

An Unusual Case of Steroid Resistant IgG4-RD Affecting the Maxillary Alveolar Process

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Abstract

Immunoglobulin G4-related disease is an autoimmune fibro-inflammatory condition which is characterised histologically by marked lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis. Immunostaining reveals IgG4+ plasma cells. Immunoglobulin G4-related disease affecting the head and neck region is becoming increasingly recognised and generally shows a good initial response to steroids. Common manifestations within the head and neck include the orbit and the salivary glands. This article presents a rare case of immunoglobulin G4-related disease originating in the alveolar process of the maxilla with orbital and maxillary sinus involvement which was unresponsive to management with steroids.

Case Report

A 37 year old Somalian woman was referred to the Oral and Maxillo-Facial Surgery department with a 4 month history of progressive swelling of her right cheek. She had multiple presenting complaints including paresthesia and neuropathic pain affecting the V2 and V3 regions of the right trigeminal nerve. She had difficulty opening her mouth. She was not experiencing any visual issues at this initial presentation. However, she was experiencing subjective hearing impairment of the right ear. These symptoms had a gradual onset on a background of her being systemically well. She was taking only intermittent vitamin D supplements.

Examination

Examination showed a defined swelling over the right maxilla which was tender to palpation. Mouth opening was reduced. Examination of cranial nerves I, II, III, IV, VI, VIII, IX, X, XI and XII was unremarkable. However, testing of cranial nerve V revealed that she had reduced perception to light touch over the site of swelling. Normal sensory perception was maintained elsewhere in the V1 and V3 regions and the contralateral face. Hearing was reduced on the right side on whisper test.

Investigations

An ultrasound scan revealed an irregular, hypoechoic lesion in the soft tissues of the right cheek. The lesion was deep to the subcutaneous tissue and lacked any significant internal vascularity. A computed tomography scan and magnetic resonance imaging of the head and neck defined;

A 5cm mass centred on the right maxillary alveolus and hard palate extending into the right buccal space, right masticator

space and right inferior orbital fissure. Destruction of the right maxillary alveolus and hard palate, with involvement of the right infra-orbital and greater palatine nerves.

A tissue biopsy of the site was taken to confirm diagnosis. This showed a storiform pattern of stromal fibrosis with an intense inflammatory infiltrate including lymphoid follicles with reactive germinal centres. Obliterative vasculitis was seen. Of note, there was an increased number of IgG4+ plasma cells on immunostaining suggesting a IgG4 fibrosclerotic lesion. (Figure 2a,b,c,d)

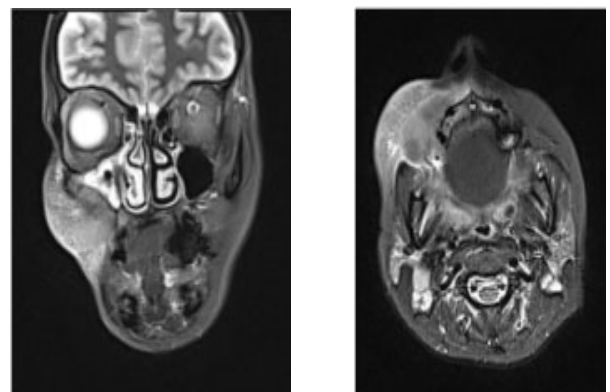


Figure 1a: Coronal view

Figure 1b: Axial view of the MRI head showing an aggressive focal lesion causing destruction of the right maxillary alveolus/hard palate and the maxillary sinus with extension to the right buccal space, right masticator space and the right inferior orbital fissure with involvement of the right infraorbital and greater palatine nerves.

Serum IgG4 levels were within normal range and IgG1 levels were elevated. Diagnosis of immunoglobulin G4-related disease was thus confirmed on the basis of clinical and histopathological findings outlined above.

Treatment

The patient was urgently referred to the Rheumatology team who started her on a course of prednisolone however there was no response to management with steroids. The swelling progressed with subsequent right sided proptosis and ptosis. She was therefore started on cyclophosphamide and rituximab. This subsequently showed an improvement clinically and symptomatically.

