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"ZYGOMYCOSIS (MUCORMYCOSIS) AND REVIEW OF THE LITERATURE"

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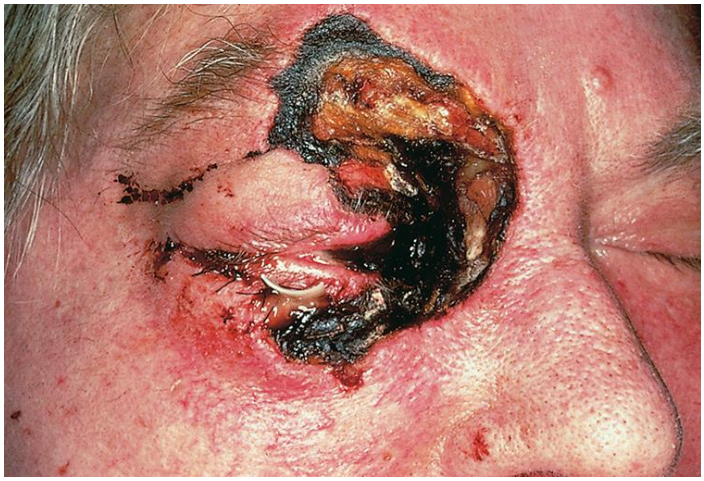
Abstract : Mucormycosis is an oppourtunistic fungal infection due to organism ot the zygomycetes class and the order of Mucorales that can cause various types of infections.Fungal infection is an uncommon complication after renal transplantation we describe a rare form of Mucormycosis in the renal graft. An infected large perigraft collection was drained,but the patient became anuric and septic.Mucormycosis is an emerging invasive fungal infection,primarily affecting immunocompromised patients. Pulmonary mucormycosis is relatively uncommon but an important opportunistic fungal infection in immunocompromised persons. Among immunocompromised patients, an important clinical emergency could be represented by mucormycosis. Zygomycosis is a rare fungal infection seen most often in associated with prolonged neutropenia. According to the latest recommendations diagnosis is based on direct examination of clinical specimens, and or histopathology, and culture. We performed a Pubmed Search on reports of patients with mucormycosis treated with Posaconazole.

Key words: Immunocompromised patients, rhinocerebral mucormycosis, diabetes mellitus, posaconazole, etc.

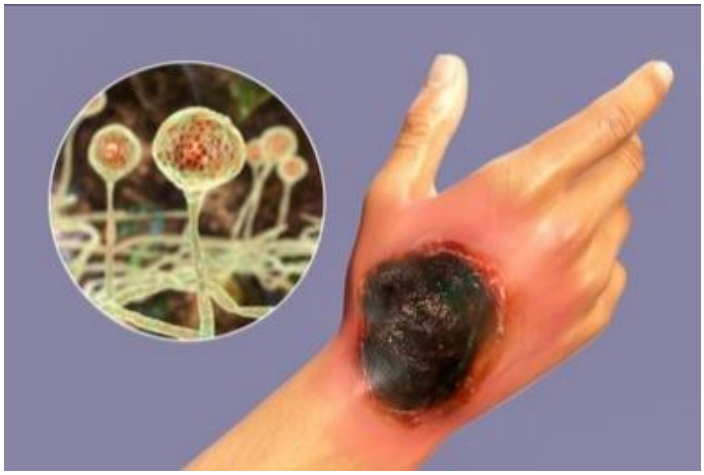
I. Introduction :-

Infection is the major cause of death in this patient population [1] .Indeed in a recent autopsy study 102 renal transplant recipients, fungal infection were responsible for 27.5% of infectious deaths[2]. Mucormycosis is usually a rapidly progressive and frequently fatal infection in renal transplant patients[3]. Rarely mucormycosis developed in the kidney allograft itself[4].Mucormycosis reffere to a spectrum of disease presentations caused by fungi of the class Zygomycetes, order Mucorales. These ubiquitous organisms are common in habitants of decaying matter.(e.g.moldy bread). The vast majority of mucormycosis infections have been descibed in patients with systemic or local conditions that are associated with a severely immunocompromised state (e.g. diabetes mellitus, HIV, malignancies chemotherapy,burns etc.)[1]. Mucormycosis has been reported in recipients of kidney, liver, lung, heart and bone marrow transplants [5]. The fungus enters the body through either the respiratory tract, the digestive tract or a damaged skin barrier. Mucor infection within the renal graft as occurred in our patients, is a rare complication. We found only three previous reports of similar cases [4] [6].

