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Acute and Chronic Rhinosinusitis, Pathophysiology and Treatment

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ABSTRACT: *Acute sinusitis (ARS) and chronic rhinosinusitis(CRS) is a common condition worldwide.CRS is due to the infection and inflammation of paranasal sinuses. Frequent clinical manifestations of ARS include persistent symptoms with nasal discharge or cough or both, presentation with fever accompanies purulent nasal discharge, and worsening symptoms. Complications of CRS have five stages, preseptal cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess and cavernous sinus septic thrombosis. Most acute sinusitis generally of viral origin, e,g. rhinoviruses, corona viruses,and influenza viruses. Bacterial pathogen include Streptococcus pneumonia, Haemophilus influenza and Moraxella catarrhalis. Bacteria found in biofilms have their antibiotic resistant increased up to 1000 times when compared to bacteria free living of same species. Sinusitis also results from fungal invasion in patients with diabetes, immunedeficiencies, and AIDSor transplant patients. Bacterial and viral sinusitis are difficult to distinguish. The diagnosis of acute sinusitis should be on clinical presentation in most patients CT scan of sinuses is useful for patients with complications and in patients in whom sinus surgery is considered. MRI may have a role in the diagnosis of fungal rhinitis. The benefit of Functional Endoscopic Sinus Surgery (FESS) is its ability for a more targeted approach. Recently developed treatment by balloon sinuplasty is promising. A short-course of antibiotics is helpful in clinically diagnosed bacterial sinusitis without complicating factors.*
KEY WORDS: *Chronic Rhinosinusitis, Patho physiology ,and Treatment*

I. INTRODUCTION

Sinusitis, also known as **rhinosinusitis**, is inflammation of the paranasal sinuses. It can be due to infection, allergy, or autoimmune problems. Most cases are due to a viral infection and resolve over a course of 10 days. It is a common condition, with over 24 million cases in the Unites States [1].Evidence of maxillary sinusitis has been found in human archeological specimens discovered in Africa, North America, and Europe[2].Hippocrates recognized the association between high arched palate, nasal obstruction, headache, and discharging ears-probably what today would be called rhinosinusitis associated with otitis media. The first accurate description of the paranasal sinuses was by Vesalius in the 16thcentury, and the first documented cases of documented cases of supportive sinusitis were by Antonio Molinetti in Venice in 1697[3].Classification of sinusitis or rhinosinusitis include a)acute rhinosinusitis-a new infection that may last up to four weeks and can be divided symptomatically into severe and non-severe; b) recurrent acute rhinosinusitis four or more separate episodes of acute sinusitis that occur within one year; c)sub-acute rhinosinusitis-an infection that lasts between four and 12 weeks, and represents a transition between acute and chronic infection)chronic rhinosinusitis-when the signs and symptoms last more than 12 weeks; and e)acute exacerbation of chronic rhinosinusitis exacerbate, but return to base line treatment. All these types of sinusitis have similar symptoms, and are thus difficult to distinguish. Acute sinusitis is very common. Roughly ninety percent of adults have had sinusitis at some point in their life [4,5].Diagnosis of acute bacterial of viral sinusitis by imaging, Xrays,computed tomography(CT) or magnetic resonance imaging(MRI) is generally not recommended unless complications develop, for chronic sinusitis nasal endoscopy, and clinical symptoms are also used to make positive diagnosis[6,7],A tissue sample for histology and cultures also be collected[8].Cultures obtained via endoscopy or by sinus aspiration, bacterial pathogens isolated in order of frequency include *Streptococcus pneumoniae, Haemiphilus influenza*,Anaerobes, *Streptococcal* spp, *Moraxilla catarrhalis*, *Staphylococcus aureus*, methicillin resistant *Staphylococcus aureus*(MRSA) and others[9].Recommended treatments for most cases of sinusitis include rest and drinking enough water to thin mucus, antibiotics are not recommended for most cases Decongestant nasal sprays containing oxymetazoline may provide relief. However ,if symptoms do not resolve within 10 days, amoxicillin is to use first for treatment with amoxicillin/clavulanate being indicated when symptoms do not improve [10,6,7].There is limited evidence to support short treatment with oral cortico- steroids for chronic rhinosinusitis with nasal polyps[11]. Surgery should only be considered for those people who do not benefit with medication [11].The paper reviews the current literature, pathophysiology and treatment of acute and chronic rhinosinusitis.

