

Isolated Nasal Amyloidosis: A Case Report

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Summary. *Amyloidosis is a rare condition characterized by the deposition of abnormal protein filaments into the extracellular tissue. Only 16 cases of true primary idiopathic amyloidosis localized in the nose and the paranasal sinuses have previously been reported. We present a case of localized amyloidosis involving the sinonasal cavities and the nose in a 53-year-old woman. Our patient was operated on as a typical case of chronic rhinosinusitis with polyps, but after 2 years, the patient came back with severe symptoms of nasal obstruction and pain in the frontal and maxillary regions with proptosis of both eyes. Magnetic resonance imaging revealed sinonasal-intraorbital masses. Primary amyloidosis (AL type) was confirmed by tissue biopsy. A systemic workup for additional amyloid deposits revealed no evidence of other diseases. Extended surgery produced a symptomatic improvement.*

Introduction

Amyloidosis is a rare condition characterized by the deposition of abnormal protein filaments into the extracellular tissue. Localized amyloidosis is a slowly progressive disease that does not respond to medical therapy. The most frequent types of amyloidosis are immunoglobulin light-chain amyloidosis (AL, primary, as in the present case) and serum amyloid A protein-associated amyloidosis (AA, secondary). The distinction between the localized and the systemic disease is important because localized amyloidosis can be managed conservatively or surgically with a good prognosis, whereas systemic amyloidosis is associated with significant morbidity and mortality (1). Primary amyloidosis of the head and the neck is extremely rare and usually occurs in the larynx. Only 16 cases of true primary idiopathic amyloidosis restricted to the sinonasal tract have previously been reported in literature (2). We present a case of a large extension of sinonasal-intraorbital AL amyloid masses and good surgical treatment results.

Case Report

A 53-year-old woman presented to the Centre of Ear, Nose and Throat Diseases with a 2-year history of slowly progressive nasal stuffiness, associated with rhinorrhea, loss of smell, and recurrent

episodes of sinusitis and bilateral epistaxis. A short time ago, her symptoms rapidly worsened: proptosis of both the eyes with a slight vision impairment and severe facial pain developed, and she was referred to our center. Two years ago, the patient was operated on in our center as a typical case of rhinosinusitis with polyps, which had lasted for about 1 year. Ethmoidectomy with the enlargement of the natural ostium for all the sinuses was performed, but the final diagnosis of AL amyloidosis was made. The postoperative period was without any significant complications; the patient regained the sense of smell after 1 month, and breathing through the nose became satisfactory. A complete examination to detect a systemic cause was done by therapists and hematologists, but the results were negative. During the last year, the patient became symptomatic again with slowly worsening symptoms of nasal obstruction, loss of smell, and recurrent episodes of sinusitis followed by the administration of antibiotics and topical nasal steroids.

On her first stay in our center in 2010, an endoscopic examination revealed nasal polyps arising from both the middle meatus with thick serous secretion and some edematous masses on the posterior edge of the right inferior turbinate. Computed tomography (CT) revealed a complete opacification of all the sinuses. The patient denied any history of a familial or hereditary disease or any notable allergies. During the second visit in 2012, an endoscopic examination demonstrated erythematous masses

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completely obstructing the bilateral middle meatus and the olfactory clefts that were bleeding due to a mild trauma. Proptosis of both eyes, greater on the left side, was evident.

Magnetic resonance imaging (MRI) revealed multiple inhomogeneous masses with septations, involving the ethmoidal cells with a predominant expansion to the left maxillary, frontal, and sphenoidal sinuses. A marked deformation and erosions of the left orbital wall were also evident with a dis-

location of the intraorbital structures (the medial rectus muscle and the optical nerve). Additionally to the amyloid masses, the paranasal sinuses were filled with secretions and hypertrophic mucosa (Fig. 1). After an intravenous injection of a contrast agent (10 mL of gadopentetate dimeglumine), only a partial septal and peripheral enhancement was noticed in the masses (Fig. 2). Although an amyloid itself usually does not enhance with the administration of contrast material, a peripheral