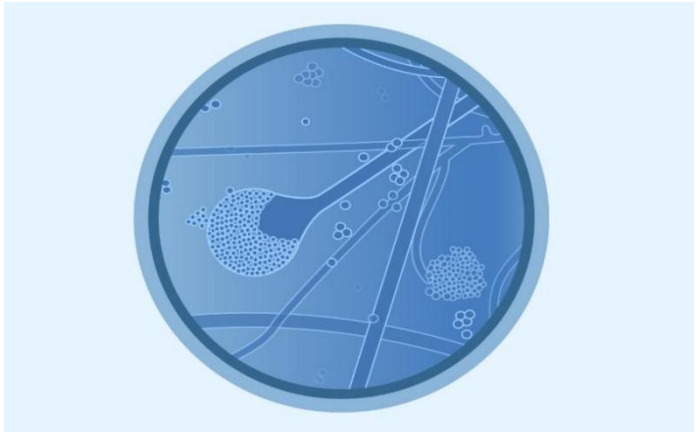
Zygomycosis is the third most common causes of fungal infection after candidasis and aspergillosis[7][8]. Intestinal zygomycosis is extremely rare andit is difficult to obtain a histological diagnosis, although it may be possible by means of computerised tomography guided biopsyof abnormal mucosa[9]. Zygomycosis has a high mortality of 70-100 %, but some patients may be cured by surgical excision and Amphotericin. " The diagnosis of Zygomycosis is rarely suspected and antemortem diagnosis is made in only 23-50 % of cases".Zygomycosis is rare invasive fungal infection, which is most often seen in immunocompromised patients, particularly during prolonged neutropenia. It is caused by various members of the phycomycetes, such as rhizopus, mucor and absidia[7-10].



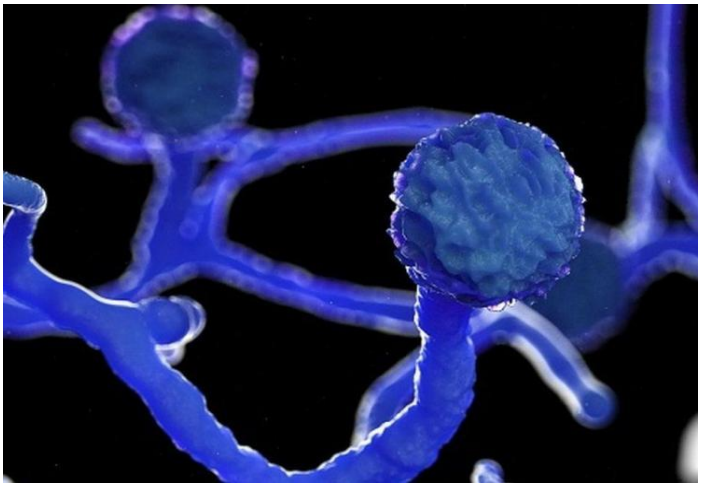
Img. 1. Skin Mucormycosis.



Img. 2 . Skin Mucormycosis.



Img.3.Mucormycosis



Img.4. Mucormycosis.

Gastrointestinal zygomycosis has been reported in neonates. It is presents as necrotising enterocolitis and invariably fatal [11][12]. In the neutropenic phase, inflammation of the ileum is often caused by typhiltis post chemotherapy. However, this condition resolves spontaneously when the neutrophil count recovers. Neutropenic fever can be common presenting feature of Zygomycosis [9-12]. The treatment of choice is amphotericin, preferably the lipid formulation, because adequate dosage can be delivered with reduced renal toxicity. The common prophylactic antifungal agents such as fluconazole and itraconazole are not active against the fungus[8-12].The new triazole antifungal agent posaconazole, has been compared with amphotericin B, voriconazole and itraconazole in in-vitro studies. Posaconazole was significantly more active than voriconazole and other agents[7-10].

Mucormycosis reffers to different diseases caused by fungal infection the most common organism is the Rhizopus species[13]. The major route of infection is through inhalation ,and when the spores are deposited in the nasal turbinates ,rhinocerebral disease developed.[14]. The rhinocerebral mucormycosis causes significant morbidity and requires rapid diagnosis with aggressive medical and surgical therapy[15]. According to anatomic localisation ,mucormycosis can be classified as ,Rhinocerebral ,Pulmonary ,Cutaneous ,Gastrointestinal and Disseminated[16]. Most patients with rhinocerebral disease have diabetes (especially with ketoacidosis) and this was typically observed in our patients as he was developing COVID-19 infection [17].

As it was shown that the mortality rate of rhinocerebral mucormycosis is possibly reaching 50-70 % and the mortality rate associated with disseminated disease is approaching 100 % [18]. Disseminated mucormycosis involving the lungs and brain at Post-mortem study [19].

Risk factors-There are multiple risk factors for mucormycosis such as haematological malignancies and neutropenia ,but the infections are also seen in transplant patients, diabetic patients or following trauma or burns [20]. The clinical presentation depends not only on the underlying disease ,but also on the species involved[21]. Many species can cause mucormycosis and recently emerging and or new species have been reported , such as Saksenaea erythrospora or Rhizopus homothallicus [22][23]. Histopathology is also strongly recommended . Immunohistochemistry is possible by using monoclonal
antibodies that are commercially available ,but it needs trained personnel and specialized laboratories[24].

A communicable disease ,also known as an infectious disease ,could be defined as “an illness caused by a specific infectious agent or it’s toxic product that results from

transmission of that agent or it's products from an infected persons ,animal or reservior to a susceptible host ,either directly or indirectly through an intermediate plant or animal host ,vector or in animate enviornment ".Infectious disease can occur as both endemic (disease constantly present in a population or in certain geographical area) and epidemic (sudden increase in the number of cases ,higher than expected).When an epidemic is geographically very extensive and affects many individual of the population ,it is called a pandemic [25]. In recent years ,mucormycosis ,a fungal infection caused by Mucorales ,is becoming an interesting and alarming phenomenon [26] because of the increase in cases ,the high mortality rates ,and the lack of effective antifungal treatments . In the past ,it was considered a rare infection and limited to patients with severe immune alterations (for e.g.- Patients suffering from AIDS ,diabetes ,organ transplants , or other conditions associated with immunosuppression [27].

In recent years ,the epidemilogy of mucormycosis has shown an alarming trend especially in countries such as India & China ,a rise in incidence especially among patients with uncontrollerd diabetes mellitus has been observed [28]. The most frequently isolated from patients are Apophysomyces (A .Variabilis), Cunnighamella (C . bertholletiae), Lichethmia (L. corymbifera L.raosa), Mucor (M.circinelloides) ,Rhizopus (R.pusillus), and Saksenaea (S.vasiformis) [27]. Pulmonary mucormycosis is realtively uncommon infection that occurs mostly in immunocompromised persons. The first case of pulmonary mucormycosis was described in 1876 by Furbringer [29].

Mucormycosis often subsumed under the term zygomycosis is a rare ,but severe and often life threatening disease [30].Rhinocerebral, pulmonary, cutaneous and disseminated infections are among the most common entities [34]. Disease is the most common of the so-called rare invasive fungal disease (IFD) [31]. However, insulin and non-insulin dependent diabetes mellitus play a major role as risk factors in some regions of the world ,whwere they outnumber patients with iatrogenic immunosuppression [32].Posaconazole is a well tolerated extended spectrum compound and exhibits in-vitro activity against mucorales [33].

3.Signs & Symptoms :-

Neutropenic fever can be common presenting feature of Zygomycosis [9].

Rhinocerebral disease may be manifest as unilatera hedache, facial pain ,numbness , fever , hyposmia & nasal congestion ,which progressess the black discharge [17].

Patients may present with non specific symptoms such as fever , abdominal pain , & diarrohea [9].

2.TREATMENT :-

2.1.Antibiotic :-

Four elements are fundamental for a successful tretment :- Rapid diagnosis, Reduction of predisposing factors ,(if possible), surgical debridment of infected tissues & appropriate antifungal therapy [27]. Two case series have been reported so far, described the first 24. Patients treated with posaconazole as salvage therapy for active mucormycosis who were enrolled in an open label , non randomized multicenter compassionate use trial [36]. Surgical debridment which may begin as a diagnostic procedure & antifungal compounds are corner stones in the treatment of mucormycosis [34]. The new triazole antifungal agent , posaconazole , has been compared with amphotericin B , voriconazole & itraconazole in in-vitro studies . Posaconazole was significantly more active than voriconazole & other other agents [35].

2.2.Surgery :-

Antifungal therapy only is often unable to completely control mucormycosis because of it's rapid progression furthermore , it frequently has insufficient penetration of anti-infective agents into the site of infection due to the mulyiple distinctive characteristics of the disease (the angioinvasion , thrombosis, tissue necrosis). Therefore, the antifungal agent may be ineffective in vivo , even if the in vitro test has shown a discrete susceptibility[37].

2.3.Antifungal Therapy :-

In vivo and in vitro laboratory studies & some clinical studies have demonstrated the efficacy of amphotericin B (AMB)[38]. However the optimal dosage of amphotericin B for the treatment of mucormycosis (as ready occurs with many antifungal agents and mycoses is still undetermined lipid formulation of amphotericin have a significantly lower toxicity on kidney function compared to amphotericin B deoxycholate & can be safely administered at higher doses over a longer period of time)[39].

4.Conclusion :-

Pulmonary mucormycosis is a serious and life threatening condition specially if follow COVID-19 infection in immunocompromised patients with coexisting medical illnesses as a diabetes mellitus , and further imposed by heavy use of steroids , we need to ruminate on whether the patient developes the skin lesions and necrosis or neurological manifestations.

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