

TITLE: Pediatric Rhinosinusitis

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Introduction

Rhinosinusitis is manifested clinically by an inflammatory response involving the upper respiratory airway tract including the following: the mucous membranes (possibly including the neuroepithelium) of the nasal cavity and paranasal sinuses, fluids within these cavities, and/or underlying bone. Broadly speaking, rhinosinusitis is defined as an inflammation and/or infection involving the nasal mucosa and at least one of the adjacent sinus cavities. Traditionally this condition was called sinusitis but the Task Force on Rhinosinusitis believes that for issues of clarity the entity should be referred to as rhinosinusitis to reflect that the condition affects the nasal passages and the sinus mucosa simultaneously. Rhinosinusitis syndromes are discussed in temporal terms and the disease state is categorized by how long symptoms have been present.

Acute rhinosinusitis (AS) is defined as the persistence and worsening of upper respiratory symptoms for greater than a 7-day course, which is the typical duration of a viral illness, but lasts less than 4 weeks. Subacute rhinosinusitis (SAS) is defined as nasal symptoms lasting 4 weeks to 12 weeks. The infectious pathogens involved in SAS are similar to those found in AS. 11 Acute Bacterial Rhinosinusitis (ABS) is the fifth most common diagnosis, in the primary care setting, prompting antibiotic administration and accounts for 0.4% of ambulatory diagnoses. The economic burden of this disease is greater than \$1.77 billion per year. Acute rhinosinusitis may lead to chronic rhinosinusitis (CRS).

CRS diagnosis is symptom based and requires persistence of patient complaints of mucosal inflammation for more than 3 consecutive months despite optimal medical therapy or episodes have occurred more than four times a year with persistent radiographic changes. Chronic Recurrent Rhinosinusitis (CRRS) consists of multiple episodes of sudden worsening of CRS with return to baseline between episodes. Typically the acute symptoms are alleviated but the chronic symptoms persist. Rhinosinusitis is rarely life threatening, but the close proximity of

the paranasal sinuses to the central nervous system, the multiple fascial planes of the neck, and the associated venous and lymphatic channels can lead to serious complications.

Background

The incidence of pediatric rhinosinusitis varies amongst various publications from 5-10%, most of these children progressed from an upper respiratory tract infection. A smaller subset of those patients will go on to develop chronic rhinosinusitis. True incidence and prevalence is hard to determine because many children are treated empirically without necessarily obtaining radiographic evidence of sinus disease.

Signs and symptoms of rhinosinusitis include: Day and night cough, purulent nasal discharge, nasal airway obstruction, headache, irritability, or facial pain, fever, and postnasal drip. The single most common symptom in children is nasal discharge followed closely by cough.

Embryology

Classic anatomic treatises attribute initial paranasal sinus development to lateral nasal wall ridges called ethmoturbinals. A series of five to six ridges first appear during the eighth week of development; through regression and fusion, however, three to four ridges ultimately persist the first ethmoturbinal regresses during development; its ascending portion forms the agger nasi, while its descending portion forms the uncinat process. The second ethmoturbinal ultimately forms the middle turbinate, the third ethmoturbinal forms the superior turbinate, and the fourth and fifth ethmoturbinals fuse to form the supreme turbinate. These structures are all considered to be ethmoid in their origin. An additional ridge, the maxilloturbinal, arises inferior to these structures. This ridge ultimately forms the inferior turbinate but is not considered ethmoid in its embryologic origin.