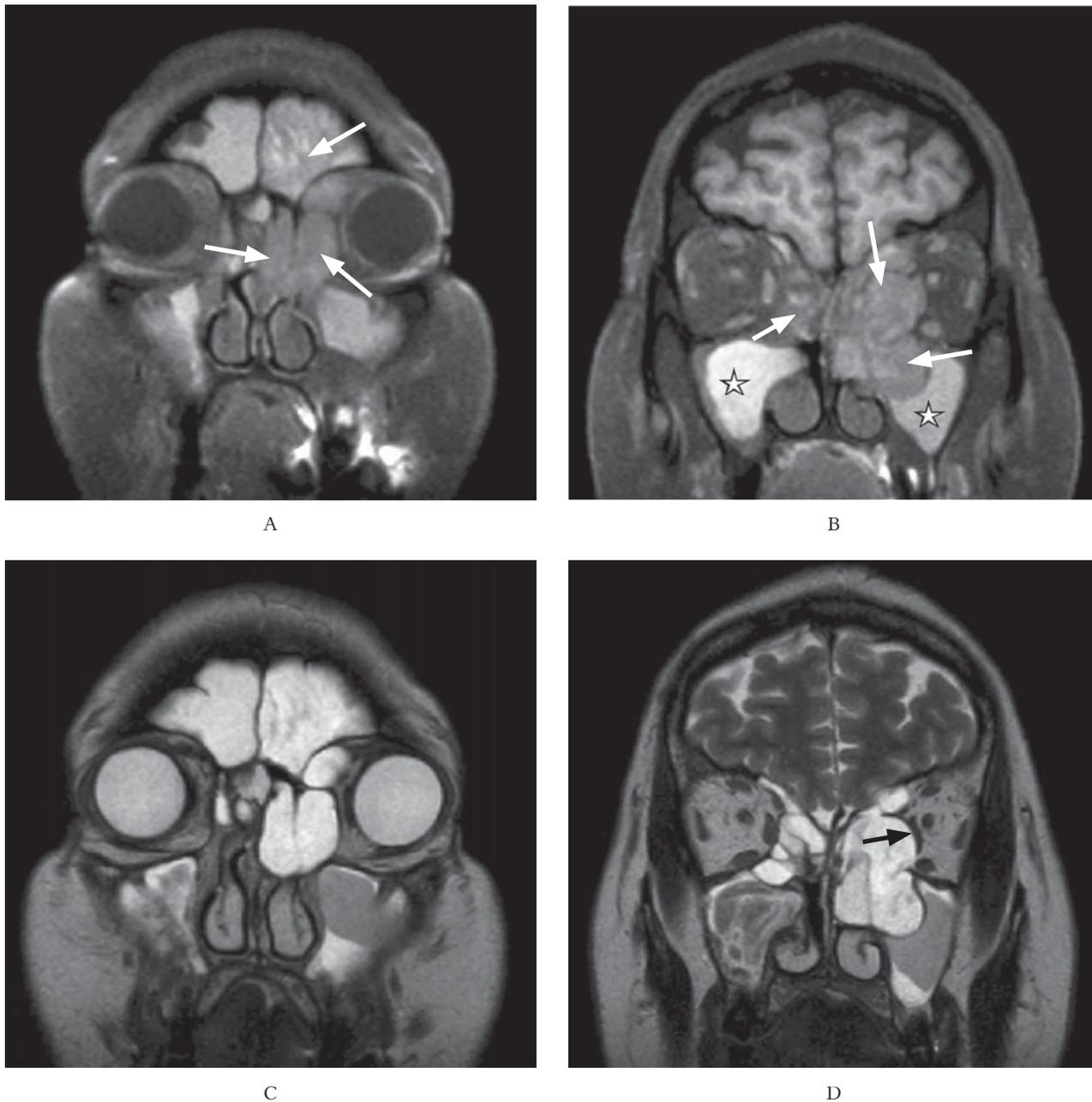


Fig. 1. Coronal T1- and T2-weighted images

Coronal T1-weighted images (A and B) with fat suppression demonstrate predominantly hypointense, inhomogeneous masses (arrows), mostly involving the left sinonasal cavity, and entrapped secretions in the maxillary sinuses (stars). Coronal T2-weighted images (C and D) also demonstrate an inhomogeneous and dominantly high signal in the masses with a marked deformation of the intranasal structure and the left medial orbital wall (arrowhead).

