Hard palate perforation in acute lymphoblastic leukemia due to mucormycosis – a case report

Dipti R. Samanta · Surendra N. Senapati · Praveen K. Sharma · B. S. Shruthi · Prajna Bimoch Paty · Gitanjali Sarangi

Received: 11 November 2008 / Accepted: 24 February 2009
© Indian Society of Hematology and Transfusion Medicine 2009

Abstract Palatal perforation can occur due to trauma, infection and malignancy. Mucormycosis is a rare opportunistic fungal infection caused by an organism of class zygomycetes. Rhinocerebral mucormycosis is the most common type of mucormycosis that typically starts in maxillary antrum in immunocompromised patients. Invasion of surrounding structures leads to necrotizing ulcer of the hard palate and ultimately leads to perforation. Here, we report a case of perforation of the hard palate due to mucormycosis in a eight years child having acute lymphoblastic leukemia (ALL), who was on prolonged chemotherapy and corticosteroid therapy. This case is being reported for its rarity. The aim of presenting this case report is to emphasize that the infection due to mucormycosis should be included in the differential diagnosis of hard palate perforation in ALL patients who are immunocompromised.

Keywords Hard palate perforation · Mucormycosis · Acute lymphoblastic leukemia · Immunocompromised

Introduction

Palate perforation can occur due to trauma, bacterial infection leading to osteomyelitis, viral infection like herpes zoster, fungal infection such as mucormycosis, aspergillosis, prolonged cocaine abuse and malignancies. Mucormycosis is an opportunistic deep fungal infection caused by genera *mucor*, *rhizopus*, *absidia* and *cunninghamella* collectively known as *Phycomycetes* [1]. Usually, mucormycosis presents as an acute infection and manifests as rhinocerebral, pulmonary, gastrointestinal, cutaneous or disseminated forms [2]. More than 50% of the patients present with rhinocerebral disease, 10% patients have pulmonary, cutaneous or disseminated forms and 2% of patients have renal and gastrointestinal involvement [3]. In rhinocerebral type, the disease process begins in the nose, paranasal sinuses or palate [2]. This fungus invades the arteries, forms thrombi within the blood vessels that reduces the blood supply leading to the necrosis of the palate [4]. The patients of diabetes mellitus with ketoacidosis and patients of leukemia having impaired immunity are more prone for mucormycosis infection. Palatal perforation due to mucormycosis is rare entity [5]. Here, we report a case of palatal perforation due to mucormycosis in a eight year old child of acute lymphoblastic leukemia (ALL) for the documentation due to its rarity.

Case report

An 8-year-old boy clinically presented with intermittent fever and abdominal pain for past six months. The clinical evaluation of the patient revealed anemia, bilateral cervical lymphadenopathy of level I and II lymphadenopathy with hepatosplenomegaly. The hematological profile of the patient revealed anaemia (haemoglobin-8 gm%), leucocytosis (TLC-32000/cmm) with thrombocytopenia (platelet count 42,000/cmm) and 80% premature cells. After

D. R. Samanta¹ · S. N. Senapati¹ · P. K. Sharma¹ · B. S. Shruthi¹ · P. B. Paty² · G. Sarangi²

¹A. H. Regional Cancer Centre,
Cuttack, Orissa, India

²S.C.B Medical College, Cuttack,
India

R. D. Samanta (✉)

E-mail: diptiranasamanta@rediffmail.com

two days of supportive care with intravenous antibiotics and platelet transfusion, bone marrow evaluation was done which was suggestive of 80% MPO negative blasts, based on which he was diagnosed as a case of ALL-L1 on morphology. Immunohistochemistry of the patient showed HLA DR, CD10 and CD19 positive. The patient was treated with MCP-841 protocol (a combination chemotherapy of vincristine, daunomycin, leucogenase, oral prednisolone and intrathecal methotrexate as induction). The patient had frequent febrile neutropenia after each week of therapy for which he was given empirical intravenous antibiotics and granulocyte macrophage colony stimulating factor when ever necessary. He was also given frequent blood transfusion due to anaemia. When the patient was in the fourth week of induction treatment of MCP-841 regimen, he complained of nasal pain and a detailed clinical evaluation the patient was found to have broadening of nasal bridge and an ulcer crater of size 3x3cms in the hard palate with a necrotic eschar on it (Fig: 1). X-ray of the paranasal sinuses showed haziness of the right maxillary sinus. A biopsy of the lesion was taken under local anaesthesia which revealed nonseptate mucormycotic hyphae with acute right angle branching invading blood vessels without any evidence of malignant cells. The tissue culture also revealed the growth of mucormycosis hyphae (Fig. 2). The patient was referred to the surgical oncology department and after thorough evaluation, he had undergone surgical debridement of the necrotic area. He was subsequently treated with liposomal Amphotericin-B at the dose of 1 mg/kg of bodyweight. His disease was under control after which a palatal prosthesis was given. Now, the patient is on remission induction chemotherapy.

