Locally destructive skull base lesion: IgG4-related sclerosing disease

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ABSTRACT

A unique case of IgG4$^+$ sclerosing disease was diagnosed in the sphenoid sinus, a previously unreported location, and was treated in a novel manner. This study describes the clinical presentation and management of IgG4 sclerosing disease in the paranasal sinuses. A retrospective case review and review of the medical literature were performed. A 38-year-old woman with a 2-year history of constant frontal headaches presented to our clinic. Imaging showed bony destruction of the sphenoid sinus and sellar floor. The patient underwent a right-sided sphenoidotomy with debridement and biopsy. Pathological evaluation showed a dense plasmacytic infiltrate with >150 IgG4$^+$ cells/high-power field. She was subsequently started on a nasal corticosteroid with improved patency of the sphenoid antrostomy. We report an unusual case of a middle-aged woman who presented with IgG4-sclerosing disease (IGSD) isolated to the sphenoid sinus. Although our knowledge concerning treatment in extrapancreatic organs is lacking, there is evidence that glucocorticoid treatment improves nasal sinus opacification on CT findings (Sato Y, Ohshima K, Ichimura K, et al., Ocular adnexal IgG4-related disease has uniform clinicopathology, Pathol Int 58:465–470, 2008). This case study and literature review adds to the growing literature describing IGSD in the head and neck and more specifically isolated to the sphenoid sinus with preliminary data concerning local control with topical steroids.

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IgG4-related sclerosing disease (IGSD) is a newly described entity in otolaryngology. It primarily presents as mass lesions with symptoms related to the site of involvement. IGSD was first described as autoimmune pancreatitis and later known as IgG4-related sclerosing pancreatitis.[1] It has been characterized histologically by extensive infiltration of IgG4$^+$ plasma cells and fibrosis. Although rare, IGSD in the head and neck is most commonly described in the submandibular glands (chronic sclerosing sialadenitis),[2] lacrimal glands (IgG4-related chronic sclerosing dacryoadenitis),[3] and bilateral parotid and lacrimal glands (Mikulicz's disease).[4–6] IGSD in the nasal septum and maxillary sinus was first described in 2009,[2,7] followed by ethmoid sinus involvement a year later.[8] To our knowledge, this is the first report describing IGSD within the sphenoid sinuses causing a significant amount of skull base bony destruction and the first attempt at treating IGSD with topical steroids as an adjuvant to surgery.

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CLINICAL SUMMARY

A 38-year-old otherwise healthy woman presented to our clinic with a history of seasonal allergies with a 2-year history of constant frontal headaches. She denied nasal obstruction or symptoms of chronic rhinosinusitis. Her preoperative CT scan showed aggressive bony destruction of the sphenoid sinus involving the ventral and anterior portion of the inferior wall, the posterior aspect of the planum sphenoidale, and anterior wall and floor of the sella (Fig. 1). An MRI was also obtained showing the mass lesion in the sphenoid sinus, which is isointense to gray matter on T2-weighted imaging with diffuse enhancement on T1-weighted images (Fig. 2). There was no other evidence of head and neck involvement after review of the MRI and CT scan. The patient underwent a right-sided sphenoidotomy with debridement and biopsy of the sphenoid mass.

Pathological evaluation showed a dense plasmacytic infiltrate with >150 IgG4$^+$ cells/high-power field (hpf). There was a dense infiltrate of CD138$^+$ plasma cells that were a polyclonal mixture of κ- and λ-light chain-bearing cells. The plasma cells were negative for CD56. Few nodules of CD20$^+$ B cells were present