II. PATHOPHYSIOLOGY

Pathogenesis of rhinosinusit is involves three key elements: narrow sinus ostia, dysfunction of the ciliary apparatus, and viscous sinus secretions. The narrow caliber of the sinus ostia sets the stage for obstruction to occur. Factors that predispose the ostia to obstruction include those that result in mucosal swelling and those that cause direct mechanical obstruction.0f these multiple causes viral upper respiratory infection (URI) and allergic inflammation are the most frequent and most important. During episodes of acute rhinitis, a completely patent ostia is present only 20% of time [12].When obstruction of sinus ostium occurs, there is transient increase in pressure within the sinus cavity. As oxygen is depleted in this close space, the pressure in the sinus becomes negative relative to atmospheric pressure. This negative pressure may allow the introduction of nasal bacteria into sinuses during sniffing or nose blowing [13].When obstruction of the sinus ostium occurs, secretion of mucous by mucosa continues, resulting in accumulation of fluid in the sinus. A study of adult volunteers investigated the role of nose blowing in introducing nasal fluid, and possibly microbes with the fluid, into the sinus cavities. Serial computed tomography (CT) scans showed that up to 1 ml of viscous fluid was propelled into the sinus when volunteers blew their noses. This one potential mechanism for nasal fluid and flora to contaminate the sinuses, particularly during common cold [14].However, young children who do not blow their noses still develop acute bacterial sinusitis, so there must be multiple factors that play a role in the development of acute infection [15].

Dysfunction of mucocilary apparatus also contributes to the pathogenesis of sinusitis. During viral colds, both the structure and the function of the mucociliary apparatus are impaired. In a study of children with viral URI,nasal mucosal biopsies were performed for the examination of the ultrastructure of the cilia. Dysmorphic ciliary forms involving micro tubular abnormalities were observed during the acute phase(7days) of illness. Progressive loss of ciliated cells was observed throughout the illness in a patch pattern [16].In a study of documented viralURI in adults. mucociliary clearance was measured with the use of a solution of dyed saccharin. Mucociliary clearance times, measured by taste and color, were significantly slower during acute phase of illness. Presumably these same changes in structure and function of the nasal mucosa during viral URI occur also in the sinus mucosa. This attributes to the reduced clearance of material and increases the likelihood of sinus cavity [17,].The quality and characters of sinus secretions also play a role in the pathogenesis of sinusitis. Cilia can beat only in fluid media. The mucous blanket in the respiratory tract consists of two layers. The *sol* phase is thin, low-viscosity layer that envelops the shaft of the cilia and allows the cilia to beat freely. A more viscous layer, the gel phase, rides on *sol* phase. Alterations in the mucous layer, which occur in the presence of inflammatory debris, as in infected sinus, may further impair ciliary movement [15].

Historically, it was believed that a reduction in airflow through the nasal passages contributes to the development of rhinosinusitis. However, an extensive review of this hypothesis found no convincing evidence that diminished airflow is a factor in sinus pathology [18].Except in experimental models; the histological findings during acute sinusitis were not well characterized until recently. In the rabbit model of acute sinusitis, histological changes include epithelial desquamation edema, and goblet cell hyperplasia.Of note is the distinct loss of ciliated cells from the epithelium [19].Berger and colleagues[20] examined biopsies of 11 humans who had acute sinusitis and surprisingly, found that epithelial layer of sinus remained intact. In contrast, the lamina propria showed edema and massive infiltration of neutrophils and mononuclear cells, including lymphocytes and plasma cells.Occasionally aggregates of inflammatory cells with micro abscesses were also detected. Thrombosed blood vessels and deep necrotic foci were observed in patients with complications of acute sinusitis. Immunohistologic staining showed T lymphocytes scattered throughout the lamina propria , with dense aggregates of B lymphocytes. An analysis of cytokine production in sinusitis showed that interleukin-8 (IL-8), a potent chemoattractant for neutrophils, is upregulated in the sinus during acute infection [21].In patients with acute sinusitis, healing of mucous occurs over a period of weeks after infection. In a study in which serial magnetic resonance imaging was performed in patients with acute bacterial sinusitis, clinical symptoms resolved within three days of treatment in most patients. Radiographic changes took much longer to show improvement, with only half of the sinuses showing resolution of opacification by 10 days. It took up to 56 days for 80% of the sinuses to be aerated [22].

