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Case report

Case report: Nasopharyngeal mucormycosis, atypical presentation in a seventy-year-old diabetic lady

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ABSTRACT

Introduction and importance: Mucormycosis is rare type of infection yet, it is common in patient with Diabetes Mellitus and immune deficiencies. Mucormycosis mostly target the rhino-orbito-cerebral region, hence the common presenting symptoms are nasal symptoms followed by orbito-cerebral symptoms.

Case presentation: Here, we present a diabetic lady with unusual presentation of mucormycosis. This old lady present with long history of left dull ear pain and decrease in hearing, nasopharyngeal exam revealed a mild bulging in the fossa of Rosenmuller region. The mild bulging reported as left nasopharyngeal heterogonous soft tissue mass extending to the left external auditory canal and skull base by CT scan. Excisional biopsy was taken and found to be nasopharyngeal mucormycosis

Conclusion: Mucormycosis is a fatal infection which require early diagnosis and emergent intervention.

1. Introduction

Mucormycosis is a rare type of fungal infections, yet it's considered as a fatal infection. Its spread through inhalation of the fungal spores mostly. Usually, the first symptoms to be present in a patient with mucormycosis infection are nasal symptoms such as nasal crusting, unilateral or bilateral nasal obstruction and tissue necrosis. Other common clinical presentation could be orbito-cerebral symptoms: headache, facial paresthesia or anesthesia, ptosis, proptosis, retro-orbital pain, and total blindness [1–4]. However, mucormycosis with an ear pain and decreased hearing as presenting symptoms are rare and this is the first case reports of its kind to best of our knowledge.

Diabetes Mellitus, neutropenia, lymphopenia, organ transplant and recently COVID-19 are the commonest predisposing factors in this type of infections [2–8]. Diabetes Meletus is a key factor of developing mucormycosis through three different hypotheses: 1- impaired neutrophil function, 2- decreased binding of transferrin to iron and 3- increased GRP-78.

The treatment of choice of mucormycosis is amphotericin B. It is preferred to start amphotericin B after surgical debridement of the necrotic tissues. [8]

Here we present a case of an old diabetic lady present to ENT outpatient clinics, Al-Farwaniya hospital, which is a community hospital located in Al-Farwaniya And its serves an estimated on million people, accounting for 30 % of the country's total population.

This work has been reported in line with the SCARE 2020 criteria [9].

2. Case report

A seventy-year-old Kuwaiti lady, known case of uncontrolled Diabetes Mellitus and was on irregular treatment with Lantus 20 units once daily (she was uncompliant neither to Lantus nor to follow up), blood sugar monitoring was infrequent. She also had chronic renal disease, hypertensive on Zestril 10 mg once daily, Zestoretic 20 one tab daily and Norvasc 5 mg once daily and pacemaker on anticoagulants. Presented to the outpatient office in the department of ENT complaining of gradual, progressive left deep ear pain, pain started to be bearable then it became very severe. She also complains of gradual decrease in hearing on the left ear, as well as facial asymmetry for a long period. There was no tinnitus, no discharge nor itching. And this was her first time to experience this complaint. Family history was unsignificant.

On Examinations, she was conscious, oriented, and alert, febrile, and vitally stable.

Otoscopic exam showed: Left ear: edematous and very painful on touch, Tympanic membrane was not visible. Ear pack was inserted in the

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left external canal. Re-examination after packing and antibiotic showed polypoidal mass in the inferior-posterior part of the left external canal, mass was taken as biopsy for histopathology and came as inflammatory mass. Right ear: unremarkable examination.

Cranial nerve exam: Facial nerve exam: gross exam showed slight weakness with effort on the right side, resting appearance was normal, dynamic appearance: mild oral and forehead asymmetry, she was unable to raise her eyebrows completely on the right side and she was able to close her eyes completely with minimal effort, when she was asked to smile her mouth dropped slightly to the right side. (Grade 2 left facial palsy). Hypoglossal nerve exam showed hypoglossal nerve palsy. Other cranial nerve exams were unremarkable.