In addition to the ridge and furrow development, a cartilaginous capsule surrounds the developing nasal cavity and has an important role in sinonasal development. Bigham et al. highlighted the role of the cartilage capsule through cross-sectional histologic analysis of fetal specimens. At 8 weeks, three soft-tissue elevations or preturbinates are seen that correlate to the future inferior, middle, and superior turbinates. At 9 to 10 weeks, two cartilaginous projections invade into the soft tissue preturbinates. An additional soft tissue elevation with an underlying cartilaginous bud emerges at this time, corresponding to the future uncinat process. This structure enlarges, and by 13 to 14 weeks, a space develops lateral to the structure that corresponds to the ethmoidal infundibulum. By 16 weeks, the future maxillary sinus begins to develop from the inferior aspect of the infundibulum. The cartilaginous structures resorb or ossify as development progresses. The cartilaginous capsule, therefore, plays an important role in sinonasal development

The ethmoid sinus is commonly referred to as “the labyrinth” due to its complexity and intersubject variability. Fortunately, several rhinologists and surgeons have reduced the complex ethmoidal labyrinth of the adult into a series of lamellae on the basis of embryologic precursors. These lamellae are obliquely oriented and lie parallel. With experience, these structures are relatively easy to recognize during surgery and are invaluable in maintaining orientation in

ethmoid procedures. The first lamella is the uncinata process; the second lamella corresponds to the ethmoidal bulla; the third is the basal or ground lamella of the middle turbinate; and the fourth is the lamella of the superior turbinate. The basal lamella of the middle turbinate is especially important, as it divides the anterior and posterior ethmoids. The frontal, maxillary, and anterior ethmoids arise from, and therefore drain into, the middle meatus. The posterior ethmoid cells arise from, and therefore drain into, the superior and supreme meati, while the sphenoid sinus drains into the sphenoethmoid recess. The lamellae are relatively constant features between human subjects, making intraoperative recognition important.

Anatomy

There are four paired paranasal sinuses: the frontal, sphenoid, ethmoid, and maxillary. The maxillary and ethmoid sinuses begin to develop during gestation; the maxillary sinuses grow rapidly until age 3 years, and then again from the ages of 7 to 18 years, while the ethmoid air cells grow from 3 or 4 cells to 10 to 15 cells per side by the age of 12. The sphenoid sinuses develop at approximately 6 years of age and the frontal sinuses develop around 9 years of age. Up to 5% of adults may not fully develop one or both of the frontal sinuses. Therefore, absence of well-aerated sinuses on radiological examination in the young child does not necessarily define a pathologic condition. While the anatomy of children's sinuses is similar to that of adults, children's sinuses are significantly smaller in size, which often makes clinical evaluation more difficult.

Examination of the nasal cavity of a child will show three outgrowths from the lateral nasal wall called turbinates. The nasolacrimal duct drains immediately underneath the inferior turbinate, and the nasolacrimal sac is encased in thin bone immediately superior to the inferior turbinate. The maxillary sinus, frontal sinus and anterior ethmoid sinuses (the anterior group of sinuses) drain in the region of the middle turbinate while the posterior group of sinuses (posterior ethmoid and sphenoid sinuses) drain at the superior turbinate. The area named the osteomeatal complex is considered the primary site of obstruction leading to stasis of secretions and recurrent sinus disease. Anatomically this area is bounded by the anterior border of the middle turbinate medially and the lateral nasal wall laterally.

Mucociliary Clearance

Mucociliary clearance is very important for the well being of the paranasal sinuses. Evidence of this is demonstrated when there are aberrations of cilia which inevitable result in cilia dysfunction and paranasal sinus disease. The natural ostia of the paranasal sinuses are not always located in areas that will spontaneously drain, therefore cilia play a big role in allowing dependant areas to drain adequately. When discussing ciliary function it is important to consider the following factors: number of cilia, their structure and their coordinated activity. If any one of those factors is altered it will lead to decreased mucociliary clearance.

Cilia work optimally at a temperature of 37 degrees celcius and humidity near 100%. Cilia are located on the respiratory epithelium they are responsible for clearance of mucus which may contain bacteria and/or other noxious micro foreign bodies. To aide in their function the respiratory epithelium contains goblet cells, they account for roughly 20% of the epithelium. Cilia account for the other 80%.