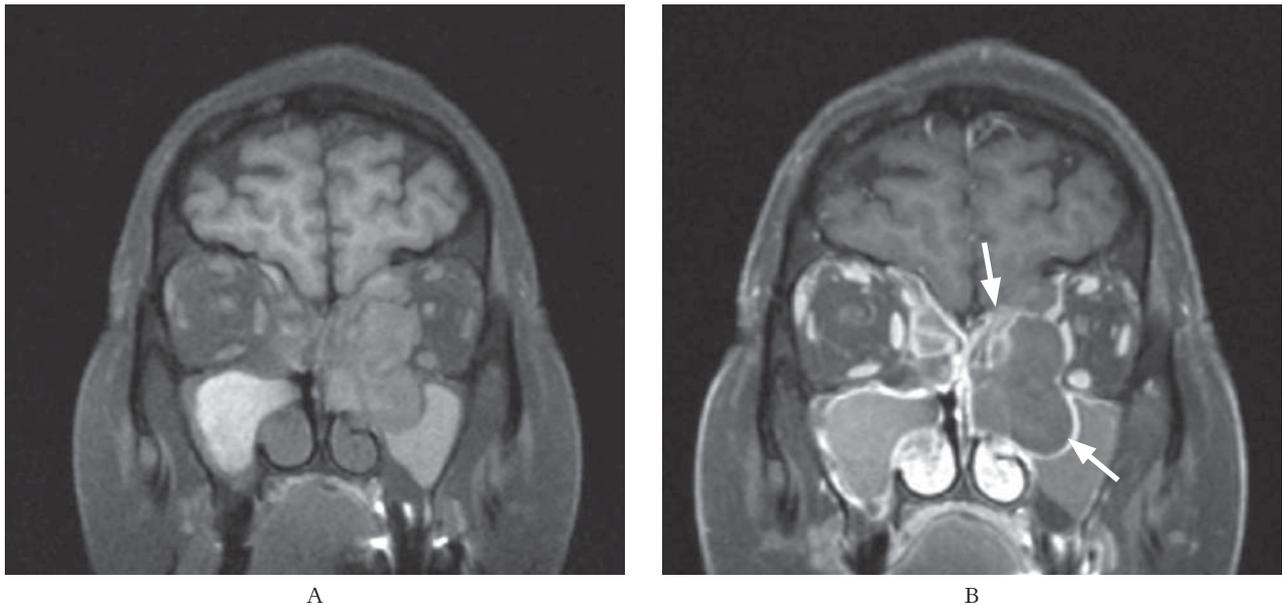


Fig. 2. Precontrast (A) and contrast-enhanced (B) coronal T1-weighted images with fat suppression demonstrating only a peripheral enhancement of the lesion (arrows)

enhancement in the region of amyloid deposits has been noted in previous reports. This may be due to a giant cell reaction against a foreign body that is evoked around amyloid deposits (2). The lack of enhancement of amyloid deposits helps distinguish them from cellular tumors, all of which enhance to varying degrees (3).

The aim of the surgery was to provide a symptomatic relief of nasal obstruction (Fig. 3), decompress the left orbit, and improve other symptoms. The surgery was performed with power instruments (shaver and drill) to remove the bulging masses from the nasal cavity and the adhesions between the septum and the lateral nasal wall. The affected tissue was precisely dissected, and all the sinuses were largely exposed. During the operation, the lamina papyracea (the medial ethmoidal bony wall of the left orbit) on the left side was found to be partially destroyed, so the remnants of the bony pieces were removed. By pressing the eyeball externally, the movement of all the intraorbital content of the left eye was noticeable through the lateral nasal wall. Total ethmoidectomy was performed with the enlargement of the sphenoid and the frontal sinus natural ostium. Draf type II A procedure for opening the frontal sinuses was performed. Bilateral maxillectomy (type II) was performed (the intraoperative view is presented in Fig. 4). During the surgery, a large amount of thick whitish mucus under the pressure was drained from the sinuses.