Nasopharyngeal scope: Showed only mild bulging in the fossa of Rusenmuller region with normal mucosa.

Pure tone audiometry and tympanogram was requested but couldn't be done due to her present health condition.

She was admitted as a case of left malignant otitis externa; and was immediately put on IV Tazocin and Fortum. Meanwhile, all baseline investigations done on admission, and COVID19 nasopharyngeal swab was negative.

The second day of admission she developed sudden slurred speech so urgent Computerized tomography of ear and skull base was requested and urgent neurology consultation was sent.

Urgent CT scan reported as: left nasopharyngeal heterogonous enhanced soft tissue mass lesion (Fig. 1) with related bone erosion and destruction of related part of skull base (clivus, jagular foramen and carotid canal) as well as external auditory canal. With suspected jugular thrombosis (Fig. 2) likely of neoplastic region. Also, opacity of left middle ear and mastoid noticed (Fig. 3). Nasal sinus reported as clear, except mild mucosal thickening of the left sphenoidal sinus. Magnetic resonance imaging could not be done due to the old pacemaker, refused by the radiologist consultant.

The patient underwent surgical debridement of the diseased tissues and biopsy of nasopharynx and left ear mass once more as the mass had regenerated under general anesthesia was done by ENT department team, Farwaniya Hospital; a nasopharyngeal swab for screening of COVID-19 24 h prior to surgery was done and resulted negative [10].

Histopathology result of the biopsy reported as: fungal hyphae broad with right angle branching in keeping with mucormycosis.

IV Tazocin and Fortum were discontinued and urgent consultations with microbiology team, and clinical pharmacology team was done; liposomal amphotericin b was started, which can be used safely in critically ill patient. So, beside liposomal amphotericin b, the patient was managed by insulin to control her blood sugar which is a key factor

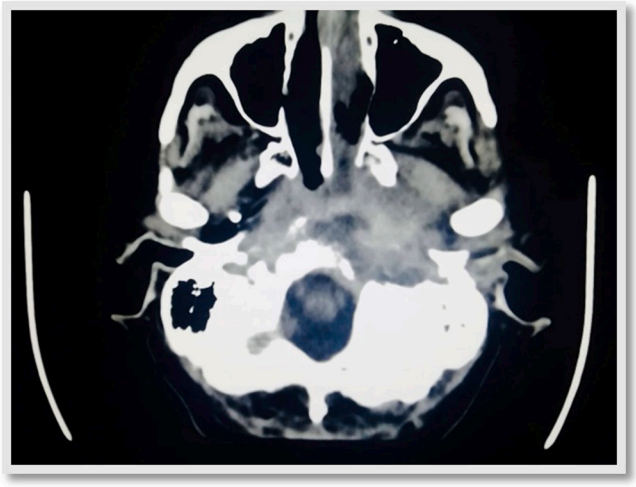

Fig. 1. Fairly defined heterogenous enhanced soft tissue mass lesion is seen in the left nasopharyngeal region extending to left external auditory canal.

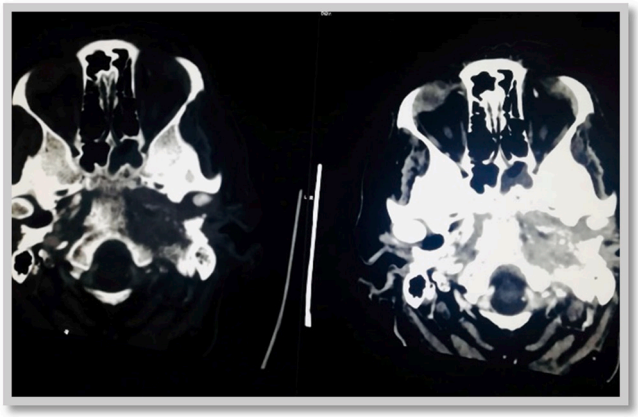

Fig. 2. Non-enhancement proximal segment of left jugular vein near to skull base region.