The normal structure of cilia is a highly conserved 9+2 structure seen even in the simplest unicellular organisms. The outer configuration of the cilia contain 9 doublet microtubules, each one of those microtubules contains an inner and outer dynein arm as well as a radial head and spoke which interacts with the inner 2 single microtubules in the cilia. Knowledge of this is important because there are several diseases in which missing inner or outer dynein arms lead to dysfunction of the entire ciliary structure. An example of such a disease is Inherited Primary Ciliary Dyskinesia. It is an autosomal recessive trait with extensive heterogeneity. It results in defects of either the inner or outer dynein arms, total or partial defects. The deficiency of these structures leads to decreased beat frequency, outer arms are more detrimental to the beat frequency.

There are other diseases in which the cilia are functionally normal, yet they are overwhelmed by superimposed disease process. In cystic fibrosis, the cilia are functionally normal, however because of the thick mucous produced by the defective sodium channels the cilia are unable to clear the mucus effectively. To some extent ciliary function is eventually affected in cystic fibrosis. Ciliary function is also affected in chronic rhinosinusitis, further worsening the disease.

Pathophysiology

Nasal endoscopy has led to a better understanding of the etiology of sinus disease in children. The fundamental principle in development of sinus disease is that obstruction in the drainage pathways of the sinuses results in stasis of secretions, leading to sinus disease. The obstruction may be anatomic, physiologic, or a combination of the two. Other conditions such as allergy, gastroesophageal reflux, air pollution, first- or second-hand smoke, and day care environments may increase the incidence of sinus disease.

Obstruction of the osteomeatal complex may be caused by bony anatomic variation, or mucosal inflammation from allergy, infection, irritation, and other intranasal pathology. This obstruction leads to cessation of normal sinus drainage patterns and results in the stasis of secretions with resultant sinusitis. Although the pediatric literature has focused predominantly on the maxillary sinus as the source of sinusitis, anterior ethmoid cells are involved with equal frequency. When the ostium of a sinus becomes obstructed, gas exchange becomes impaired within the normally aerated sinus, favoring growth of anaerobic bacteria and promoting infection. Ciliary dysfunction within the sinus mucosal lining worsens, leading to further stasis of secretions and thickening of the mucous membranes in the sinuses. This leads to repeated or chronic sino-nasal infections.

In general, the pathophysiology of rhinosinusitis relates to impairment of mucociliary clearance, mucosal inflammation and any condition leading to decreased ventilation through a patent sinus ostium. Normal sinus drainage can be affected by GERD, Allergic rhinitis, viral URIs, immune deficiency and asthma.

Gastroesophageal reflux disease: Recent studies suggest that patients with chronic rhinosinusitis have an increased prevalence of gastroesophageal reflux. Many patients, especially children, experience improvement in their chronic sinonasal symptoms after therapeutic trials of antireflux therapy. GER is theorized to have direct effects on nasal mucosa, initiating an

inflammatory response associated with edema and impaired mucociliary clearance. Phipps in 2000 reported the results of a prospective trial in which pediatric patients referred for chronic rhinosinusitis were evaluated for gastroesophageal reflux. 19 of 30 patients (63%) were found to have esophageal reflux by pH probe. Six of the 19 patients (32%) demonstrated nasopharyngeal reflux. Fifteen of the nineteen patients had improvement of their sinonasal symptoms after treatment of GERD. Bothwell in 1999 reported that 89% of pediatric candidates for functional endoscopic sinus surgery avoided surgery with treatment for GERD.

Allergy is a known contributing factor to both acute and chronic rhinosinusitis. Allergic rhinitis creates edema of the nasal passages, blocking proper drainage of the sinus cavities. This may lead to an episode of acute sinusitis or contribute to the chronic inflammation of those with chronic rhinosinusitis. Patients with refractory chronic sinusitis or history of atopy should be considered for allergy testing.