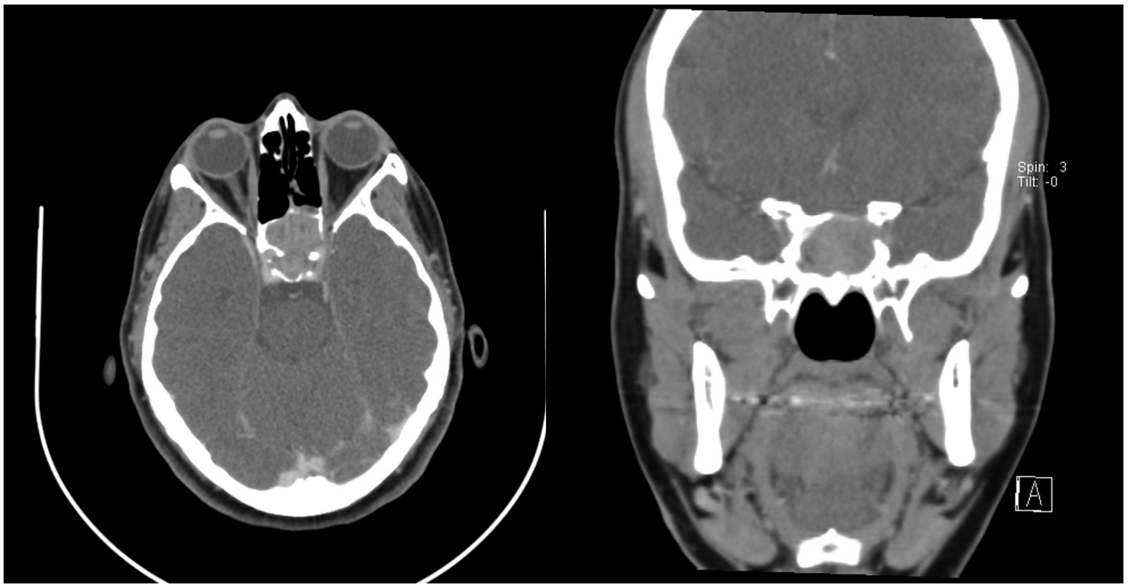

Figure 1. *Preoperative (A) axial and (B) coronal CT scan showing an aggressive mass within the sphenoid sinus. There is bony destruction of the anterior wall of the sphenoid sinus and the anterior portion of inferior wall, in addition to destruction of the posterior aspect of the planum sphenoidale and the anterior wall and floor of the sella turcica.*

