An unusual cause of acquired tracheo-oesophageal fistula in a patient undergoing chemotherapy

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Abstract:
Fungal infection is a common complication following intensive chemotherapy for acute myeloid leukemia. Fungal infections commonly involve the lungs, paranasal sinuses or the skin. Our patient was evaluated for complaints of a choking sensation in the throat, and was found to have a trachea-oesophageal fistula with an eroding growth, which on biopsy was proven to be mucormycosis. Even with unusual presentation such as this, a high index of suspicion for an infective etiology is required in patients following high dose chemotherapy.

Keyword: acute myeloid leukemia, fungal infection

Key Messages:
A high index of suspicion for infective etiology is required in patients post-chemotherapy, even in a non-neutropenic setting.

Introduction:
Fungal infection is a common complication of induction therapy for acute myeloid leukemia. Prolonged severe neutropenia secondary to intensive chemotherapy (ANC < 500/mm3 lasting for more than 3 weeks duration) is a risk factor for the development of fungal infection. As fungal infections usually cause pneumonia, sinusitis and skin nodules, presentation at these sites elicits immediate escalation of antifungal therapy. Presentation at unusual sites, and unusual presenting complaints may result in a delay in diagnosis which may prove fatal.

Case History:
A 23 year old female diagnosed to have acute myeloid leukemia, had been previously treated with standard induction therapy (Cytosine 200mg/m2 and Daunorubicin 45mg/m2). She was found to have bulk residual disease, and was given salvage chemotherapy (FLAG-Ilda protocol as follows: Day 0 to +5 Inj. Neupogen 500µgm IV once daily in 250ml 5% dextrose, Day +1 to +5 Inj. Fludarabine 50mg IV once daily
in 100ml NS, Day +1 to +5 Inj. Cytosine 3.5gm, Day +1 to +3 Inj. Idarubicin 17mg once daily). Antifungal prophylaxis with alternate day Amphotericin was initiated, however this was changed to Voriconazole after 2 weeks in view of nephrotoxicity. She was started on daily growth factor injections after excluding residual disease by bone marrow. Febrile neutropenia was managed with broadspectrum antibiotics, and all blood cultures remained negative. In view of persistent fever, a high resolution CT thorax was done which did not show any evidence of fungal infection. She became afebrile with recovery of neutrophil counts (Day +23 ANC 1600/mm3). As oral intake was encouraged, the patient complained of a choking sensation in the throat, and profuse coughing while attempting to take sips of water. CT scan of the neck revealed a soft tissue mass in the peritracheal space, infiltrating the trachea and oesophagus, with a tracheo-oesophageal fistula. She was taken for emergency biopsy and elective intubation and was shifted to the ICU for ventilation. On the same day, she had an episode of massive hemoptysis through the endotracheal tube, and despite all attempts at hemostasis, the bleeding could not be controlled. She died on Day +28 post-chemotherapy. The biopsy from the tracheal mass was later reported as Mucor (Figures 1 & 2 showing biopsy from tracheal lesion with aseptate fungal hyphae - H&E 40X and GMS 40X).

Discussion:
Fungal infection is a major cause of mortality following intensive chemotherapy for acute myeloid leukemia(1). The prolonged neutropenia that follows chemotherapy predisposes patients to developing fungal infections. While fungal pneumonia accounts for the major proportion of fungal infections, sinusitis and skin nodules also account for a large proportion of cases. Other sites of fungal infection are cerebral parenchyma, and bloodstream (5). Zygomycosis in particular involves the oro-facial region and lungs (5). The epidemiology of fungal infections are changing, with an overall decrease in Aspergillus species, and increase in non-Aspergillus molds, which are frequently resistant to Amphotericin (2). In an epidemiological study of fungal infections in 1108 patients with hematological malignancies, 69% of all infections occurred in acute myeloid leukemia, of which over half were due molds, aspergillus being the commonest (310/356 mold infections). The highest fungal infection attributable mortality rates were due to zygomycosis (64%) (1). Similar mortality rates have been described in a study of mucomycosis in 59 haematological patients, with only 63% of patients with mucormycosis succumbing to the disease (5). Mucormycosis was the cause of death in 87% of patients in this cohort. A high index of suspicion for fungal infections needs to be maintained for neutropenic patients, as these infections may present at unusual sites, with breakthrough infections while on antifungal therapy and may flare up after neutrophil recovery, such as described in this case. In the case described, Amphotericin was changed to Voriconazole due to nephrotoxicity. As mucor is resistant to Azoles, in this patient there was progression while on antifungal therapy (3), with erosion of the trachea, resulting in the development of a tracheo-oesophageal fistula - at which time the patient became symptomatic. The diagnosis of fungal infection in cytopenic patients usually presumptive (4), as definitive diagnosis requires biopsy or culture from sites that are often inaccessible. A high index of suspicion and early diagnosis is essential in order to initiate timely
and appropriate antifungal therapy in immuno-suppressed patients post-chemotherapy.

References:


