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Case Report of Rhino-Orbital Mucormycosis Associated with COVID-19

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Rezumat

Mucormicoză rino-orbitară asociată cu COVID-19 – prezentare de caz

Mucormicoza rino-orbitară este o infecție fungică invazivă rară cauzată de o ciupercă aparținând ordinului Mucorales. Constituie o boală fulminantă cu risc vital, cu rate ridicate de morbiditate şi mortalitate în ciuda tratamentului. Pacienții imunodeprimați sunt în primul rând afectați şi infecția survine aproape întotdeauna la bolnavi cu diabet zaharat necontrolat, îndeosebi la cei aflați în cetoacidoză diabetică. Cel de-al doilea val al pandemiei de COVID-19 pandemic a generat creşterea raportărilor de mucormicoză orbitară, în special în India. S-a sugerat pe larg faptul că terapia cortizonică prelungită asociată cu disglicemia determinată de diabet ar oferi o oportunitate excelentă pentru invazia fungică. Lucrarea prezintă cazul unui bărbat în vârstă de 64 de ani, internat în clinica noastră în septembrie 2024, cu diagnosticul prezumptiv de celulită orbitară dreaptă. Din antecedentele patologice ale pacientului se remarcă o pneumonie recentă în context COVID-19, tratată în alt spital, precum şi diabetul zaharat de tip 2 sub tratament cu insulină. După investigații paraclinice extinse şi dată fiind evoluția rapidă a semnelor clinice în ciuda terapiei intensive şi complexe instituite, s-a stabilit diagnosticul de mucormicoză rino-orbitară. Cazul de față susține ipoteza potrivit căreia triada nefastă diabet, corticoterapie şi contextul infecției COVID-19 determină risc crescut de mucormicoză şi faptul că se impun cercetări extinse pentru a găsi tratamentul optim pentru asemenea cazuri.

Cuvinte cheie: COVID-19, mucormicoză rino-orbitară, corticosteroizi, diabet, pacienți imunodeprimați

Abstract

Rhino-orbital mucormycosis is an uncommon invasive fungal infection caused by a fungus belonging to the order Mucorales. It is a life-threatening, fulminant disease with high rates of morbidity and mortality despite treatment. Immunocompromised patients are primarily affected,

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and it almost always occurs in patients with uncontrolled diabetes mellitus, especially those in diabetic ketoacidosis. The second wave of the COVID-19 pandemic emerged with increased reports of rhino-orbital mucormycosis, especially in India. It has been widely suggested that prolonged steroid therapy coupled with dysglycemia resulting from diabetes provides an excellent opportunity for fungal invasion. We report the case of a 64-year-old male admitted to our clinic in September 2024 with the presumptive diagnosis of right orbital cellulitis. The patient's history revealed recent COVID-19-related pneumonia, hospitalized in a different hospital, and type 2 diabetes mellitus with insulin treatment. After extensive paraclinical investigations, and given the rapid evolution of the clinical signs, despite intensive and complex therapy, we concluded the diagnosis of Rhino-orbital mucormycosis. Our case supports the hypothesis that the ominous triad of diabetes, corticosteroid use, and the background of COVID-19 determines the increased risk of mucormycosis, and that extensive research must be conducted to find the optimal treatment for these cases.

Keywords: COVID-19, rhino-orbital mucormycosis, corticosteroid, diabetes, immunocompromised patients

Introduction

Fungal infections, despite their high morbidity and high mortality rates worldwide, have often been neglected (1). Their considerable impact needs to be addressed by developing appropriate diagnostics and therapeutics for fungal infections (2). Mucormycosis, also known as black fungus, is a rare and life-threatening angioinvasive fungal infection, belonging to the order Mucorales, which includes Rhizopus, Apophysomyces, Rhizomucor, Lichtheimia, Cunninghamella, Mucor, and Saksenaea (3). The most common causative agent of mucormycosis is Rhizopus arrhizus (4,5). Mucorales spores dispersed in dust particles gain entry into a human host via the respiratory tract and skin or a breach in the mucosal barrier/ traumatized sites, and fungal spore germination and proliferation lead to cutaneous necrotizing fasciitis and/or disseminated mucormycosis infections (6,7). In immunocompromised hosts, the defense mechanisms break down, and Mucorales multiply rapidly upon encountering a favorable environment (8,9). The impairment of host defense mechanisms, such as decreased phago-cytosis during immunocompromising conditions, including hyperglycemia and glucocorticoid treatment, aids fungal growth and leads to disease progression (10,11). During the SARS-CoV-2 pandemic, an increase in mucormycosis cases was reported, causing severe infections in COVID-19 patients (12). Uncontrolled diabetes, as well as systemic cortico-steroid treatment, were present in most patients with COVID-19-associated mucormyco-sis, and rhino-orbital cerebral mucormycosis was the most frequent disease. Mortality was high at 49%, which was particularly due to patients with pulmonary or disseminated mucormycosis or cerebral involvement (13).

Case Report

A 64-year-old male was referred to our clinic in September 2024 with right eye pain, decreased vision, and periorbital swelling and paresthesia. The patient reported the sudden onset of the symptoms 4 days prior to the presentation. The patient's history revealed recent COVID-19-related pneumonia, hospitalized for 20 days in another local hospital (with hospital discharge on the same day of the presentation to our clinic), and type 2 diabetes mellitus with insulin treatment. The patient was admitted with the presumptive diagnosis of right orbital cellulitis.

The initial clinical examination revealed a conscious, cooperative patient, afebrile, with satisfactory general condition, right facial hemi-paresis, right eye: BCVA (best corrected visual acuity) - 0.80, IOP (intraocular pressure) 40 mmHg, superior palpebral ptosis with intense red edema, celsian signs present, intense conjunctival hyperemia with chemosis, limited and painful ocular movement in all directions; all other right eye structures were typical, with normal reactive pupil. In the left eye: BCVA -1, IOP 14 mmHg, regular non-painful ocular movements in all directions, typical ocular structures, normal reactive pupil. The fundus examination was regular in both eyes.

Initial blood tests revealed leukocytosis (17.41 * 10^3/mcL) with neutrophilia (16.72 * 10^3/mcL), high blood glucose (434.98 mg/dL), microcytic

hypochromic anemia, high elevated levels of: C-reactive protein (16.87 mg/dL), fibrinogen (813 mg/dL), urea (96,54 mg/dL).

Initial cranial and orbital CT-scan revealed frontomaxillary and ethmoidal sinusitis, with observation of right orbital cellulitis.

Based on the clinical and paraclinical findings, we initiated systemic treatment with broad-spectrum antibiotics, steroidal and nonsteroidal anti-inflammatories, diuretics and analgesics, associated with topical therapy with broad-spectrum antibiotics and steroidal and non-steroidal anti-inflammatory medication.

The otorhinolaryngology examination formulated the diagnosis of chronic frontomaxillary and ethmoidal sinusitis and recommended continuing with the systemic broad-spectrum antibiotic treatment and intranasal decongestant applications.

Two days following the admission, we observed the onset of a slight right nasolabial sulcus ecchymosis, and the systemic steroidal anti-inflammatory medication was stopped, and anti-fungal medication (Fluconazole) was added, as a prophylactic treatment of mycosis due to aggressive systemic antibiotic treatment. Although there was ongoing suspicion of a sinusoidal source of infection, we also suspected a cavernous sinus thrombosis complication, and we opted for a neurology examination, which recommended a cerebral CTA (Computed Tomography Angiography), then MRI (Magnetic Resonance Imaging) with angiography (14).

In addition to the neurological examination, we asked for an internal medicine examination for the follow-up blood works, which revealed evolution towards aggravation and sepsis suspicion. The internal medicine examination recommended screening tests for MRSA (Methicillin-resistant Staphylococcus aureus) and ESBL (Extended-spectrum Beta-lactamase), both of which were shown to be negative, hemocultures in a febrile state, and continuous monitoring of vital functions. During hospitalization, the patient developed no febrile state.

Cerebral MRI with angiography revealed right orbital cellulitis with massive inferior eyelid edema with presumed sinusoidal origin, frontomaxillary and ethmoidal sinusitis, and right cavernous sinus thrombosis under observation.

Based on the neurology re-evaluation, according to MRI findings, we immediately started anticoagulant treatment, but the patient's condition progressively worsened. In the next two days, despite therapy, the nasolabial sulcus ecchymosis extended periorbitally, frontally and palpebrally on the left side, also at the roof of the mouth on the right side (*Figs. 1, 2*). Moreover, new similar ecchymosis appeared on the limbs.

