CASE REPORT

Unusual cause of maxillary sinus mass with proptosis

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SUMMARY

We report a case of a 21-year-old Indian man with an 8-month history of left-sided headache, maxillary sinus mass, proptosis and swelling of the left temple, whose contrast-enhanced CT scans of the paranasal sinuses showed an enhancing, destructive soft tissue mass involving the left maxillary sinus, orbit, infratemporal fossa and anterior cranial fossa, suggestive of a malignancy or chronic granulomatous disease. Histopathological examination of the sinus mass, which was debulked and partially excised via an endoscopic approach, suggested a diagnosis of immunoglobulin G4-related sclerosing disease of the maxillary sinus. Subsequent immunohistochemical staining and biochemical tests confirmed the diagnosis. We highlight the importance of considering this increasingly recognised but rare entity that can mimic a malignant lesion with its clinical and radiological features but which, unlike the latter, has a very good prognosis with appropriate treatment.

BACKGROUND

Mass lesions involving the maxillary sinus with associated proptosis and headache in Indian patients suggest the presence of a neoplasm or chronic granulomatous disease. This theory is further reinforced when radiological evaluation of such a patient reveals a bone-destructive enhancing mass within the sinus. This case illustrates the need to also consider immunoglobulin G4-related sclerosing disease (IgG4RSD), a relatively rare but increasingly recognised entity, as a differential diagnosis. A literature review shows that IgG4RSD is a rare autoimmune condition characterised by infiltration of the involved organs with IgG4-positive plasma cells and T lymphocytes. The presentation is variable depending on the organ system involved. IgG4RSD often preferentially involves exocrine organs and was first described in association with autoimmune pancreatitis in 2003.¹ Involvement of the paranasal sinuses is particularly rare. Diagnosis is based on the presence of characteristic histopathological features of lymphoplasmocytic infiltrates of IgG4-positive plasma cells along with fibrosis, positive quantitative immunohistochemistry and raised serum IgG4 levels. The precise aetio-pathogenesis of IgG4RSD is not clear.

CASE PRESENTATION

A 21-year-old man presented to the outpatient services, with slowly progressive proptosis of the left eye, of 8 month's duration. This was associated with left-sided facial pain and headache. He had no

visual disturbances, restriction of eye movements, nasal obstruction or epistaxis. There was no relevant medical or family history. He was a labourer by profession.

General examination showed diffuse fullness of the left cheek and temple. There was no tenderness over the mass. The oral cavity, region of hard

Figure 1 (A and B) Contrast-enhanced coronal and axial CT sections of the paranasal sinus showing an ill-defined enhancing mass (black arrow) within the left nasal cavity, and maxillary sinus eroding the floor of orbit and extending to the left infratemporal fossa.

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Figure 2 (A–C) Photomicrography of immunoglobulin G4 (IgG4)-related sclerosing disease. (A) H&E staining $\times 200$ showing dense lymphoplasmacytic infiltration (thin red arrow), sclerosing fibrosis (thick red arrow) and obliterative phlebitis (thin black arrow). Immunohistochemistry shows brown staining of (B) IgG4-positive cells (arrow) and (C) IgG-positive cells (arrow). The ratio of IgG4/IgG-positive plasma cells is $>70\%$ and the IgG4-positive plasma cell count was 60–70/high-power field.

palate and gingivobuccal sulcus were normal. Endoscopic examination of the nasal cavity was normal. Examination of the left eye showed axial proptosis with mild restriction of ocular movements on lateral gaze. The patient's visual acuity was normal bilaterally. Gross neurological examination was normal. Systemic examination was normal.

INVESTIGATIONS

Contrast-enhanced CT scan of the paranasal sinus (figure 1A, B) showed an enhancing soft tissue mass centred in the left maxillary antrum with extensive bony destruction of the anterolateral and posterior sinus walls causing extension of the mass to the ipsilateral cheek, pterygopalatine fossa and infratemporal fossa. There was associated erosion of the pterygoid plates. Superiorly, the mass extended through the floor of the orbit into the lateral extraconal compartment pushing the lateral rectus muscle medially with resultant proptosis. The lacrimal gland, inferior orbital fissure and superior orbital fissure were also involved. There was intracranial extradural extension of the mass along the anterior temporal pole, with no obvious parenchymal invasion.

A preliminary diagnosis of left-sided maxillary sinus malignancy/fungal sinusitis was made and the patient planned for endoscopic biopsy of the lesion under hypotensive anaesthesia.

Intraoperatively, although the middle meatus looked normal on the left side, the maxillary antrum was found to be filled with a firm, fibrous mass with moderate vascularity. The specimens were sent for histopathological examination as well as fungal and acid-fast bacilli (AFB) culture.

Histopathological findings (figure 2A) showed areas of storiform fibrosis, obliterative phlebitis and dense aggregates of plasma cells mixed with lymphocytes in the subepithelium. On immunohistochemistry (figure 2B,C), the IgG and IgG4 cells were stained differentially. The number of IgG4 plasma cells was 60–70/high-power field. The ratio of IgG4/IgG-positive plasma cells was more than 70%. The diagnosis of IgG4RSD was confirmed.