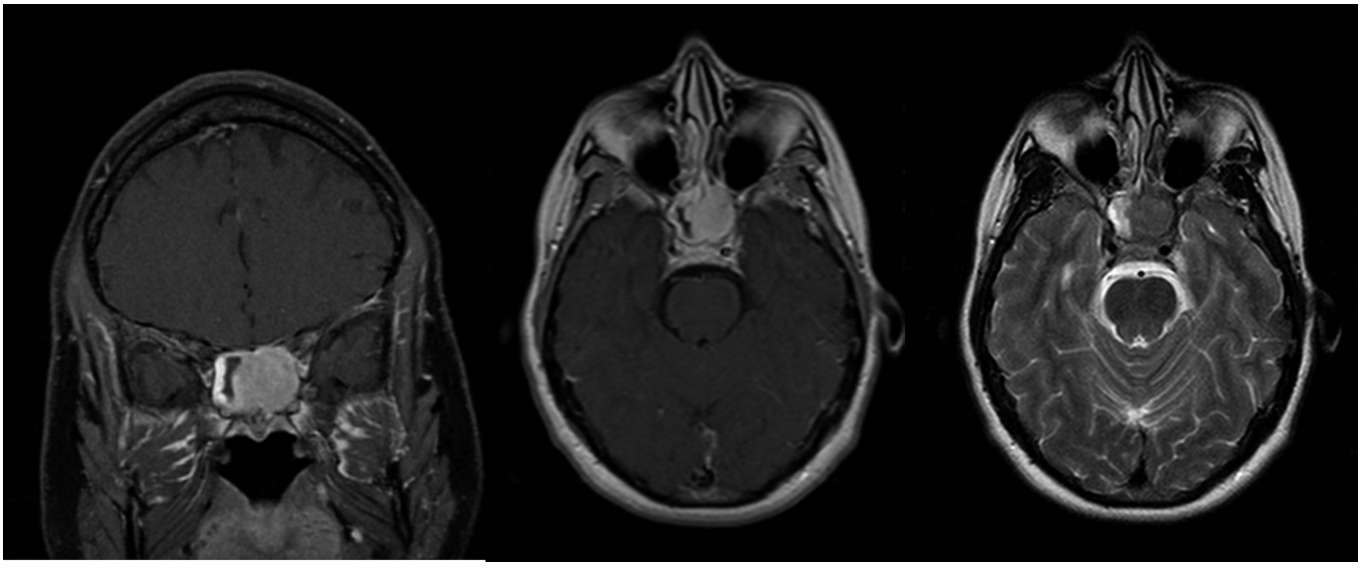

Figure 2. *Preoperative (A) coronal T1, (B) axial T1, and (C) T2 MRI. The mass lesion in the sphenoid sinus is isointense to gray matter on T2-weighted imaging with diffuse enhancement on T1-weighted images. The pituitary gland is distinctly visualized and separate from the mass.*

along with scattered $CD3^+$ T cells. Acute and chronic inflammation with fibrosis was present throughout the tissue sample. These pathological findings were consistent with the diagnosis of IGSD of the sphenoid sinuses (Fig. 3)

A full body PET/CT was obtained to rule out potential extra sphenoidal sites of involvement. The PET/CT showed no evidence of active disease. One-month postoperative evaluation showed a patent sphenoid antrostomy without evidence of recurrence (see Fig. 5 *A*). Serum plasma levels of IgG4 at baseline was 20 mg/dL, which was found to be within normal physiological levels (1–291 mg/dL), further implicating this to be a local destructive focus of IGSD in the paranasal sinuses. However, at her 2-month postoperative visit she showed evidence of disease recurrence in the sphenoid sinus with partial opacification of the sphenoid sinuses on CT imaging and occlusion of the sphenoid antrostomy (Figs. 4 and Fig. 5 *B*). She was subsequently started on fluticasone, a nasal corticosteroid, which improved the patency of the sphenoid antrostomy (Fig. 5 *C*).

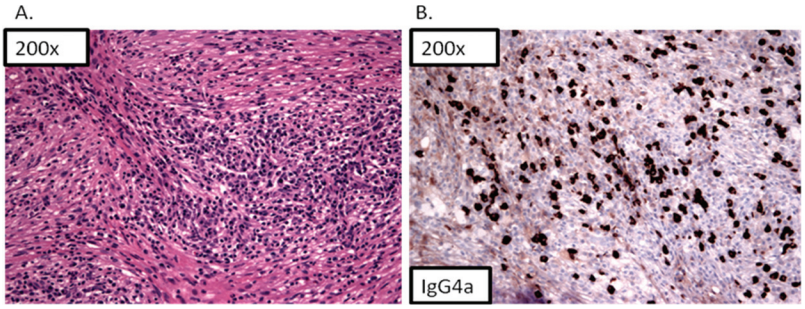

Figure 3. *(A) Hematoxylin and eosin (H & E) stain showing acute and chronic inflammation with fibrosis present throughout the tissue sample. Plasma cells were CD138$^+$ with a mixture of κ- and λ-light chain-bearing cells. (B) Dense plasmacytic infiltrate with >150 IgG4$^+$ cells/high-power field (hpf).*

