Intranasal Eosinophilic Angiocentric Fibrosis: A Rare and Suspicious Appearing Lesion

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ABSTRACT

Objectives*:* The aim of this report is to describe a case of eosinophilic angiocentric fibrosis (EAF) and raise its awareness in head and neck pathology by discussing its clinical course, histological features, diagnosis, and management options.

Study design: Retrospective case report.

Methods: The medical records of a patient with EAF were reviewed at a tertiary medical center. The PubMed database was searched for keywords “eosinophilic angiocentric fibrosis” and “intranasal.”

Results*:* Here we report a case of intranasal EAF in a 49-year-old male who presented with a several month history of right-sided lateral nasal skin swelling and a 10-year history of chronic congestion. On physical examination, patient had a non-pigmented, rubbery right-sided nasal skin lesion. Nasopharyngoscopy revealed a submucosal intranasal lesion of the right middle vault. Punch biopsy and fine needle aspiration revealed no malignancy. Final pathologic diagnosis after surgical excision revealed extensive perivascular “onion skin” fibrosis, consistent with EAF. A comprehensive review of the literature revealed less than 60 reported cases of EAF.

Conclusion*:* EAF is a benign fibrosing vasculitis of unknown etiology that affects mucosal surfaces of the sinonasal and upper respiratory tracts. Patients commonly present during the fifth and sixth decades of life with chronic symptoms of nasal obstruction, sinusitis, epistaxis, and breathing difficulties. The non-specific presentation and rarity of disease should raise suspicion of more common differentials, including Wegener’s granulomatosis, Churg-Strauss syndrome, and granuloma faciale. Although the clinical course is slow growing, management remains challenging due difficulties in establishing diagnosis and high risk of recurrence with a propensity for progressive local destruction.

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INTRODUCTION

First described in 1983 by Holmes and Panje as intranasal granuloma faciale (GF), it was later re-named EAF by Roberts and McCann in 1985 after reporting three similar cases with identical histopathological features.[1,2] EAF is a rare tumefactive lesion affecting mucosal surfaces of the upper respiratory and sinonasal tracts. It represents a benign, non-fatal fibrosing vasculitis of unknown etiology that is characterized by two distinct histological stages with pathognomonic perivascular “onion-skin” fibrosis.[3,4] Men and women are equally affected and present during the fifth and sixth decades of life with symptoms of nasal obstruction or swelling, epistaxis, breathing difficulties, and sinusitis.[5,6] The clinical course is slowly progressive and locally destructive with a tendency to recur.[3,5] Originally thought to be a mucosal variant of GF, the etiology of EAF remains unknown with many suggesting an allergic or trauma-inciting event, while others believe it is part of a spectrum of IgG4-related sclerosing disease (IgG4-RSD).[5,7]

Since the mid-1980s, less than 60 cases of EAF have been reported in the literature.

CASE REPORT

A 49-year-old Caucasian male with no past medical history presented with a several month history of a progressively enlarging, right-sided swelling over the lateral nasal skin and a 10-year history of breathing difficulties previously attributed to a deviated septum. He denied history of atopy, prior nasal trauma or surgery, or any associated symptoms of facial pain, sinusitis or anosmia. He is a lifelong non-smoker.

On physical evaluation, patient had a non-pigmented, non-mobile, rubbery, subcutaneous right-sided nasal lesion. Nasopharyngoscopy revealed a 90% left-sided nasal septal deviation and a submucosal intranasal lesion of the right middle vault. Both punch biopsy and fine needle aspiration (FNA) of the skin lesion revealed no evidence of malignancy. Lab work-up included complete blood count (CBC), eryhtrocyte sedimentation rate (ESR), antineutrophil cytoplasmic antibodies (ANCA), immunoglobulin E (IgE) titers, and peripheral eosinophils. All labs were within normal limits, except for a mildly increased ESR. Concerned with a sampling error in light of the suspicious-appearing mass, patient elected to proceed with surgical resection.

Patient underwent a transcolumellar approach open rhinoplasty with resection of a friable and firm violaceous lesion overlying the right upper lateral cartilage. A septoplasty with bilateral submucosal inferior turbinate resection was also performed for concurrent deviated septum and nasal obstruction. The cartilaginous septum had an irregular appearance that was yellow in color with a sponge-like quality. Frozen pathology was consistent with an inflammatory process. Final pathologic diagnosis revealed extensive fibrotic changes including areas of whorled fibrosis without cellular atypia, active vasculitis or true granuloma formation. Both tissue and serum testing of IgG4 plasma cells revealed rare IgG4 cells relative to IgG. Immunostains for Melan A, CD34, S100, EMA, androgen-receptor, b-Catenin, SMA, PR, ALK-1, CK AE1/AE3, and desmin were all negative.

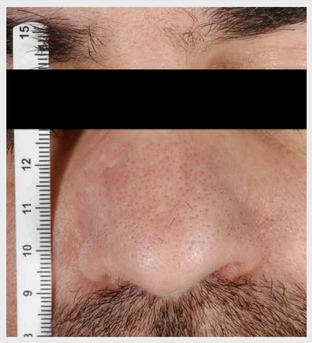

Figure 1. Subcutaneous, intranasal lesion overlying right lateral nasal wall.