Microbiological smears for fungus and AFB were negative. The serum IgG4 level was raised at 1968 mg/L and this was consistent with the diagnosis of IgG4RSD. A work up for any systemic involvement of the disease including an ultrasound of the abdomen, chest X-ray and liver function tests, was normal.

DIFFERENTIAL DIAGNOSIS

In view of the findings of an enhancing, destructive mass involving the maxillary sinus with skull base and intracranial extension on CT scan, the differentials included chronic granulomatous lesions such as tuberculosis or chronic granulomatous fungal sinusitis or malignancy. The relatively long history and age of the patient were less in favour of a malignancy, despite the CT findings. Negative fungal and AFB smear and culture results, together with the characteristic histopathological and immunohistochemical findings, led us to the diagnosis of IgG4RSD.

IgG4 disease is characterised histologically by the presence of dense lymphoplasmacytic infiltration, obliterative phlebitis and fibrosis (figure 2). Positive immunohistochemistry findings along with a raised serum IgG4 further confirmed the above diagnosis as per the current diagnostic criteria² (box 1).

TREATMENT

Based on previous reports,^{3 4} the recommended treatment of IgG4RSD is high-dose oral steroid. A dose of 1 mg/kg body

Box 1 Diagnostic criteria for immunoglobulin G4-related sclerosing disease

1. Triad of dense lymphocytic infiltration, obliterative phlebitis and storiform fibrosis
2. IgG4 counts: 10–200/high-power field
3. IgG4/IgG ratio $>40\%$

weight prednisolone was started. As the patient weighed 52kg, he was given oral prednisolone at a dose of 50 mg for 2 weeks followed by tapering dose for 3 months, following which he was reviewed.

OUTCOME AND FOLLOW-UP

Following the 3 months of oral steroid therapy, the patient's facial pain and headache had resolved, and the proptosis, cheek and temple swelling had reduced considerably. Exophthalmometry showed a 5 mm reduction in proptosis. Serum IgG4 levels also reduced to 1218 mg/L from the pre-operative levels of 1968 mg/L. A repeat contrast-enhanced CT scan of the paranasal sinuses revealed a reduction in the mass lesion within the nasal cavity, middle meatus and the infratemporal fossa (figure 3A, B). Given the clinical and radiological

Figure 3 (A and B) Contrast-enhanced coronal and axial CT scan sections of the paranasal sinus on follow-up after 3 months showing a reduction in the mass in the nasal cavity, middle meatus and infratemporal regions.

improvement, the patient was continued on oral steroids and will be reviewed in 3 months' time.

DISCUSSION

IgG4RSD is a multiorgan systemic condition caused by extensive lymphoplasmacytic infiltration with rich IgG4 abundant plasma cells. The head and neck is the second most common site for involvement by IgG4RSD, after the pancreatobiliary system.⁵ However, involvement of the paranasal sinus is quite rare, with only six adult cases reported previously in the English literature. Of the paranasal sinuses, the order of involvement is maxillary sinus^{6–10} followed by sphenoid sinus.^{8–11} Nasal septal involvement⁷ has also been described.

Histopathological examination of the involved tissue is diagnostic. The current criteria proposed by Deshpande *et al* are listed in box 1. Our patient fulfilled all of these criteria.

The disease is believed to have an autoimmune origin, although the precise mechanism of the pathogenesis is unclear. There are reports that suggest a common mechanism involving several autoantibodies, including antilactoferrin and anticarbonic anhydrase III, present in the exocrine glands and in the nasal mucosa.¹² This triggers an immune-mediated reaction involving T-helper type 2 cells and regulatory T cells.¹³

Raised IgG4 levels, as seen in our patient, occur in up to 60–70% of patients with IgG4RSD.² This feature is not consistently seen and, hence, has not been included in the diagnostic criteria (box 1).

IgG4RSD shows a good response to oral steroid therapy, as seen in patients with autoimmune pancreatitis with IgG4RSD.³ There is a lack of data regarding the relapse rates in those with sinonasal involvement. However, the relapse rates in those with pancreatic involvement are in the range of 30–50%, although corticosteroid therapy significantly reduced the recurrence.^{14–15} A few patients who have a relapse or do not tolerate steroids can be treated with immunomodulators such as azathioprine and rituximab.¹⁶ Previous reports of patients with maxillary sinus involvement have shown a good prognosis with oral steroid therapy,^{6–9} except in one case where rituximab had to be given along with steroids for stabilising the disease.⁸

Learning points

- ▶ Immunoglobulin G4-related sclerosing disease (IgG4RSD) is an autoimmune condition characterised by abundant IgG4 plasma cells and lymphocytes in the involved tissues.
- ▶ IgG4RSD can masquerade as malignancy by virtue of its extensive bony erosion.
- ▶ The mainstay in the diagnosis is histological confirmation along with positive immunohistochemistry based on well-defined criteria.
- ▶ The disease shows good response to steroid therapy. Rarely, immunomodulators may require to be used as adjuvant therapy.

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