A histopathological examination (Fig. 5) revealed the deposits of amorphous eosinophilic material involving the vessels and the lamina propria,

consistent with an amyloid structure. The deposits were of the AL type, as demonstrated by an immunohistochemical examination (Fig. 6).

The patient again underwent a thorough systemic workup, including liver and renal function testing, serum alkaline phosphatase, urine analysis, chest x-ray, abdominal ultrasound, ECG, echocardiogram, abdominal fat aspiration, and rectal biopsy to rule out the foci of systemic amyloidosis.

Oral antibiotics and intravenous infusions of saline were administered postoperatively. After 2 months, the sinuses remained widely open, and only some small edematous polyp-like masses were noticed on the lateral nasal wall. Topical nasal steroids were administered additionally and the masses disappeared. There was a significant improvement in the patient's symptoms of nasal obstruction and facial pain, and the sense of smell returned after 2 months postoperatively. The patient's eyeballs returned to the normal position. In our case, we had an excellent outcome with no signs of recurrence and clinical symptoms at 6 and 18 months postoperatively (Fig. 7).

Discussion

Amyloids are pathological proteinaceous substances deposited among cells in various tissues and organs of the body in a variety of clinical entities (4). The diagnosis depends on the findings from biopsy specimens.

Amyloidosis is a generic term that refers to the extracellular tissue deposition of fibrils composed of low-molecular-weight subunits of a variety of pro-

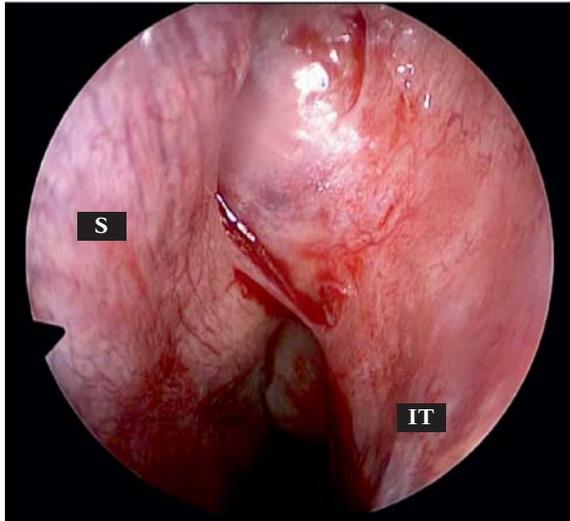


Fig. 3. The intraoperative endoscopic view showing significant adhesions between the septum and the lateral nasal wall
S, septum; IT, inferior turbinate.

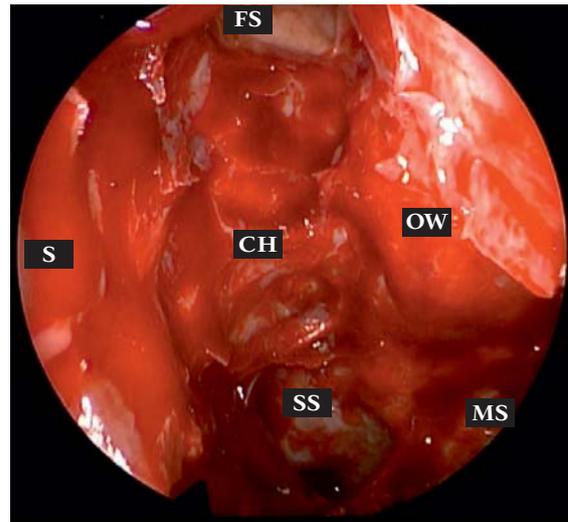


Fig. 4. The intraoperative endoscopic view after the removal of the bulging masses from the nasal cavity (total ethmoidectomy with the enlargement of the sphenoid and frontal sinus natural ostium, Draf type II A procedure for opening of the frontal sinuses, and bilateral type II maxillectomy)
FS, frontal sinus; MS, maxillary sinus; SS, sphenoid sinus; S, septum; CH, choana; OW, orbital wall.