A history of frequent otitis media, pneumonia and sinusitis may suggest a primary or secondary immunodeficiency state. Serum IgG, IgA, IgM and IgE should be evaluated as well as ability to respond to polysaccharide capsular antigens of *S. pneumoniae* and *H. influenzae*. Patients identified with immune dysfunction may require IVIG therapy. Genetic counseling for the patient and family may be appropriate. Immunization against *S. pneumoniae* and *H. influenzae* are suggested.

Sinusitis and asthma are frequently associated; controversy exists over whether they are manifestations in different parts of the respiratory tract of the same underlying disease process or whether a causal relationship exists wherein sinusitis worsens bronchial asthma. Zimmerman found a 31.2 % incidence of radiographic paranasal sinus abnormalities in asthmatic children compared to 0% in controls. Treatment of sinusitis, whether medical or surgical, has been shown in multiple studies to decrease use of broncodilators, normalize pulmonary symptoms and improve subjective asthma symptoms.

Cystic fibrosis is inherited as an autosomal recessive trait; the mutations associated with CF affect the CFTR protein which is expressed mainly in the epithelial cells of airways and gastrointestinal tract. Multiple different CFTR mutations have been characterized in CF patients. Patients with cystic fibrosis develop chronic pulmonary disease in childhood, sinusitis and nasal polyposis, pancreatic insufficiency and focal biliary cirrhosis. Cystic fibrosis patients presenting to the otolaryngologist usually have already been diagnosed with CF; however, some patients may be undiagnosed and present first to the otolaryngologist with sinonasal symptoms. Not all cystic fibrosis patients with chronic rhinosinusitis have nasal polyps but nasal polyps in the pediatric age group are rare. If cystic fibrosis is suspected, a sweat chloride test or referral for genetic evaluation should be made. Nasal cultures positive for pseudomonas or *S. aureus* are suggestive of CF. Recent studies suggest that heterozygous mutations in the CFTR gene are associated with chronic rhinosinusitis as well as isolated chronic pancreatitis, allergic bronchopulmonary aspergillosis and congenital bilateral absence of the vas deferens. Raman found that seven of fifty-eight pediatric patients (12.1%) with chronic rhinosinusitis harbored CFTR mutations; the expected rate is 3-4%. Wang found a 7% incidence of CFTR gene mutations in 123 chronic rhinosinusitis patients compared to 2% in a control group.

Treatment

Treatment of pediatric rhinosinusitis is different from treating adults with chronic rhinosinusitis. Initial aims of treatment are to target the cause of the rhinosinusitis. As discussed above the causes of rhinosinusitis are very diverse and therefore attention should be directed during the history and physical to attempt to elucidate which one of the factors is leading to CRS. Initial therapy is directed at treating the infection with appropriate antibiotics for susceptible microbes. Chronic Rhinosinusitis should be treated with a 4 to 6 week course of beta lactam stable antibiotic. Adjuvant therapy with nasal steroids should be employed as well as antihistamines especially if underlying allergic condition suspected. Mucolytics may be used to help thin secretions and consider reflux treatment if suspicion of GERD is high.

Surgical therapy is a step-wise approach. If medical therapy fails first line of treatment is adenoidectomy, nasal endoscopy with/without antral lavage or directed opening of a sinus cavity which is seen to be blocked on CT scan. Tonsillectomy may be performed also if patient has OSA or recurrent strep throat. Finally a conservative FESS should be considered if child is not improving after having instituted medical and initial surgical therapy.

Conclusion

Pediatric rhinosinusitis remains a diagnostic dilemma in many children. Newer technology has helped us diagnosis and allowed us to treat patients that were previously inadequately or not treated at all. While the management of pediatric rhinosinusitis is primarily aggressive medical therapy, surgical management is appropriate for certain patients. Further inquiry is required to expand our understanding of the etiology and natural history of sinus disease in children with additional insight into defining the indications for specific forms of medical and surgical therapy.

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