It has been hypothesized that ***biofilm bacterial infections*** may account for many cases of antibiotic refractory chronic sinusitis [23].Biofilms are complex aggregates of extracellular matrix and interdependent microorganisms from multiple species, many of which may be difficult or impossible to isolate using standard clinical laboratory techniques [24].Bacteria found in biofilms have their antibiotic ***resistant increased up to 1000 times*** when compared to free living bacteria of same species. A recent study found that biofilms were present on mucosa of 75% of patients undergoing surgery for chronic sinusitis [25].

III. ETIOLOGIC AGENT

The nasal cavity is heavily colonized with respiratory flora, which can easily contaminate materials obtained from paranasal sinuses. In classic studies of the bacteriology of sinusitis, specimens of sinus secretions were obtained by puncture of the maxillary antrum to reduce the risk of nasal contamination. Infection is defined as bacterial colony count of at least 10^4 colony-forming units per milliliter (CFU/ml) of aspirated materials[26].Acute sinusitis is usually precipitated by an earlier respiratory tract infection, generally of viral origin, mostly caused by rhinoviruses, coronaviruses, and influenza viruses, other caused by adenoviruses ,human para influenza viruses, human respiratory syncytial virus, enteroviruses other than rhinoviruses, and metapneumovirus. If the infection is of bacterial origin, the most common three causative agents are *Streptococcus pneumoniae, Haemophilus influenza, and Moraxellacatarrhalis*[6].Until recently *Haemophilus influenza* was the most common bacterial agent to cause sinus infections.However, introduction of *H.influenzae* type B(Hib) vaccine has dramatically decreased *H.influenzae* type B infections and now non-type *H.influenzae*(NTHI) are predominantly seen in the clinics. Other sinusitis-causing bacterial pathogens include *Staphylococcus aureus* and other streptococci species, anaerobic bacteria and less commonly, gram negative bacteria. Viral sinusitis typically lasts for 7 to 10 days [6] whereas bacterial sinusitis is more persistent. Approximately o.5% to 2% of viral sinusitis results in subsequent bacterial sinusitis. It is thought that nasal irritation from nose blowing leads to the secondary bacterial infection [14].Acute episodes of sinusitis can also result from fungal invasion. These infections are typically seen in patients with diabetes or immune deficiencies (e.g., AIDS or transplant patients on immunosuppressive anti—rejection medication) and can be life threatening. In type 1 diabetics, ketoacidosis can be associated with sinusitis due to mucromycosis. *Aspergillus, Bipolaris, Curvularia* and *Exserohilum* have been associated with fungal sinus disease [27,28].Chemical irritation can also trigger sinusitis, commonly from cigarette smoke and chlorine fumes[29].Rarely, it may be caused by a tooth infection[6].

Chronic sinusitis represents a multifactorial inflammatory disorder, rather than simply a persistent bacterial infection. A combination of anaerobic and aerobic bacteria, are detected in conjunction with chronic sinusitis. Also isolated are *Staphylococcus aureus* (including methicillin resistant *S.aureus*-MRSA) and coagulase-negative Staphylococci and Gram negative enteric organisms can be isolated[6].Attempts have been made to provide a more consistent nomenclature for subtypes of chronic sinusitis.The presence of eosinophils in mucous lining of the nose and paranasal has been demonstrate for many patients, and this has termed ***eosinophilic mucin rhinosinusitis***(EMRS).Cases of EMRS may be related to an allergic response, but allergy is not often demonstrated, resulting in further subcategorization into allergic and non-allergic EMRS[30].A more recent, and still debated, development in chronic sinusitis is the role that fungi play in this disease. It remains unclear if fungi are definite factor in the development of chronic sinusitis and if they are, what the difference may be between those who develop the disease and those who remain free of symptoms. Trials of antifungal treatments have mixed results [27].

IV.CLINICALMANIFESTATIONS

The pathogenesis of sinusitis and viral URI are similar, the clinical manifestations of these two diseases overlap greatly. Nasal symptoms such as congestion and discharge are prominent in viral URI. Nasal discharge has a predictable pattern in its progression-from clear and watery, to mucoid and thick, and finally to colored and opaque before resolving [31].The clinical presentation of acute community- acquired bacterial sinusitis falls into three predictable patterns. **The first** is that of persistent symptoms, characterized by nasal discharge or cough or both that last longer than 10days without improvement. Because the symptoms of a viral URI are expected to improve by 10 days, it is the lack of improvement that is a sign of an acute bacterial process. Accompnying symptoms may include periorbital edema, malodorous (Halitosis-bad breath) breath or low grade fever. The nasal discharge may vary in character from thin and mucoid to thick and purulent. **The second** presentation is characterized by the onset of severe symptoms. Fever accompanies purulent nasal discharge that is present over 3-to 4 –day period. These patients often appear ill. Worsening symptoms characterize **the third** presentation [32,33].These patients have an initial regression of symptoms of cough, nasal discharge, and congestion but then worsen again within 10 days of illness. Worsening may be signaled by new onset of fever, increasing nasal discharge, congestion or daytime cough[32].Patients with chronic rhinosinusitis have symptoms for at least 12 weeks. The presentation of each patient is characterized by anterior or posterior mucopurulent drainage and nasal obstruction .Facial pain or pressure, as well as hyposmia are frequently present in patients with chronic sinus disease[15].The physical examination is of limited utility in the diagnosis of sinusitis,mainly because of similarity of findings between patients with a viral URI and those with a bacterial process. Mucopurulent discharge may be found on the nasal mucosa. The mucosa itself is erythematous and mildly edematous.Facial tenderness over the maxillary or frontal area may be present ,but this is an unreliable finding. Periorbital edema and mild discoloration of the skin below the eyelids is occasionally observed.

Malodorous breath in the absence of dental disease or exudative pharyngitis may accompany acute sinusitis. Chronic sinusitis is characterized by facial discomfort and the presence of mucopurulent discharge in the middle meatus. Polyps may be present in the nasal cavity or the middle meatus [15]. Infection of eye socket is possible, which may result in the loss of sight and is accompanied by fever and severe illness.Another complication is infection of bones (osteomyelitis) of forehead and other facial bones-**Pott's puffy tumor**[33].Sinus infections can also cause middle ear problems due to the congestion of nasal passages. This can be demonstrated by dizziness "a pressurized or heavy head", or vibrating sensation in the head, Post-nasal drip is also a symptom of chronic rhinosinusitis. Halitosis is often is often stated to be a symptom of chronic rhinosinisitis, however gold standard breath analysis techniques have not been applied. Theoretically there are several possible mechanisms of both objective and subjective halitosis that may be involved [34].A 2004 study suggested that up to 90% of "sinus headaches" are actually migraines[35].The confusion occurs in part because migraine involves activation of the trigeminal nerves, which innervate both the sinus region and the meninges surrounding the brain. As a result, it is difficult to accurately determine the site from which pain originates. People with migraines do not typically have the thick sinus discharge that is common symptom of sinus infection [36].