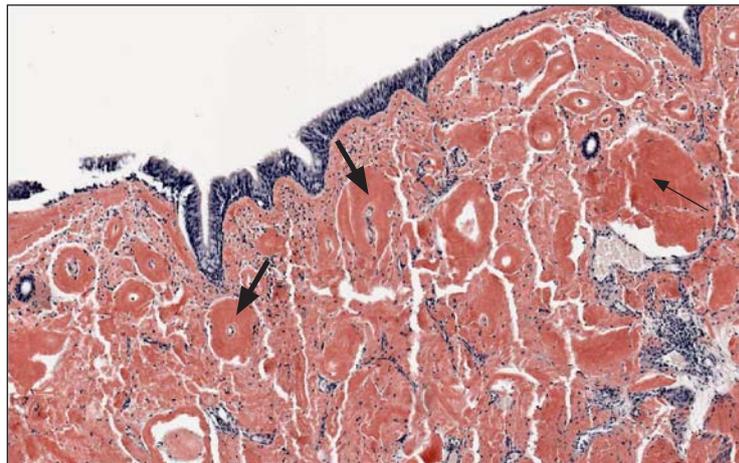


Fig. 5. Tissue stroma full of amorphous eosinophilic KR+ substance (arrows)
Immunohistochemical AmyAA (-); Ig kappa/Ig lambda nonspecific (+++) reaction.

teins, many of which circulate as constituents of the plasma. If the deposition in one or more parts of the body is extensive, it may interfere with the organ or the tissue function and even lead to death.

The most frequent types of amyloidosis are AL (primary) and AA (secondary) amyloidosis. AL amyloidosis occurs due to the deposition of the protein derived from immunoglobulin light-chain fragments. Secondary (AA) amyloidosis is a disorder characterized by the extracellular tissue deposition of fibrils that are composed of the fragments of the serum amyloid A (SAA) protein, an acute phase

reactant. AA amyloidosis occurs as a complication of an underlying chronic inflammatory process (rheumatoid arthritis, juvenile chronic polyarthritis, chronic infections, etc.). The other types of amyloidosis are myeloma-associated, localized, age-related (senile) systemic, dialysis-related, and heritable (familial) amyloidosis.

Amyloid deposition in the head and neck region can occur as an isolated pathology or can be part of systemic amyloidosis (5). The larynx is the most frequent site of involvement in the head and neck region, followed by the base of the tongue, the tra-

