

**RESEARCH ARTICLE****GRANULOMATOUS AND CHRONIC INVASIVE FUNGAL SINUSITIS: AN OVERVIEW.****Saleh Khalid Alqaryan.*****Manuscript Info******Manuscript History:***

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Sinusitis is one of the most common chronic disease placing a huge impact on the health care system and the economy. Fungal sinusitis is subject to many different factors which include diabetes mellitus, hematological malignancies, steroids, liver cirrhosis and others. It is divided into noninvasive and invasive fungal sinusitis. Invasive fungal sinusitis includes acute fulminant, granulomatous and chronic invasive subtypes. This article aims to shed some light over the chronic form of invasive fungal sinusitis and warrant clinicians about its progressive and notorious prognosis.

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Introduction:-

Fungal sinusitis constitutes up to 9% of sinusitis. Globally, *Aspergillus fumigatus* and *Aspergillus flavus* are the most common fungi affecting the sinuses,(1) however, India seems to be the exception to this rule as its rates of zygomycosis are higher than those of aspergillosis.(2) Incidence of invasive fungal rhinosinusitis has demonstrated an incremental pattern of growth in recent years with a mortality rate that reaches up to 80%.(3) Invasive fungal sinusitis can be defined based on histologic evidence of fungal hyphae within the mucosa, submucosa, bone, or blood vessels.(4) The ubiquitous nature of fungal spores aids in their colonization of the respiratory passages. Invasive fungal rhinosinusitis is subject to many factors, which include diabetes mellitus, hematologic malignancies, iatrogenic immunosuppressants, and HIV.(3)

Invasive fungal rhinosinusitis can be divided into acute and chronic forms. The acute form, which is also referred to as acute fulminant, usually occurs in immunocompromised patients and persists for approximately four weeks.(5) A diagnosis of the chronic form indicates that the symptoms have usually extended beyond 12 weeks. This form can be further divided into chronic and granulomatous subtypes. The difference between these two subtypes is based solely on their histopathological characteristics as the chronic type is marked by the dense accumulation of the hyphae, angiocentric invasion, and the involvement of the surrounding area, while the granulomatous form is characterized by non-caseating granuloma with foreign bodies or giant cells, vasculitis, vascular proliferation, and perivascular fibrosis.(4) Furthermore, the chronic subtype resembles the acute form in that it affects those who are immunocompromised. In contrast, the granulomatous subtype mainly affects immunocompetent patients and *Aspergillus flavus* is most commonly the cause.(6)

Diagnosis:-

The importance of an early diagnosis of invasive fungal sinusitis cannot be overstated. In order to ensure precise treatment, it is vital that the fungal sinusitis is correctly classified during the diagnostic stage.(8) There are several different qualifications for the diagnosis of granulomatous fungal sinusitis and chronic invasive fungal sinusitis.(8) In both cases, the patient will present with the traditional symptoms of chronic sinusitis, which typically include headache, facial/sinus pressure, discharge, nasal stuffiness, and a cough.(7, 9) In addition to these symptoms, the individual will present with persistent sinusitis with no changes to mental status or fever, although he or she may

present with orbital apex syndrome, which is categorized by a decrease in vision and immobility of the oculus.(7, 9, 10) In the case of granulomatous invasive fungal sinusitis, all of the symptoms associated with long-standing sinusitis will be present, and proptosis will likewise be present; in both cases, a nasal cavity examination is likely to reveal little in the way of evidence, while the eye exam is likely to lead to a diagnosis.(7, 9)

To confirm a diagnosis of invasive fungal sinusitis, histological evidence of the presence of fungus within the tissues is needed.(12) Regarding imaging, CT is the modality of choice as it shows the soft tissue extension and the bony erosion caused by the disease. Additionally, CT is useful both preoperatively and in the patient's follow-up. MRI can aid in making the diagnosis and it is used to reveal the cranial invasion.(5, 11, 12) Additional means of diagnosis include endoscopic biopsy, partial debridement of the sinus cavity, and histological examination of the inflamed area.(5, 11) The results of such methods of diagnosis are used as a means of identifying the type of fungal sinusitis that is present in the individual, which in turn determines the medical treatment that will follow. Moreover, patients that have been diagnosed with one of the forms of invasive fungal sinusitis will most likely exhibit elevated levels of Immunoglobulin E.