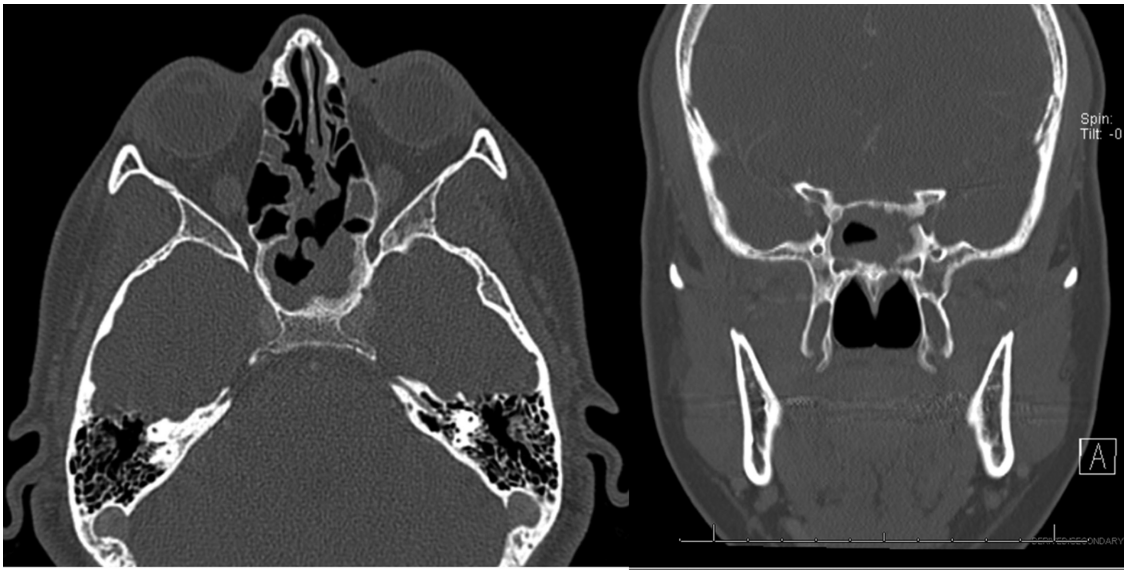

Figure 4. *(A) Axial and (B) coronal 2-month postoperative CT scan showing partial opacification and recurrence of IgG4 sclerosing disease in the sphenoid sinus. This imaging corresponded to the patient's 2 month postoperative nasal endoscopy with sphenoid antrostomy obstruction and polypoid-like mucosal changes (Fig. 5 B).*

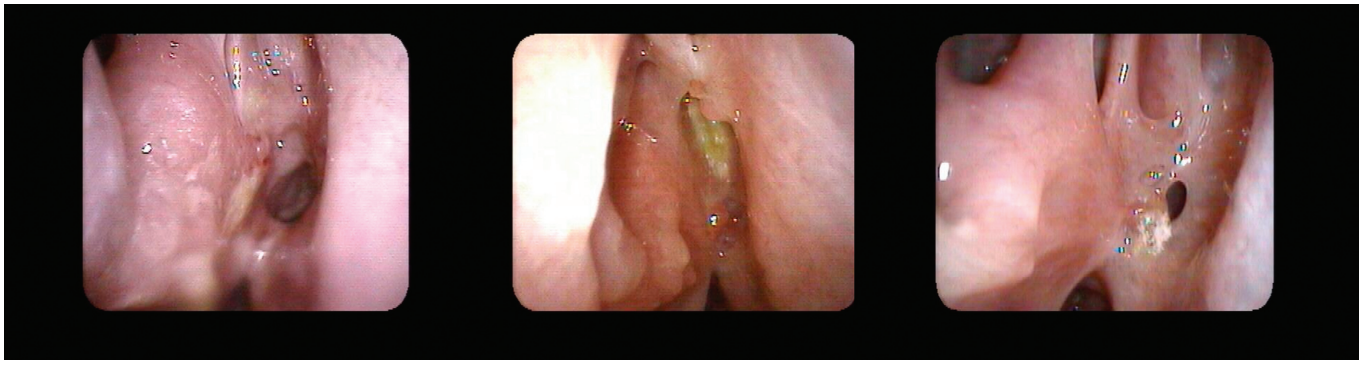

Figure 5. *(A) One-month postoperative nasal endoscopy showing a wide sphenoid antrostomy. (B) Two-month postoperative nasal endoscopy with sphenoid antrostomy obstruction and polypoid like mucosal changes. (C) Five-month postoperative nasal endoscopy after starting a nasal corticosteroid shows an improved and widely patent sphenoid antrostomy.*

DISCUSSION

IGSD is becoming a more recognized inflammatory disease that most frequently presents in older men and has been shown to involve the pancreas, thyroid,[9] submandibular glands,[10] lacrimal glands,[4] temporal bone,[11] and pituitary gland,[10] with rarely described presentation in the nasal cavity and paranasal sinuses.[2,3] We report an unusual case of a middle-aged woman who presented with IGSD isolated to the sphenoid sinus.