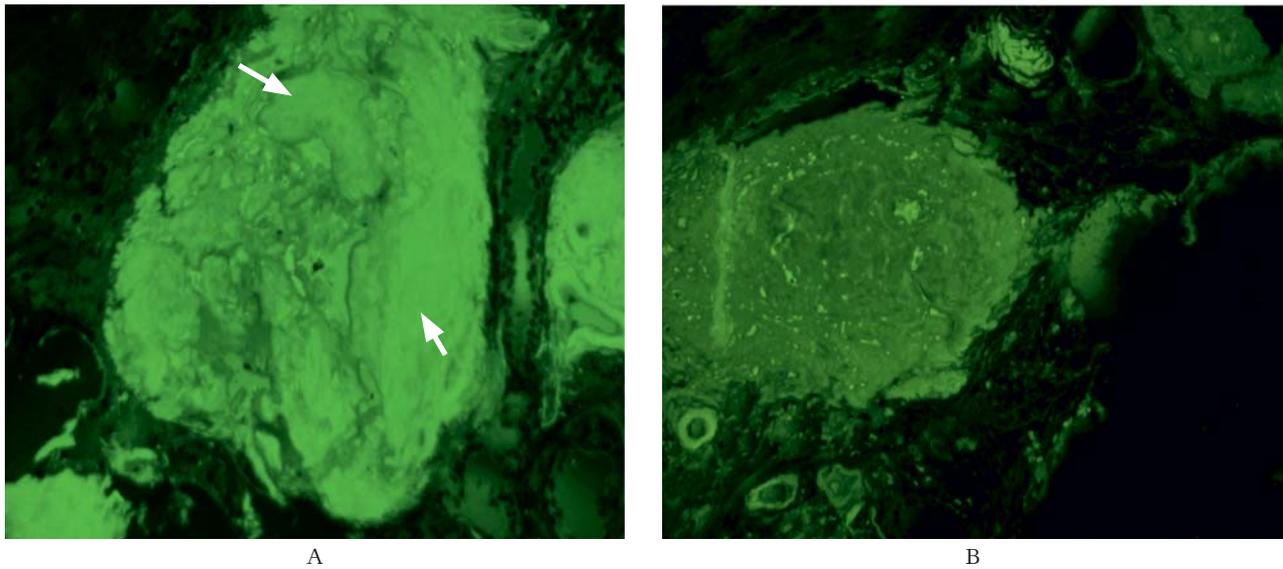


Fig. 6. Immunofluorescence examination

The amyloid deposits stained for Ig lambda (++) (arrows, A) and were negative for Ig kappa (B).

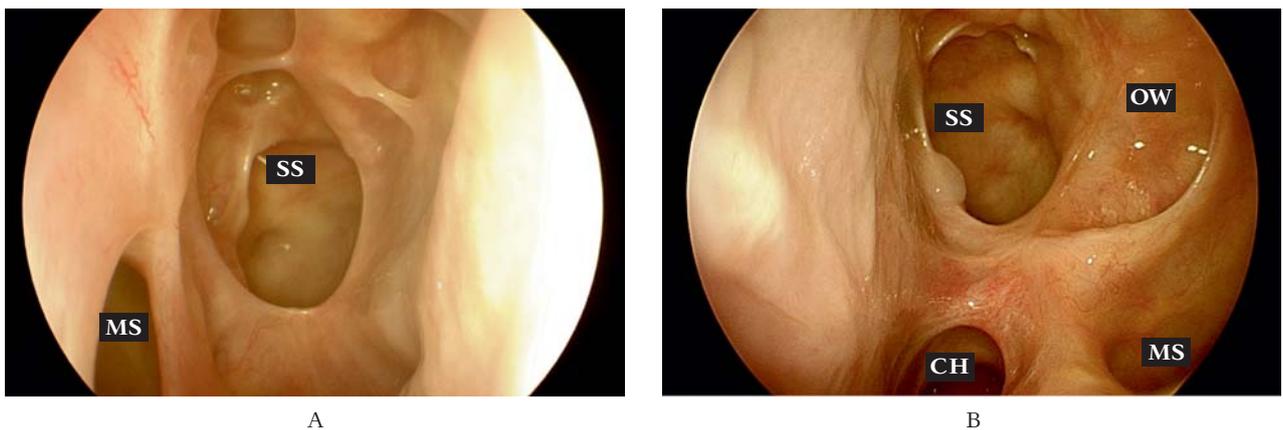


Fig. 7. The endoscopic view in the right (A) and left (B) maxillary sinuses with an excellent outcome, and no signs of recurrence and clinical symptoms in 18 months after operation

MS, maxillary sinus; SS, sphenoid sinus; S, septum; CH, choana; OW, orbital wall.

chea, the pharynx, and the nasal cavity (6). Generally, systemic amyloidosis does not involve the head and neck region; thus, the presence of amyloid masses in this region is more likely to be the localized type. To evaluate systemic amyloidosis, an abdominal fat pad aspirate has been shown to have a specificity of 92%–100% and an estimated sensitivity between 75% and 90% (7). Rectal biopsy showing a sensitivity of 84% has also been used (1).

Isolated nasal amyloidosis is extremely rare and is a localized, idiopathic, primary process composed of AL, kappa or lambda light-chain amyloids. Mufarrij et al. (8) found 7 cases reported in literature from 1935 to 1990. Prasad et al. (9) found 23 previously reported cases of isolated sinonasal amyloido-

sis. However, in 2012, Naidoo et al. (2) performed the literature review, identified only 15 previously described cases of true idiopathic isolated sinonasal amyloidosis, and presented their case. The initiating factors remain obscure though some authors claim that a surgically induced trauma to the paranasal mucosa could incite reactive amyloid deposition. In the present case, the patient had no history of previous surgical procedures of the nose before the first episode of the disease.