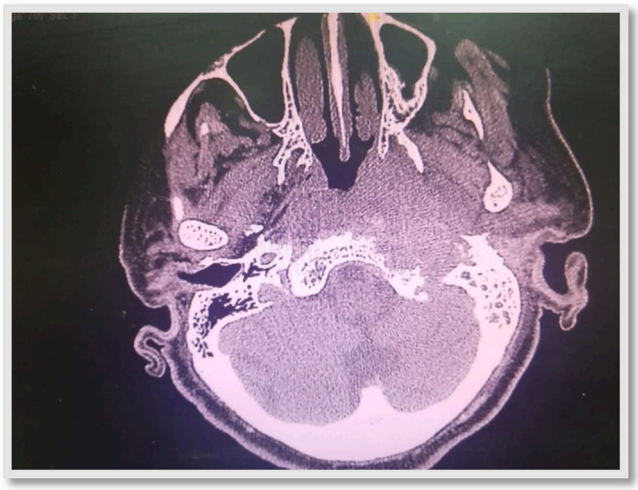

Fig. 3. Soft tissue thickening is seen almost filling the middle ear cavity completely extend through the aditus-ad-antrum to mastoid antra and air cell.

in treating mucormycosis infections. Tablets Eliquis was administered in view of jugular thrombosis. During the treatment course patient developed hypothermia (core body temperature = 33 °C), AKI in top of CKD (creatinine = 249 μmol/L) and hyponatremia (sodium = 117 mEq/L) medical, microbiology and nephrology consultation was done and was advised to stop liposomal amphotericin b and start Posaconazole syrup 5 ml twice daily. Patient conditions continue to worsen, she developed septic shock (Temp 33 °C, WBC = 39 10^9/L, blood pressure = 70/40 HR 120 pulse/min). She was shifted to intensive care unit (ICU) and started on levophid infusion. Unfortunately, the patient died after several days in the intensive care unit.

3. Outcome

Patient was admitted under the care of ENT team, in between was consulted with medical, cardiology, nephrology, and neurology regarding the treatment plan. Patient developed septic shock and shifted to ICU. She was continuing Posaconazole syrup, insulin infusion and levophid infusion. Unfortunately, the patient died in the intensive care unit (ICU).

4. Discussion

Zygomycosis was first described in 1885 by Paltauf [11] and later

coined as Mucormycosis in 1957 by Baker [12] an American pathologist for an aggressive infection caused by Rhizopus. It has since been found out that various fungi of the genus Rhizopus, Mucor, Absidia, Rhizomucor and Cunninghamella can lead to this angioinvasive disease with very high morbidity and mortality.

Hyperglycemia, COVID-19, steroid use are the commonest cause factors of mucormycosis infections [13–18].

Diabetes mellitus diminishing the inflammatory response of immune cell against mucormycosis by impairing neutrophil function through increase the oxidative stress which leads to defective chemotaxis of neutrophil and impairs the motility of phagocyte (due to metabolic reprograming) [19] as well as Overexpression of GRP78 (glucose-regulated protein) is noted specifically in nasal epithelial cells [20], mucor will attach to these receptor and invade the blood vessels causing ischemia and necrosis. In DKA (Diabetic ketoacidosis) the binding of transferrin to iron that will lead to excessive free iron. This will form an ideal, favorable environment for mucormycosis growth [21].

Steroid decrease the immunological response by inhibiting the NF-κB pathway which is a transcription factor involved in the immunological mediators. Steroid use also directly inhibits the genes which synthesize various cytokines such as IL-1, 2, 3, 4, 5, 6, 8 and IFN-γ. It also induces apoptosis of T cells, thus decreasing the T cell response against the pathogen which will increase the risk of opportunistic pathogens infections such as mucormycosis [19].