Complications of rhinosinusitis. The close proximity of the brain to the sinuses makes the most dangerous complication of sinusitis, particularly involving the frontal and sphenoid sinuses, infection of the brain by the invasion of anaerobic bacteria through the bones or blood vessels .Abscesses, meningitis and also life threatening conditions may result. In extreme cases the patient experience mild personality changes,headache, altered consciousness, visual problems, seizure, coma and possibly death[33],Sinus infection can spread through anstomosing veins or by direct extension to close structures. Orbital complications were categorized by Chandler et al. into five stages according to their severity that include1)preseptal cellulitis 2)orbital cellulitis 3)subperiosteal abscess 4) orbital abscess and 5)cavernous sinus septic thrombosis. Contagious spread to orbit may result in periorbital cellulitis, subperiosteal abscess, orbital cellulitis, and abscess.Orbital cellulitis can complicate acute ethmoiditis if anterior and posterior ethmodal veins thrombophlebitis enables the spread of infection to the lateral or orbital side of the ethmoid labyrinth. Sinusitis may extend to the central nervous system, where it may cause cavernous sinus thrombosis, retrograde meningitis, and epidural, and brain abscess[37].

V.DIAGNOSIS

The symptoms and signs of viral rhinosinusitis so closely overlap those of a bacterial process, the challenge to clinicians is to identify those patients with upper respiratory symptoms who have acute bacterial sinusitis and would benefit from treatment with an antibacterial agent. Several studies have attempted to correlate signs and symptoms with the results of the radiographic studies or cultures obtained through endoscopy(neither of which is a gold standard).Many of these studies have methodologic issues[15].Williams and associates studied 247 men with suspected sinusitis using four plain radiographic views as the standard of diagnosis[38].The signs and symptoms that showed the most consistent correlation with abnormal radiographs were maxillary toothache, poor response to decongestant, colored nasal discharge by history, purulent rhinorrhea on examination, and positive trans illumination on physical examination. When all five factors were present, clinicians predicted sinusitis correctly 92% of the time. Individual symptoms associated with the rhinosinusitis failed to have the sensitivity and specificity needed to correctly diagnose patients with sinusitis. However, abnormal radiographs are not the gold standard. Lacroix and colleagues found a correlation between facial pain colored discharge and/or abnormal radiographic findings and response to antimicrobial treatment. However, when these three findings were present concurrently, the sensitivity was only 69% and the specificity 64% insufficient to be relied upon in the clinical setting [39].The duration of respiratory symptoms is useful in discerning which patients have probable acute bacterial sinusitis. Studies on the microbiology of sinusitis in children showed that if rhinorrhea persisted at least 10 days with no improvement, that bacterial burden in the sinuses was high [40].This finding was further validated by a study in children in an outpatient setting using plain radiographs as a confirmatory diagnostic test. Of 2000 children with respiratory complaints,135 had at least 10 days of symptoms. Radiographic evidence of sinusitis was present 92.5% of these patients, demonstrating a strong correlation between at least 10 days of symptoms and the presence of sinus disease[41].Kenny and workers correlated the severity of patients symptoms with findings on CT of the sinuses. Patients 8 to 82 years of age with symptoms of acute or chronic sinusitis were asked to rank symptom severity. When patients rated symptoms of fatigue, lack of sleep, nasal discharge, stuffy nose, or a decreased sense of smell as severe, there was a strong correlation with abnormal findings on CT scans of the sinuses. In this study, symptoms of facial pain and headache did not correlate well with CT evidence of sinus disease [42].

Acute sinusitis Bacterial and viral sinusitis are difficult to distinguish .However, if symptoms last less than 10 days, it is considered viral sinusitis. When symptoms last more than 10 days, it is considered bacterial sinusitis [6].Imaging by either, CT or MRI is generally not recommended unless complications develop. Pain caused by sinusitis is sometimes confused for pain by pulpitis (toothache) of maxillary teeth, and vice versa. Classically, the increased pain when tilting the head forwards separates sinusitis from pulpitis[6].