Treatment:-

The mainstay of the management of invasive fungal sinusitis is a combination of surgical debridement and antifungal agents.(16)

Medical Treatment:-

Depending on the patient's age and additional diagnoses, certain treatment options may be taken. However, the preferred primary course of action to tackle any form of fungal sinusitis is surgery to treat the infection.(15) For the treatment of chronic invasive fungal sinusitis, surgery is mandatory; in the case of granulomatous fungal sinusitis, surgical debridement is the primary recommendation.(15)

Antifungal treatment for fungal sinusitis includes triazoles (itraconazole, voriconazole, posaconazole), polyenes (amphotericin and its lipid formulations), and other agents (echinocandins and flucytosine). Amphotericin B covers *Aspergillus* spp., *Candida* spp., and *Cryptococcus* spp. The fungicidal activity of triazoles makes them the antifungal of choice to combat *Aspergillus* spp. In contrast to other triazoles, posaconazole is particularly effective against zygomycetes.(16) One of the limitations of amphotericin B is its nephrotoxicity. This adverse effect can be mitigated by administering its lipid formulation.(1)

In the treatment of either subtypes, surgery is typically followed by an intravenous regimen of amphotericin B or itraconazole to assist in preventing recurrence of infection and to remove the residual disease.(12, 15, 17, 20) Many experts currently prefer voriconazole over amphotericin B as it exhibits better results, fewer adverse effects, and greater tolerability.(18, 19)

Surgery:-

Surgery is the preferred treatment option for all forms of fungal sinusitis.(15, 24-28) Surgery is most successful in treating the illness and preventing its recurrence if followed by a drug regimen lasting for a period of weeks to a period of months, depending on the severity of the infection and other comorbidities that the patient may have.(15, 24-28) The necessity of surgical treatment relates to the fact that it significantly decreases the viral load.(29) There are several different types of surgery that may be used to remove the fungal infection and the choice of surgery used in the completion of the event will depend on the preferences of the surgeon, the severity of the infection, and the health conditions of the patient.(25-28)

Approaches to tackle this disease can be divided into three categories. Firstly, an endonasal approach alone should be undertaken if the lesions are not intimately connected to vital structures which include the optic nerve, internal carotid artery, and cavernous sinus. Secondly, a combined transcranial and endonasal approach is indicated for safe eradication of fungal sinusitis with intracranial extension. Thirdly, a transcranial approach alone is reserved for intracranial complications caused by isolated sphenoidal sinus involvement.(12) If the disease is advanced, then the surgical procedure would be more aggressive and may aim to eradicate the infected tissue by orbital exenteration or maxillectomy.(29)

Complications:-

In spite of the management, the general prognosis of invasive fungal sinusitis is poor.(5) Potential complications can be divided into three categories: surgery-related, drug-related, and disease-related. Common complications for sinus surgery include, but are not limited to, bleeding, damage to the patient's vision or to the structure of the patient's eye, typical complications associated with anesthesia, and even intracranial complications.(30) Patient may acquire a secondary infection in the hospital at the site of the surgical incision.(25-28) Drug-related complications can manifest in the nephrotoxicity of amphotericin B and visual disturbances and photosensitivity of voriconazole.(5) The disease-related complications can be further divided into three types. First are the local complications, which include mucocele, osteomyelitis, and Pott's puffy tumor. Second are the orbital complications, which may include preseptal edema, orbital cellulitis, orbital abscess, and cavernous sinus thrombosis. Third are the intracranial complications, which include brain injury, CSF leak, and meningitis or encephalitis.(30, 31)

Conclusion:-

There seems to be an increase rate of cases of granulomatous and chronic invasive fungal sinusitis. The importance of early diagnosis cannot be overemphasized. Diagnosis is usually based on histopathology. CT and MRI can aid the diagnosis and treatment. Combination of aggressive surgical debridement and appropriate antifungal agents yield the best outcome.

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