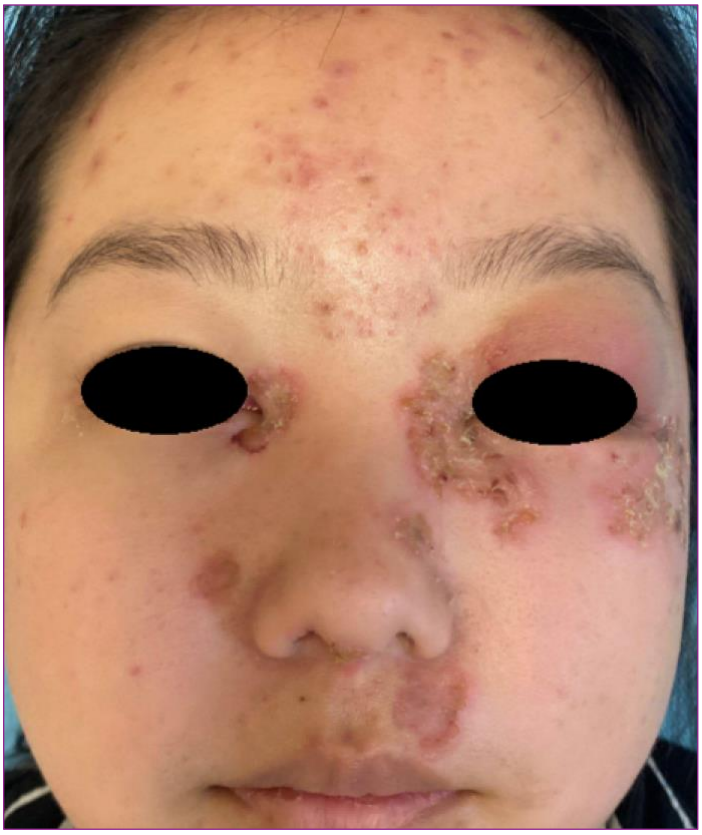

Figure 1. Bilateral honey-yellow to white-brown crusts on an erythematous base localized to the periorbital area and nasolabial folds. Chronic left orbital swelling is also present.

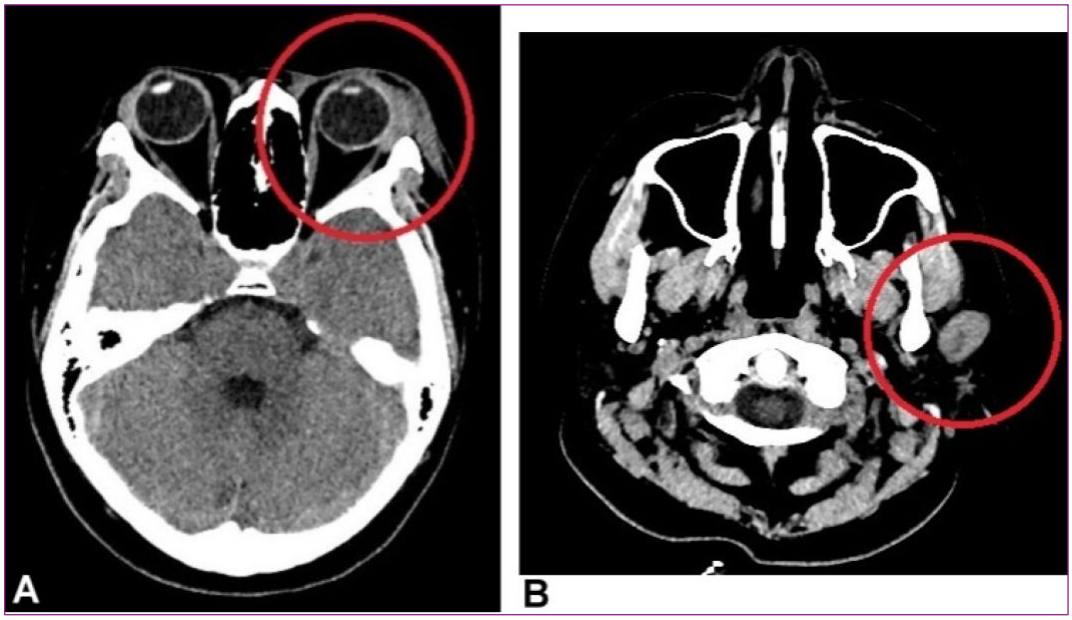

Figure 2. (A) Computerized Tomography of the head showing left lacrimal gland enlargement. **(B)** Computerized Tomography of the head showing left parotid gland enlargement.

Figure 3. Progression of orbital swelling from left-sided to bilateral (left to right).

IgG4-RD classification criteria by the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) don't require a definitive biopsy or an elevated serum IgG4 level. Rather, the diagnosis of IgG4-RD has shifted to a holistic assessment of the clinical picture.[4] One study found that serum IgG4 levels have poor specificity and predictive values for IgG4-RD.[5] In our patient with normal serum IgG4 levels and atypical but non definitive histopathology, her clinical presentation alone led to the diagnosis of IgG4-RD.

Due to the rarity of IgG4-RD, secondary manifestations remain a topic requiring further exploration. There are few case reports documenting dermatoses in the setting of IgG4-RD. Malkani et al reported a 30-year-old woman who presented with migratory panniculitis in the setting of IgG4-related cholangitis and pancreatitis.[6] Kakuchi et al reported a 60-year-old man who presented with nodular skin lesions on the scalp and neck that demonstrated histopathological findings consistent with IgG4-RD.[7] Chiang et al discussed the case of a 34-year-old woman who presented with bilateral conjunctival masses consistent with ligneous conjunctivitis and met criteria for IgG4-RD.[8]

CONCLUSION

We report a case of facial impetigo presenting as a manifestation of IgG4-RD. The etiopathology of impetigo makes it likely that abnormalities in the skin due to IgG4-RD could prime the skin for the inoculation of streptococcal bacteria.[9] We postulate that the breached skin barrier in the orbital area of this patient's face likely contributed to the subsequent skin infection. Our patient was treated with oral antibiotics for the impetigoand found relief of her IgG4-RD symptoms on continuous rituximab infusions. Although systemic steroids remain a first-line treatment for IgG-related diseases, rituximab infusions are a useful option for steroid-resistant cases such as ours.[10] Rituximab is also the only drug that can be utilized without concurrent steroid therapy.[10] Other steroid-sparing options such as disease-modifying anti-rheumatic drugs (DMARDs) like azathioprine, tacrolimus, cyclophosphamide, and methotrexate can also be considered but are utilized alongside steroid therapy.[11] In summation, we present this case to emphasize that patients with underlying autoimmune conditions such as IgG4-RD are potentially at risk for superimposed superficial skin infections. Rituximab may be considered for steroid-resistant cases of IgG4-RDs without concurrent corticosteroid therapy.

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