CASE REPORT

Immunoglobulin G4-related disease of the paranasal sinuses

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SUMMARY

Immunoglobulin G4-related disease (IgG4-RD) is becoming increasingly documented. It was first described in relation to autoimmune pancreatitis. Features of the disease include tissue infiltration by IgG4 plasma cells with associated fibrosis and the growth of pseudotumours. A 71-year-old woman presented with increasing right cheek swelling and mild proptosis. Ten years earlier, she had a similar presentation and was diagnosed with an inflammatory pseudotumour. Examination revealed a lesion in the right nasal cavity. CT and MRI confirmed a mass within the right maxillary antrum extending into the nasal cavity. Endoscopic biopsies showed florid plasma cell infiltrate with marked increase in IgG+ plasma cells. Immunostaining expressed IgG4 (70%). She was started on a course of prednisolone and her symptoms resolved. IgG4-RD is becoming an emerging disease entity. Its involvement in the paranasal sinuses can mimic nasal tumours. Major surgical resection should be avoided as patients can often be treated medically.

BACKGROUND

Immunoglobulin G4-related disease (IgG4-RD) was first reported in relation to autoimmune pancreatitis in 2001.¹ Histologically, it is characterised by tissue infiltration by IgG4+ plasma cells and associated fibrosis. It is known to involve the head and neck. We report a rare case involving the paranasal sinuses and the diagnostic and management considerations regarding the disease.

CASE PRESENTATION

A 71-year-old woman with increasing right cheek swelling and mild proptosis was referred to our tertiary unit. She had no nasal obstruction, double vision or visual disturbance. Her medical history included hypertension and hypothyroidism. Ten years earlier, under the care of the maxillofacial team in a different region, she underwent a right medial maxillectomy via a Weber Ferguson approach for a similar presentation. At that time, a histological diagnosis of an inflammatory pseudotumour was made. Regular follow-up for the next 4 years showed no signs of recurrence.

Examination revealed a lesion in the right superior nasal cavity with no associated lymphadenopathy.

INVESTIGATIONS

MRI and CT confirmed a mass within the right maxillary antrum extending into the nasal cavity

(figure 1) but not crossing the midline. The tumour extended to the inferomedial wall of the orbital margin (figure 2) and the frontonasal duct region with obstruction of the right frontal sinus. Biopsies were obtained endoscopically. Histopathology showed a florid plasma cell infiltrate with a marked increase in IgG+ plasma cells. Immunostaining showed the expression of IgG4 (70%) and IgG2 (50%).

As a result, IgG serum subtype levels were performed. The serum IgG4 level was 1.6 g/L (normal range 0.030–2.010 g/L). Other IgG serum subtype levels were in the normal range.

TREATMENT

She was referred to the rheumatology team and started on a course of prednisolone.

OUTCOME AND FOLLOW-UP

Following the commencement of prednisolone, her facial swelling and proptosis resolved within 6 months. She, however, developed side effects to the steroids, including muscle weakness, diabetes and fatigue. Consequently, she was started on mycophenolate and weaned off prednisolone. At her 14-month review, she was noted to have some new nasal obstruction symptoms and was referred back to the local ear, nose and throat (ENT) team. Flexible nasoendoscopy and MRI revealed a new lesion arising from the right middle turbinate and situated anteriorly in the nasal cavity.

Her new presentation was discussed at the local multidisciplinary department team (MDT) meeting and she was recommenced on a lower dose of regular prednisolone in addition to mycophenolate.

After 20 months, examination revealed a reduction in size of the lesion. Nonetheless, it was felt by the MDT that she would gain the most clinical benefit from an endoscopic surgical debulking procedure so she could be maintained on a low dose of steroids which were providing the best symptomatic response. This was performed and was uneventful.

She continues to be followed up regularly by the rheumatology team and at 28 months after the initial diagnosis is asymptomatic. She remains on mycophenolate and low-dose prednisolone with no further significant side effects.

DISCUSSION

IgG4-RD is a fibroinflammatory condition that can cause tumour-like growths in multiple different

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Figure 1 MRI scan showing tumour involving the right maxillary sinus and nasal cavity

organs. Its key features include a distinctive histopathological appearance and an increase in IgG4+ plasma cells in the tissues. The histopathological characteristics include lymphoplasmacytic infiltration ([figure 3](#)), fibrosis in a storiform distribution ([figure 4](#)) and obliterative phlebitis.

A raised serum IgG4 may suggest IgG4-RD but it can be normal in up to 40% of patients. In addition, a ratio of >40%

Figure 2 CT scan showing tumour extending into the right inferomedial orbit

Figure 3 Sinonasal mucosa with underlying pronounced plasma cell infiltrate

of IgG4 to IgG+ cells is highly suggestive of IgG4-RD.² Using this criteria, our patient is in this category as they had >70% ([figure 5](#)). Both of these findings are not specific to IgG4-RD and for that reason the histopathological appearances form the basis of the diagnosis. Nonetheless, the diagnosis cannot be confirmed without IgG4 immunostaining and therefore the combination of the histopathological appearances and an increased IgG4 to IgG+ ratio or elevated IgG4+ plasma cells in the biopsy are required to make the diagnosis.²

IgG4-RD most commonly affects the pancreas. The second most frequently affected region is the head and neck of which the orbit is the most common subsite.³ There have been few documented cases involving the paranasal sinuses. A similar presentation of proptosis and facial fullness was found by Kurien *et al* in a patient with IgG4-RD of the maxillary sinus. Their patient also did not complain of nasal obstruction.⁴ Additionally, Vandjelovic *et al* demonstrated that cases relating to the paranasal sinuses are often expansive and locally destructive. Most commonly the disease affects the maxillary sinus, followed by the ethmoid sinus and then nasal septum. Of the 11 cases found in their literature review, eight were in the maxillary sinus. Furthermore, the main presenting complaint was epistaxis, with facial swelling only found in two cases.⁵

Figure 4 Fibrosis in a storiform distribution

Figure 5 (A) IgG immunostain (B) IgG4 immunostain with >70% IgG4 to IgG+ cells

Presenting symptoms include epistaxis, nasal obstruction, chronic rhinosinusitis and eye involvement. Malignancy, chronic granulomatous disease and other autoimmune processes are important differential diagnoses that can be ruled out after biopsy.

An international consensus statement for the treatment and management of IgG4-RD supports glucocorticoids as first-line treatment.⁶ Additional immunosuppressive agents also play a part in patients who do not respond fully to steroids alone or where steroids are not tolerated.⁶ Mullholland *et al* reported 90% of patients with head and neck IgG4-RD who had medical treatment alone had a remission, with 67.7% having a full remission with just steroids.³

The primary aim of surgery should be for gaining histological samples for a diagnosis. Rarely should wide surgical resection be performed because of its attendant morbidity and potential

complications. Surgical debulking may be required as in this case and in patients with highly fibrotic disease, as these cases may respond poorly to medical treatment.⁶

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Learning points

- ▶ Immunoglobulin G4-related disease (IgG4-RD) is a fibroinflammatory condition that has been reported in almost all organs and is becoming an emerging disease entity.
- ▶ Its involvement in the paranasal sinuses can mimic nasal tumours.
- ▶ It is important to be aware of the disease so the appropriate histological analysis and staining is performed to make the diagnosis.
- ▶ Patients with IgG4-RD should be treated medically and avoid unnecessary major surgical resection.

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