IGSD is characterized histologically by extensive infiltration of IgG4$^+$ plasma cells and T lymphocytes, associated with fibrosis. IgG4 is the least common of the IgG subclasses to be expressed, accounting for only

3–6% of total IgG in normal serum. Concerning diagnostic criteria, IgG4-related disease is diagnosed pathologically with certain histological and immunohistological findings. There are varying criteria for the diagnosis of IGSD; however, increased numbers of $IgG4^+$ plasma cells are required for the diagnosis and in cases with >50 $IgG4^+$ cells/hpf the reported specificity and sensitivity are 100%.[1,12,13] The serum IgG4 titer can also be used to aid in diagnosis but is elevated in only 30% of patients with IGSD and therefore not necessary for diagnosis.[12] An $IgG4^+$/IgG^+ cell ratio of >40% (normal = 3–6%) can also be used with high sensitivity and specificity, 86 and 96%, respectively. Histologically, it presents with a triad of lymphoplasmacytic infiltration, sclerosis, and obliterative phlebitis.[1] Our patient's surgical pathology contained a dense plasmacytic infiltrate with >150 $IgG4^+$ cells/hpf with acute and chronic inflammation and fibrosis throughout the tissue sample (Fig. 3), consistent with IGSD of the sphenoid sinuses. Moteki *et al.* showed IgG4-bearing plasma cell infiltrations in the mucosal tissues of patients with sinusitis associated with IgG4-related disease. IgG4-bearing plasma infiltration was indistinguishable from the control group represented by patients with common chronic rhinosinusitis, who also had IgG4-bearing plasma cell infiltrations in their nasal mucosa.[14] Thus, they caution that IGSD should be diagnosed with IgG4 serum levels. However, this new entity of extrapancreatic IGSD still has to be clearly defined and plasma serum levels of IgG4 is not a diagnostic criterion. Our patient had isolated sphenoid sinus involvement with low to normal levels of serum IgG4.

Extrapancreatic IGSD lymphadenopathy is commonly seen in up to 80% of patients with IGSD.[15] Lymphadenopathy occasionally is the first presenting symptom and can be mistaken for lymphoma. Lymph nodes are generally smaller in IgG4-related disease with absent constitutional symptoms such as fever and weight loss. Although lymphadenopathy is highly prevalent in autoimmune pancreatitis our patient presented without associated lymphadenopathy when evaluated by head and neck CT and MRI.

We posit that recognition of IGSD is important clinically because it has been proven to be steroid sensitive, thus potentially obviating the need for surgical management. Glucocorticoids have become the standard therapy for autoimmune pancreatitis, but the indications, dose, and duration of therapy continue to remain controversial.[16] For unresponsive or recurrent IGSD, rituximab and other disease-modifying antirheumatic drugs may prove to be more efficacious.[17] Although our knowledge concerning treatment in extrapancreatic organs is lacking, there is evidence that glucocorticoid treatment improves nasal sinus opacification on CT findings.[14] In this instance we did not institute preoperative oral steroid because we felt the most likely diagnosis was a lymphoproliferative disorder that would require postoperative oral steroids as a part of a multidrug therapy. In hindsight, oral steroids would be a logical and justified treatment option for patients presenting with paranasal IGSD. However, this should be weighed against the risks of steroid complications. Because of the patients history of allergic rhinitis and seasonal allergies and in light of her newly diagnosed IGSD, we elected to start her on fluticasone, a nasal corticosteroid spray. Oral steroids postoperatively could also be used and were considered. Because of resolution of opacification on postoperative imaging and patent sphenoidotomy seen on nasal endoscopy (Fig. 5 *C*) an oral steroid was not instituted. Albeit rare, lymphoma has arisen in IgG4-related chronic sclerosing dacryoadenitis, indicating the need for close follow-up.[1,4]

This case study and literature review adds to the growing literature describing IGSD disease in the head and neck. More specifically, IGSD can be found in the paranasal sinuses with preliminary data showing local control with nasal topical corticosteroids.

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