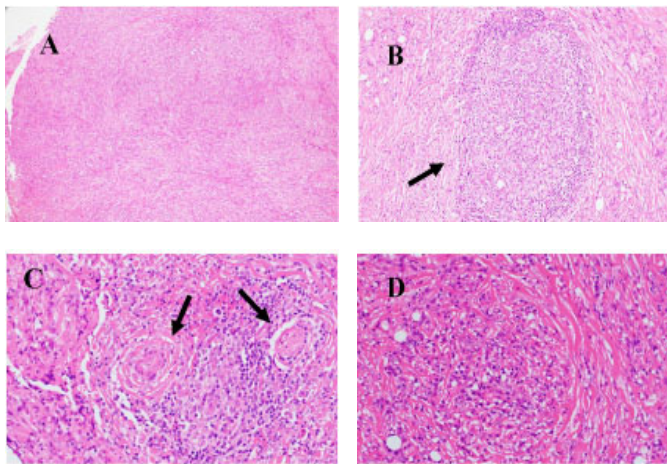


Figure 2: A tissue biopsy was sent for histopathological analysis and shows a subtle storiform pattern of fibrosis (A). B cells are assembled into a reactive germinal centre (B). There is infiltration of lymphocytes and plasma cells into the lumen of veins causing obliterative phlebitis (C). A high power slide showing a dense, mixed lymphoblastic inflammation (D).

Discussion

Clinically, immunoglobulin G4-related disease presents as a tumefactive, tissue destructive lesion [1] and often mimics malignant tumours which can complicate diagnosis [2]. It can affect multiple different organs throughout the body but is becoming increasingly recognised within the head and neck. Common sites of involvement within the head and neck include the orbits and the salivary glands [3]. Immunoglobulin G4-related disease manifesting in the maxilla is rare. There are only three reports of the disease affecting the alveolar process of the maxilla within the literature to date [4-6]. As presented in this case report, patients with immunoglobulin G4-related maxillary disease may experience swelling, facial pain [4,6] and trismus[6]. In our case proptosis and pseudoptosis occurred as the disease progressed and the orbit became involved. There was no diplopia and visual acuity was grossly intact. Pupillary reflexes were normal. Other possible symptoms that have been reported in patients with maxillary immunoglobulin G4-related disease include increasing mobility and loss of teeth [4] and dysphagia [6].

In any patient presenting with an expanding / invading mass urgent diagnosis is required to enable appropriate and time-

ly treatment (surgical excision, chemo-radiotherapy or other non-surgical treatments, as in this case). Diagnosis of immunoglobulin G4-related disease is usually based upon a combination of clinical, histopathological and serological findings. It is characterised by the presence of an intense lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis on histopathological examination. Immunostaining reveals IgG4+ plasma cells. Serum levels of IgG4 may also be raised in patients with IgG4-RD. However, elevated serum levels of IgG4 are not diagnostic of the disease [7]. Evidence suggests that many as 30% of patients with biopsy confirmed immunoglobulin G4-related disease can have normal serum levels [8]. Currently, the first line treatment modality for immunoglobulin G4-related disease is systemic glucocorticoids[2,9]. A systematic review of the therapeutic approaches to immunoglobulin G4-related disease showed glucocorticoids to have a 96% efficacy as a first line treatment [10]. This article presents a rare case of immunoglobulin G4-related disease which is non-responsive to treatment with steroids and outlines an alternative management using cyclophosphamide and rituximab. Patients treated with cyclophosphamide and concurrent steroid therapy have been shown to have a higher rate of complete remission and a lower rate of relapse in comparison to those treated with glucocorticoid monotherapy [11]. Rituximab is a third line treatment agent for immunoglobulin G4-related disease in patients who fail to respond to treatment with steroids and is used to successfully prevent further disease progression [2]. In this case report, management with a combination of these medications resulted in an improvement both clinically and symptomatically.

Conflicts of Interest

Sarah Shannon, Tun Wildan and Michael Perry declare that they have no conflict of interest

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