UCSF Benioff Children's Hospital San Francisco

Sinonasal Polyposis in a Child with IRAK-4 Deficiency

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ABSTRACT

Objective: To present a unique case of recurrent sinonasal polyposis in a patient with IRAK-4 deficiency.

Study Design: Case report and literature review

Methods: Medical records of a patient with IRAK-4 deficiency and sinonasal polyposis treated at a tertiary academic medical center were reviewed. PubMed was searched for "IRAK4 deficiency" OR "immune deficiency" AND "nasal polyps" OR "sinusitis."

Results: A 7 year-old female with a history of interleukin-1 receptor-associated kinase-4 (IRAK-4) deficiency presented to the pediatric head and neck clinic for evaluation of progressive nasal congestion and recurrent sinusitis. Her physical exam was significant for right nasal polyposis, and her computed tomography scan demonstrated complete opacification of all the paranasal sinuses. She was taken to the operating room for endoscopic sinus surgery. Intraoperative findings were notable for diffuse polyposis throughout the right sinonasal cavities and pus in right frontal sinus. Final pathological analysis was consistent with nasal polyposis with chronic inflammation and microbial culture revealed Haemophilus influenzae. A comprehensive search of the literature did not reveal any previous reports of sinonasal polyposis in patients with IRAK-4 deficiency.

Conclusions: This is the first report to our knowledge of a patient with IRAK-4 deficiency presenting with sinonasal polyposis. Sinonasal polyps are uncommon in the pediatric population. Underlying immunodeficiency has been reported as possible etiology of chronic rhinosinusitis, and Toll-like receptor dysfunction has been implicated in the development of nasal polyps. Associated diseases should be considered in children presenting with sinonasal polyposis.

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INTRODUCTION

Interleukin-1 receptor-associated kinase-4 (IRAK-4) deficiency is a rare, inherited, primary immunodeficiency associated with increased susceptibility to recurrent infections by pyogenic bacteria.[1] Most patients suffer acute bacterial infections early in life, with recurrent invasive pneumococcal infections as the hallmark of the disease. While sinusitis has been reported to be a presenting infection,[2] to our knowledge there has been no previous report of sinonasal polyposis in patients with IRAK-4 deficiency.

CASE REPORT

A 7 year-old female with a history of interleukin-1 receptor-associated kinase-4 (IRAK-4) deficiency was referred to our pediatric head and neck clinic for evaluation of progressive nasal congestion and recurrent sinusitis.

She was diagnosed with IRAK-4 deficiency in 2013 following extensive immunologic work-up for recurrent viral and bacterial infections in the setting of hypogammaglobulinemia and neutropenia. At the time of evaluation, she was receiving IVIG infusions and taking Bactrim and penicillin prophylaxis.

Prior to her referral, her mother had noted worsening congestion, rhinorrhea, and sinus pressure over several months, and on exam she had obvious polyposis filing the right nasal cavity. Notably, she did not have pulmonary or GI disease. Her computed tomography scan demonstrated complete opacification of her right paranasal sinuses with bony expansion of the maxillary sinus ostium and infundibulum. There was only partial opacification of her left ethmoid air cells (Figure 1).

She was taken to the operating room for endoscopic sinus surgery. Intraoperative findings were notable for diffuse polyposis throughout the right sinonasal cavities and purulence in right frontal sinus (Figure 2). Final pathological analysis was consistent with nasal polyposis with chronic inflammation and microbial culture revealed *Haemophilus influenza*. She was treated with nasal steroids, saline irrigations, and three weeks of Augmentin.

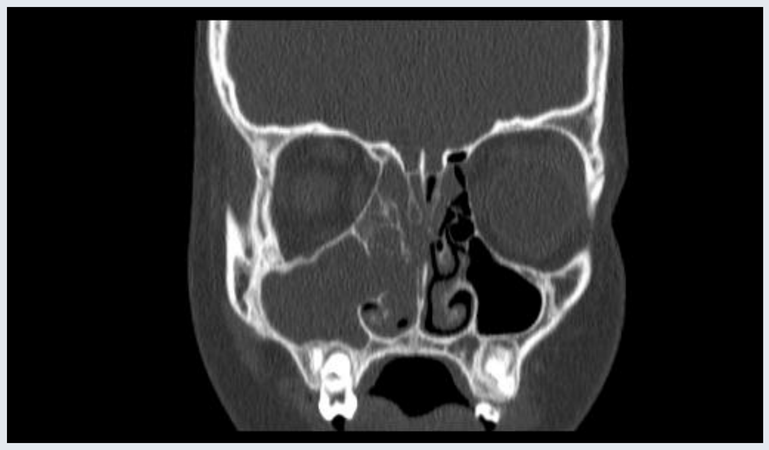

Figure 1. Coronal CT Sinus demonstrating pan-opacification in the right sinonasal cavities.