The diagnosis and management of this disorder is difficult as it can be easily confused with more typical chronic inflammatory diseases like chronic sinusitis with polyps. Sometimes, multiple biopsies from different places in the nose and the sinuses may

be required to accurately diagnose amyloidosis (10). Isolated sinonasal amyloidosis usually presents with common rhinological symptoms that depend on the site of involvement and are slowly progressive over months to years before the diagnosis. In the present case, the patient suffered from nasal obstruction, recurrent episodes of sinusitis, nasal discharge, and loss of smell for many years. The episodes of nasal bleeding are associated with the loss of vascular integrity (as the amyloid tends to infiltrate the blood vessels) or with the appearance of fragile irregular mucosa that covers amyloid masses (11).

Some authors report that the diagnosis of amyloidosis is only based on the demonstration of amyloid depositions in a biopsy specimen, as staining with Congo red leads to “apple green” birefringence under polarized microscopy or on the immunohistochemical examination of a specimen for determining kappa or lambda light-chain restriction (2, 11). Other authors, e.g., Chin et al. (3), have reported that the amyloid on MRI has the signal intensity similar to that of the skeletal muscle on T1- and T2-weighted sequences because of a highly organized ultrastructure of the amyloid, which is similar to the multilayered, myofibrillar ultrastructure of the skeletal muscle. The amyloid usually enhances minimally after the administration of a contrast agent, but a peripheral enhancement might be present. This may be caused by a giant cell reaction against a foreign body that is evoked around amyloid deposits (2). The lack of enhancement in amyloid deposits helps distinguish them from cellular tumors, all of which enhance to varying degrees (3). On CT, “fluffy” bone changes might be noted adjacent to the amyloid deposit and may suggest the diagnosis of this rare disorder. In the present case, the MRI findings were exactly the same as described above.

Primary localized sinonasal amyloidosis is a slowly progressive disease that does not respond to medical therapy. Medical treatment with topical or systemic corticosteroids and even more aggressive treatment such as chemotherapy have not been successful (12). Radiotherapy is contraindicated because it is ineffective and has significant side effects.

Most cases of amyloidosis of the nose have been treated surgically. Debulking of the mass without compromising the function of the involved organs is recommended for the treatment of localized amy-

loidosis. Despite a high rate (up to 50%) of recurrence (13), surgery at least provides a symptomatic improvement in the majority of patients. Recurrent amyloid deposits can be simply re-excised; thus, a complete removal of amyloid deposits is not recommended if this risks significant morbidity. Further surgical therapy is dictated by symptomatology. Postoperative mucosal adhesion is a common and major complication among patients; therefore, the use of Silastic splints is highly recommended, especially if both the septal and the lateral nasal wall mucosa are affected.

In summary, localized amyloidosis of the sinonasal tract is a rare disease. Limited amyloidosis is best monitored by follow-up examinations, and surgery should be reserved for more severe and extended cases.

Conclusions

We presented the case of isolated nasal AL amyloidosis, an extremely rare, localized, idiopathic, and primary entity. Generally, systemic amyloidosis does not involve the head and neck region; thus, the presence of amyloid masses in this region is more likely to be amyloidosis of the localized type. The diagnosis depends on identification in biopsy specimens because the diagnosis and management of this disorder is difficult as it can be easily confused with more typical chronic inflammatory diseases (like chronic sinusitis with polyps) and slowly progressive over months to years before the diagnosis. MRI findings with a peripheral enhancement are typical of the giant cell reaction that is evoked around amyloid deposits and helpful in determining the localization and the extent of masses. Localized amyloidosis is a slowly progressive disease that does not respond to medical therapy but can be managed conservatively (monitored by follow-up examinations), and surgery should be reserved for more severe and extended cases. Debulking of the mass without compromising the function of the involved organs is recommended for the treatment of localized amyloidosis. Despite a high recurrence rate (up to 50%), an excellent outcome at 18 months postoperatively with no signs of recurrence was achieved in our case.

Statement of Conflict of Interest

The authors state no conflict of interest.

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