Discussion

Zygomycosis is an infection caused by the fungi of the class zygomycetes comprising the order mucorales. The infection caused by fungi of order mucorales produces mucormycosis; a life threatening fungal infection uniformly affecting immunocompromised hosts in developing as well as industrialised countries. Mucormycosis is an opportunistic fulminating fungal infection of the sinonasal region first described by Plataut AP in 1885 [6]. Patients having diabetic ketoacidosis, leukemia, prolonged corticosteroid therapy, deferoxamine therapy are more prone for the development of mucormycosis [7–10]. Both the mononuclear and polymorphonuclear phagocytes of normal host kills mucorales by the generation of oxidative metabolites and cationic peptides [11]. The above oxidative mechanism is lost in diabetic ketoacidosis and prolonged corticosteroid therapy [12, 13]. The reported case was diagnosed as a case of ALL-L1 who was on prolonged chemotherapy and oral corticosteroids and hence more susceptible to mucormycosis infection.

Based upon the involvement of the anatomical sites, mucormycosis can be divided into atleast 6 clinical types

i.e. rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and miscellaneous. Rhinocerebral mucormycosis is the most common form of mucormycosis that occurs in patients having diabetic ketoacidosis, haematological malignancies and haemopoietic stem cell transplant. Patient having haematological malignancies develop mucormycosis due to prolonged corticosteroid therapy

Fig. 1 Clinical Photograph showing black eschar and perforation of hard palate

Fig. 2 Wet mount preparation showing non septate mucormycotic hyphae (Lactophenol cotton blue stain X 40)

which causes immunosuppression, chemotherapy induced neutropenia and repeated blood transfusion leading to iron overload which was also observed in the reported patient [14, 15]. Patients of rhinocerebral mucormycosis clinically present with facial pain, numbness, nasal congestion and conjunctival suffusion. The infected lesion first appears as a erythematous patch which turns into a violaceous patch followed by a black necrotic eschar due to ischaemic necrosis produced by angioinvasive property of mucormycosis. The infection results from inhalation of fungal spores through the nose which then spreads from the sinuses into the mouth and produces painful, necrotic ulceration of the hard palate [5, 16]. The reported patient had nasal pain and congestion, pain in the right maxillary sinus area followed by an erythematous tender patch at the hard palate which subsequently led to development of a perforation with a black necrotic plug of tissue.

The palatal perforation may occur due to tertiary syphilis, squamous cell carcinoma of maxillary sinus, accessory minor salivary gland tumour of the palate, extranodal NK-T cell lymphoma, Wegener's granulomatosis, acute necrotizing ulcerative gingivitis, bifosphonate treatment and long term cocaine use [17–19]. The histopathology study and culture of the fungus from the palatal lesion is essential to distinguish mucormycosis from the above mentioned diseases. The histopathology finding of mucormycosis shows necrotic and oedematous tissue with infiltration of neutrophils and presence of wide, ribbon like aseptate hyphal elements that branch at right angles. The smear cytology of the palatal perforation lesion shows presence of wide, ribbon like aseptate, hyaline, hyphal elements. In our reported case, the patient was a diagnosed case of ALL-L1 who was on chemotherapy and oral corticosteroid therapy. The patient had no history of trauma to palate, bifosphonate therapy or cocaine use. When palatal perforation was detected we thought it to be due to leukaemic infiltration responding to chemotherapy leading to perforation. However, on access of literature on internet we came across isolated case reports of mucormycosis producing palatal perforation in ALL. Accordingly, a tissue culture to isolate the fungus and histopathological study was done, which confirmed the presence of mucormycosis in this case.