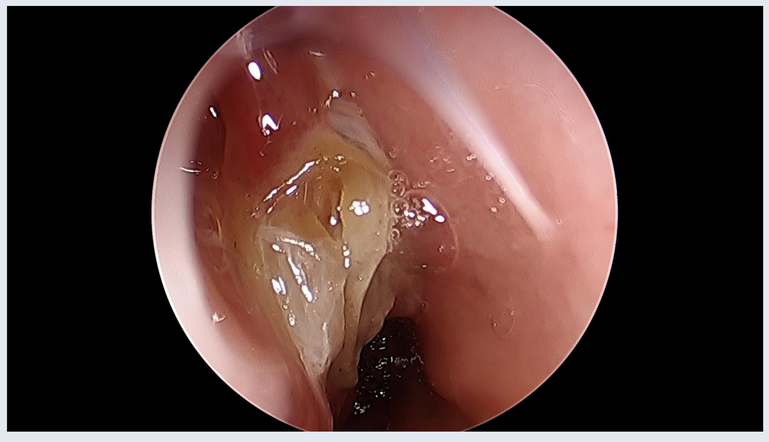

Figure 2. Intraoperative endoscopic view of the right nasal cavity with significant polypoid disease and mucopurulence

Approximately five weeks post-operatively, she experienced recurrent facial pain and congestion that did not improve after a short course of oral steroids. She was taken to the operating room for revision endoscopic sinus surgery. Findings were significant for diffuse mucopurulence and recurrent polyposis throughout the left greater than right nasal cavities (Figure 3). Cultures at that time grew multiple organisms, including MSSA, *Haemophilus influenza*, *Vibrio cholerae*, *Bacteroides fragilis*, *Corynebacterium*, and anaerobes.

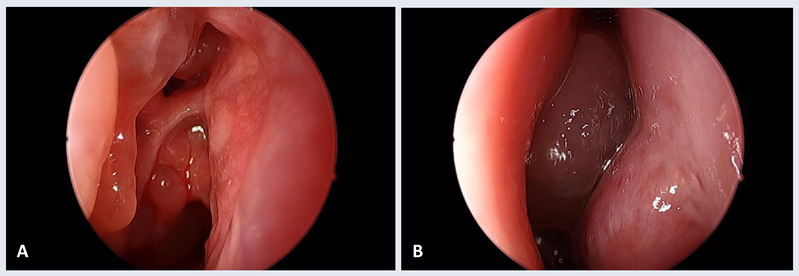

Figure 3. Intraoperative endoscopic views of the right (A) and left (B) nasal cavities revealing recurrent polyposis.

She has since been followed closely by the OHNS, Infectious Disease, and Immunology teams. She has recently started systemic oral and parenteral antibiotic therapy targeting her prior cultures as well as topical aminoglycoside irrigations for newly discovered fluoroquinolone-resistant *Pseudomonas*. At her latest follow-up, there was no evidence of recurrent polyposis.

DISCUSSION

Interleukin-1 receptor-associated kinase-4 (IRAK-4) is a member of the IRAK family and plays an essential role in mediating cellular activation in response to Toll-like receptor and IL-1 receptor activation.[1] IRAK-4 deficiency is an autosomal recessive disorder characterized by recurrent infections by pyogenic bacteria at a young age. Infections may be invasive, affecting normally sterile sites such as the brain, joints, or deep tissues, or noninvasive, most frequently affecting the skin or the head and neck region, including sinusitis. The most common organisms implicated are *S. pneumoniae*, *S. aureus*, and *P. aeruginosa*.[2] Interestingly, patients are not particularly susceptible to infections by other microorganisms such as viruses, fungi, or parasites, and the risk of infection decreases with age, even without continued treatment or prophylaxis.[2]

A comprehensive search of the literature did not reveal any previous reports of sinonasal polyposis in patients with IRAK4 deficiency. Sinonasal polyposis in children is rare. When present, it is most commonly associated with cystic fibrosis and asthma,[3] neither of which was present in our patient. However, underlying immune deficiency has been linked with chronic sinusitis,[4] and dysfunction in Toll-like receptor signaling has been linked to the development of nasal polyps.[5] Other work has also suggested a relationship with *S. aureus* enterotoxins and nasal polyposis, although the exact association remains unclear.[6] Both intravenous and topical antibiotic therapy are thought to have potential benefits in children with chronic rhinosinusitis, although there have been limited comparison studies.[7,8]

CONCLUSIONS

This is the first report to our knowledge of a patient with IRAK-4 deficiency presenting with sinonasal polyposis. Sinonasal polyps are uncommon in the pediatric population. Underlying immunodeficiency and innate immune dysfunction have been implicated in chronic sinusitis and the development of nasal polyps. Associated systemic diseases should be considered in children presenting with sinonasal polyposis.

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