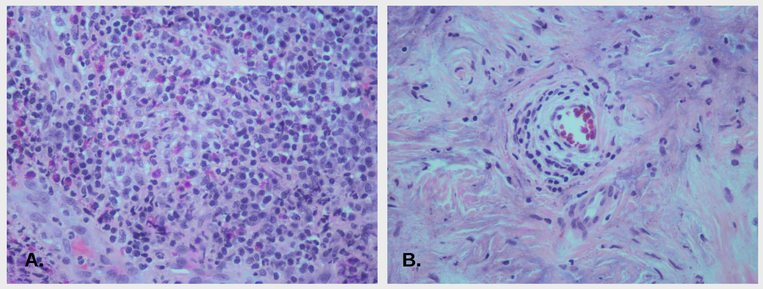

Figure 2. High power H&E stains of right nasal mass and nasal septum demonstrating (**A)** mixed inflammatory infiltrate and **(B)** classic ‘onion skin’ whorled fibrosis.

DISCUSSION

While epidemiology is elusive, EAF most commonly presents during the fifth and sixth decades of life in a 1:1 male-to-female ratio.[4,5,8,9] The most common presenting symptom is progressive nasal obstruction in 78.8%, however, presentation is often nonspecific with an average of 60 to 70 months from time of symptom onset to diagnosis.[3,5,6,9] Other symptoms may include epistaxis, breathing difficulties, sinusitis, nasal tenderness, and facial pain.[4,5,6,9] Approximately 25.0% have associated nasal deformity or swelling, often overlying the lateral nasal wall, as in our patient.[10] EAF is limited to the nasal cavity in over 90% and classically involves the nasal septum.[5]

Differential diagnoses to consider include: Wegener’s granulomatosis, Churg-Strauss syndrome, Kimura’s disease, sarcoidosis, and GF.[5,7,10] Lab work-up consists of CBC, ESR, ANCA, IgE titers, and peripheral eosinophils.[5,9] Radiographic imaging is recommended to evaluate extent of disease and exclude pulmonary involvement, a key feature of Wegener’s granulomatosis and Goodpasture’s syndrome. Rheumatology referral may be beneficial, but did not reveal any abnormalities in our patient. A punch biopsy and FNA of the right lateral nasal skin were useful in excluding malignancy, but failed to establish a diagnosis in our patient.

EAF is diagnosed by two distinct and progressive histological stages: vasculitis and fibrosis.[11] Early lesions represent an inflammatory phase with an active necrotizing vasculitis affecting capillaries and venules.[3,11] Late stage disease is characterized by decreased inflammation and extensive fibrotic changes with areas of perivascular whorled fibrosis.[3] These “onion-skin” whorls are pathognomonic for EAF.[3,6,9,7] Both stages are characterized by an abundance of eosinophils.[8] Unlike other vasculitides, EAF lacks fibrinoid necrosis and true granuloma formation.[3]

The etiology of EAF remains uncertain. Early reports described it as a mucosal variant of GF, a rare, benign vasculitis of the dermis with a tendency to develop slow-growing reddish-brown plaques on the face.[5] However, GF rarely affects mucosal surfaces and lacks concentric “onion-skin” fibrosis.[8] Other proposed etiologies include prior history of nasal surgery or trauma, atopy, or parasitic infection.[5,6,10] In a study by Fang et al., only 26.9% of cases studied had prior history of nasal trauma or surgery.[5] The thought is that these predisposing factors represent an inciting event to an abnormal proinflammatory reaction in response to trauma or surgery. However, immunosuppressive and steroid therapies have been unsuccessful in treating EAF and eosinophilia is the only apparent evidence supporting atopy or parasitic disease.[6] Our patient had no history of nasal trauma, surgery, or atopy.

Additional studies suggest that EAF may be due to underlying IgG4-RSD, a systemic disease characterized by an elevated number of IgG4 plasma cells and T-cell infiltration producing tumefactive lesions in numerous organs.[7,10] Like EAF, it is associated with allergic manifestations and shares similar histology with a rich lymphocytic infiltrate and fibrosis.[7] This correlation was reported in a series of five cases showing increased IgG4 levels in 4 out of 5.[7] However, a subsequent case series by Rimmer et al. failed to show such an association and our case further revealed no such findings.[10] Other diseases categorized as IgG4-RSD include: Reidel’s thyroiditis, Mikulicz disease, chronic sclerosing siadaldenitis and orbital pseudotumor.[7,10]

DISCUSSION

Untreated, EAF has the potential to cause cosmetic disfiguration and disability secondary to mass effect.[5,10] However, due to its rarity and benign behavior, there are no standard management guidelines. Traditionally, EAF is treated with surgical resection to establish diagnosis and provide symptomatic control.[5] Operative approaches are based on lesion location, with open rhinoplasty and lateral rhinotomy being the preferred approaches in most cases.[5]

Corticosteroids have been used to control early stages of local inflammation but are insufficient alone and associated with unfavorable side effects.[5] Immunomodulators like dapsone have also been used due to its success in treating GF, but have not been particularly effective.[5,10] Recent use of rituximab, a monoclonal antibody to CD20 used to treat IgG4-RSD, has shown positive effects in some patients, but further evidence is required.[10]

Although there are no reports of malignant transformation or death, there is a high incidence of local progression and disease recurrence.[3] In fact, complete surgical resection results in only 30% of patients having a disease-free survival.[3] EAF often recurs in the same anatomic location as the primary lesion, suggesting progressive disease rather than true recurrence.[8,10]

CONCLUSIONS

In conclusion, this case highlights the clinical course of EAF with a long period of progressive nasal symptoms often attributed to sinonasal disease. Although this disease is relatively benign, its progressive and destructive nature warrants surgical management and rheumatologic work-up to exclude systemic disease. Recurrent disease is likely and is best managed with proper follow-up and surveillance. The etiology remains uncertain and more studies are required to adequately elicit a cause.

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