The follow-up blood tests indicated an imminent shutdown of the patient's system. Under these circumstances, associated with the rapid, apparent decline of the clinical state, the patient was transferred to the Intensive Care Unit.

Because of the ongoing suspicion of the sinus source of the infection, an otorhinolaryngology re-evaluation was performed. Finally, the intranasal fibroscopic examination described the appearance of necrosis of the soft and hard tissues, most likely of a fungal nature.

Unfortunately, on the same day the fibroscopic examination was performed, the patient went into

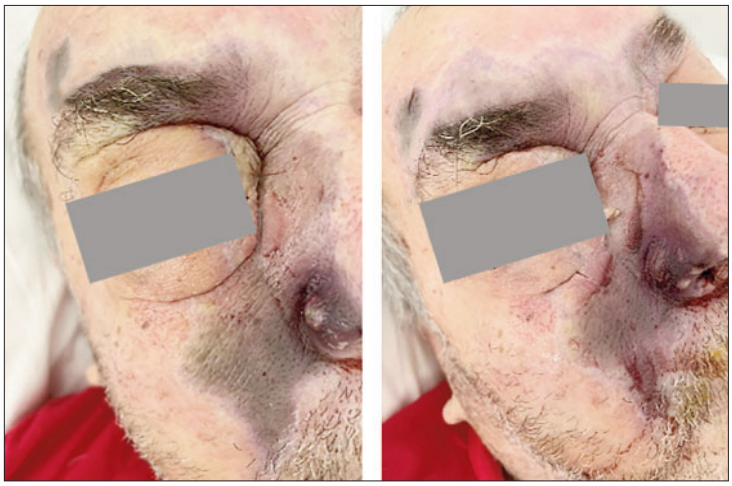

Figure 1. The expansion in surface and the increase in color of the right nasolabial sulcus ecchymosis the next day from its onset, 3 days following the admission.

Figure 2. Rapid progression of the color abnormality of the face skin, invading the right cheek and the nose, also expanding on the left half of the front, 4 days following the admission.

cardiorespiratory arrest, with failed resuscitation maneuvers and exitus.

The patient's family opted out of the autopsy examination, and there are no results to report.

In the end, the case is characterized by the very rapid onset and severe evolution of the clinical state of a diabetic patient, which developed a therapy resistant extensive orbital infectious complication, following an aggressive steroid treatment imposed by a life-threatening COVID-19 related pneumonia. Based on these aspects, associated with the appearance of the particular and extensive skin lesions and with the findings of the last intranasal fibroscopic examination, we concluded the diagnosis of rhino-orbital mucormycosis.

Discussions

The reported case is the single patient with rhino-orbital mucormycosis associated with COVID-19 in our clinic. The patient had a history of type 2 diabetes mellitus with insulin treatment. Prior to admission to our clinic, the patient received aggressive treatment for COVID-19-related pneumonia (which included corticosteroid medication) for up to 19 days. In our clinic, the patient was hospitalized for 6 days, with rapid, poor evolution and progressive extension of the infection despite all therapy, and unexpected exitus. Our case supports the hypothesis that the ominous triad of diabetes, corticosteroid use, and the background of COVID-19 determines the increased risk of mucormycosis and that extensive research is required for the optimal treatment of such cases.

COVID-19 tends to become a ubiquitous morbidity presence. Under the circumstances of COVID-19 international expansion, the risk of mucormycosis has to be well-known and reconsidered. Despite its low prevalence, the extreme severity of this complication makes it a potential extreme danger for any patient with comorbidities or with poor immunity status. Even if biological self-defense mechanisms seem to be normal before the onset of COVID-19 infection, they can become less effective afterwards. Thus, the development of immunity supporting treatments as components of mandatory current therapy protocols might offer a way towards better outcomes and lower mortality rates in this disease.

Conclusions

Sharing such cases is important in order to help improve therapy protocols for fragile patients with existing comorbidities, in their struggle against the development of various organ infections and even life-threatening viral infections. A successful treatment strategy is reaching for the proper balance between defeating abnormal immune reactions caused by the virus and supporting the host organism's immunocompetence.

Conflict of Interest

The authors declare no conflict of interests.

Ethics Approval and Consent to Participate

The case study was done by following the ethical norms of scientific research and the principles anonymity a confidentiality. The patient included in this case has provided informed consent.

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