Chronicsinusitis. For sinusitis lasting more than 12 weeks a CT scan is recommended[6].Nasal endoscopy, and clinical symptoms are also used to make a positive diagnosis[7].A tissue sample for histology and cultures can also be collected and tested. Allergic fungal sinusitis (AFS) is often seen in people with asthma and nasal polyps. In rare cases, sinusoscopy may be made. Nasal endoscopy involves inserting a flexible fiber-optic tube with a light and camera at its tip into the nose to examine the nasal passages and sinuses. This is generally a completely painless (although uncomfortable) procedure which takes between five to ten minutes to complete [8].A meta-analysis of studies comparing plain radiographs with sinus puncture and culture demonstrated a sensitivity of 90% and specificity of 61% for plain radiograph [43,] In summary, the diagnosis of acute sinusitis should be made on clinical grounds in most patients. CT of sinuses is useful for evaluation of patients with infraorbital or intracranial complications of sinusitis and for the evaluation of patients in whom sinus surgery is being considered [32].Magnetic resonance imaging may have a role in the diagnosis of fungal rhinitis and is useful in diagnosis of intracranial complications of sinusitis [15].

VI. TREATMENT

Decongestant nasal sprays containing for example oxymetazolin may provide relief, but these medications should not be used for more than the recommended period. Longer use may cause rebound sinusitis [44].It unclear if nasal irrigation, antihistamines, or decongestants works in children with acute sinusitis [45].The vast majority of sinusitis are caused by viruses and will therefore resolve without antibiotics. Antibiotics recommended only if symptoms do not resolve within 10 days[7].Antibiotics are specifically not recommended in those with mild/moderate disease during first week of infection due to risk of adverse effects, antibiotic resistance, and cost[46].Because of increasing resistance to amoxicillin the 2012 guideline of the Infectious Diseases Society of America(IDSA) recommends amoxicillin-clavulanate as the initial treatment of choice for bacterial sinusitis[47].The guidelines also recommend against other commonly used antibiotics, including azithromycin, clarithromycin and trimethoprim /silfametoxazole, because of growing drug resistance. A short-course(3-7 days) of antibiotics seems to be just as effective as the typical longer-course(10-14 days) of antibiotics for those with clinically diagnosed bacterial sinusitis without other severe disease or complicating factors[48].IDSA guideline suggest five to seven days of antibiotics is long enough to treat a bacterial infection without encouraging resistance. Guidelines still recommend children receive antibiotic treatment for ten to two weeks [47].Most recommend that antibiotics be prescribed for those patients with clinically diagnosed acute sinusitis. One such guideline recommends, watchful waiting for at least 10 days but leaves antimicrobials as an option for the clinicians [32,6]. For unconfirmed acute sinusitis, intranasal corticosteroids have not been found to be better than a placebo either alone or in combination with antibiotics [49].For cases confirmed by radiology or nasal endoscopy. Treatment with corticosteroids alone is supported. The benefi thowever, issmall [50,50].Surgery should only be considered for those people who do not benefit with medication. It is unclear how benefits of surgery compare to medical treatment in those with nasal polyps as this has been poorly studied [11,52].Maxillary antral washout involves puncturing the sinus and flushing with saline to clear the mucus. A 1996 study of patients with chronic sinusitis found that washout confers no additional benefit over antibiotics alone [53].A number of surgical approaches can be used to access the sinuses and these have generally shifted from exteral/exteranasal approaches to intranasal endoscopic ones. The benefits of **Functional Endoscopic Sinus Surgery**(FESS) is its ability to allow for a more targeted approach to the affected sinuses, reducing tissue disruption, and minimizing post-operative complications[54].The use of drug eluting stents such as propel mometasome furoate implant may help in recovery after surgery. Another recently developed treatment is **balloon sinuplasty**. This method is, similar to balloon angioplasty used to ”unclog” arteries of the heart, utilizes balloons in an attempt to expand the openings of the sinuses in a less invasive manner. The utility of this treatment for sinus is still under debate but appears promising [54]..However, surgery may be considered as a treatment option in those patients with chronic sinusitis recalcitrant to medical therapy [33].

VII. CONCLUSION

Acute and chronic rhinosinusitis have similar symptoms, although acute sinusitis is more common. Studies to correlate signs and symptoms with radiographic or culture results, have methodologic issues. A short-course of antibiotics is as effective as the longer-course Infectious Diseases Society of America (IDSA) guidelines are useful.

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