COVID-19 cause Excessive ferritin synthesis along with reduced extracellular iron transport results in high levels of intracellular iron which will lead to produce excessive reactive oxygen species that will lead into tissue damage and release of free iron into the circulation. Same concept as in DKA, the Free iron in circulation forms an ideal environment for fungal proliferation and growth [22] as well endothelial damaged and attacks induced by COVID19 will cause thromboembolic event, as we said previously mucormycosis is Angioinvasive, so united of these two factors will increase the susceptible of tissue invasions, and necrosis [23,24]. It also targets T lymphocyte causing lymphopenia which will suppress the immunity and virus form another theory that explain increased mucormycosis infection in affected patients.

As we mention before, DM and steroid leads to immunosuppression which will increase the risk of having COVID19 infection. COVID19 infection attack b cell of the pancreas that will lead to diabetogenic state [25,26]. So, it acts like a cycle of immunosuppressive state, each predisposing factor increases the risk of another one. Which make the patient more and more prone to getting mucormycosis.

Mucormycosis usually initiates on the nasal and oral mucosa and spreads to paranasal sinuses, palate, pharynx and through lamina papyracea it will spread into the orbits. The progression of the disease is by direct spread or hematogenous facilitated by angioinvasion [27]. The classical presentation in rhino-orbito-cerebral mucormycosis are nasal crusting, obstruction and swelling, facial pain and paresthesia, headache, and orbital swelling, inflammation, eyelid drooping, and proptosis [28–31]. In our case the presentation was unusual, she came with diffuse, sever ear pain and facial palsy without any rhino-orbito-cerebral compliant at the time of presentation. Mucormycosis is Angioinvasive which can cause thrombosis Whitin large arterial and venous channel, which can lead to necrotized, devitalized blackish tissues, or/and stroke.

Diagnosis is usually based on clinical history, physical examination, imaging study (CT, MRI). Gadolinium enhanced MRI is the gold standard test. Gadolinium will only reach the area with good blood supply, so it helps in diagnosis of necrotic area [32]. A definitive diagnosis is based on the demonstration of fungal hyphae typical for mucormycetes in biopsies of affected tissues [33,34]. There is a lot of ongoing research, focusing on finding non-invasive, rapid methods to detect mucormycosis infections, such as qPCR for the detection of circulating mucoralean DNA in blood or urine, serology-based and Metabolomics-Breath Test [33].

European Confederation of Medical Mycology initiated ‘One World One Guideline’ for treatment in mucormycosis [35]. It strongly advises administration of high-dose liposomal amphotericin-B and surgical debridement as first-line treatment. “Prevention is a mother of cure” so avoid infection from first place is much better than treating and managing after getting infected. That's why correction of predisposing factor has an important value [36–38]. Strict glycemic control and monitor is critical. Early detection and correction of DKA, acidosis, hypoxia, and leucopenia, judicious steroid use, prophylaxis with Posaconazole in high-risk patients (200 mg TDS) [39,40] are a necessary step in prevention. [36,41]

5. Conclusion

In summary, mucormycosis is not that common type of infection but it should be considered in any patient with predisposing immune deficiencies. Although Rhino-orbito-cerebral symptoms are the commonest presenting symptoms for mucormycosis infection our patient present with unusual ear symptoms at time of presentation. Mucormycosis is Angioinvasive which can cause venous or arterial thrombosis and can result in stroke. That's why mucormycosis patients should be followed by multidisciplinary team regarding the treatments plan.

Ethical approval

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the Editor-in-Chief of this journal in request.

Author contribution

Dr. Bashayer; data collection, writing the paper.
Dr. Hussein; data analysis and contribution.
Dr. Ahmad; data analysis and contribution.
Dr. Imtiyaz; data collection, writing paper, study concept.

Research registry

Reserchregistry.com – for all human studies.
Researchregistry7832.

Guarantor

Dr. Bashayer Alsaeedi.

Provenance and peer review

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Declaration of competing interest

There is no conflict of interest to declare by any of the authors of this study.

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