The treatment of palatal perforation due to mucormycosis consists of correction of underlying condition, antifungal therapy, surgical debridement and repair of the perforation. In our patient, after thorough evaluation, surgical debridement of all the necrotic tissue was done. Since, Amphotericin-B is nephrotoxic, the patient was treated with liposomal Amphotericin-B in a dose of 1mg/kg bodyweight with regular monitoring of the kidney functions. After controlling the infection the patient was given a palatal prosthesis with acceptable swallowing and speech function and has been planned for definitive palatoplasty at a later date. The patient is at present continuing the chemotherapy.

Conclusion

Palate perforation due to opportunistic fungal infection in immunocompromised patients of ALL who are on prolonged steroid therapy and chemotherapy is a rare event. Clinicians should be aware of such a complication of mucormycosis infection, for early diagnosis, prompt treatment and to prevent the spread to other organs. Hope for cure of this infection lies in early diagnosis and initiation of aggressive treatment approach.

References

1. Jayachandran S, Krithika C (2006) Mucormycosis presenting as palatal Perforation. *Indian J Dental Res* 17:139–142
2. Leitner C, Hoffmann J, Zerfowski M, Reinert S (2003) Mucormycosis: necrotising soft tissue lesion of the face. *J Oral Maxillofac Surg* 61:1354–1358
3. Sugar AM (2000) Agents of mucormycosis and related species. In: Mandell G, Bennett J, Dolin R. (5th ed.) *Principles and practices of infectious diseases*. Churchill Livingstone, Philadelphia New York, pp 2685–2695
4. Pogrel MA, Miller CE (2003) A case of maxillary necrosis. *J Oral Maxillofac Surg* 61:489–493
5. Regezi JA, Sciubba JJ (1993) Ulcerative conditions. In: Regezi JA, Sciubba JJ (2nd ed.) *Oral pathology clinical pathological correlations*. W B Saunders, Philadelphia, pp 52–60
6. Plataut AP (1885) Mucosis mucorina. *Virchows Arch* 102: 543–564
7. Mowat AG, Baum J (1971) Chemotaxis of polymorphonuclear leucocytes from patients with diabetes mellitus. *New Engl J Med* 284:621–627
8. Pagano L, Ricci P, Tonso A, Nosari A, Cudillo L, Montillo M, Cenacchi A, Pacilli L, Fabbiano F, Favero AD (2003) Mucormycosis in patients with haematological malignancies: A retrospective clinical study of 37 cases. *Br J Haematol* 99:331–336
9. Fain JK, Markowitz A, Khilani PV (1978) Case report of localized mucormycosis following intramuscular corticosteroid. *Am J Med Sci* 275:209–216
10. Daly AL, Velazquez LA, Barkley SF, Kauff CA (1989) Mucormycosis: association with deferroxamine therapy. *Am J Med* 87:468–471
11. Diamond RD, Haudenschild CC, Erickson NF (1982) Monocyte mediated damage to rhizopus oryzae hyphae in vitro. *Infect Immun* 38:292–297
12. Chinn RY, Diamond RD (1982) Generation of chemotactic factors by rhizopus oryzae in the presence and absence of serum: Relationship to hyphal damage mediated by human neutrophils and effects of hyperglycemia and ketoacidosis. *Infect Immun* 38:1123–1129
13. Waldorf AR, Ruderman N, Diamond RD (1984) Specific susceptibility to mucormycosis in murine diabetes and bronchoalveolar macrophage defence against rhizopus. *J Clin Invest* 74:150–160
14. Marr KA, Carter RA, Crippa F, Wald A, Corey L (2002) Epidemiology and outcome of mould infections in haemo-

- poietic stem cell transplant recipients. *Clin Infect Dis* 34: 909–917
15. Rickerts V, Böhme A, Just-Nübling G (2002) Risk factors for invasive zygomycosis in patients with hematological malignancies. *Mycoses* 45(suppl. 1):27–30
 16. Petrikos G, Skiada A, Sambatakou H, Toskas A, Valopoulos G, Giannopoulou M, Katsilambros N (2003) Mucormycosis: ten years experience at a tertiary care centre in Greece. *Eur J Clin Microbiol Infect Disease* 22:753–756
 17. Seyer B, Grist W, Miller S. (2002) Palatal perforation in long term intranasal cocaine abuse. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 94:465–470
 18. Loudon JA, Marsh WE, Allen CM. (2000) Destructive midline palatal lesion. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 89:134–136
 19. Ribes JA, Vanover-Sams CL, Baker DJ. (2000), Zygomycetes in human Disease. *Clin Microbiol Rev* 13:236–301