Rhinofacial Basidiobolus Misdiagnosed as Granulomatosis with Polyangiitis

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Abstract
We report a case of a young female, initially misdiagnosed as Granulomatosis with Polyangitis (Wegener's). Repeat histopathology and culture however revealed *Basidiobolus species*. She was managed successfully with antifungals, highlighting the need for a high index of suspicion for molds in unusual presentations.

Key Words
Basidiobolus; Granulomatosis with Polyangiitis.

Introduction
Basidiobolus species are saprophytic fungi of the order Entomophthorales; Class Zygomycetes found in the soil, decaying vegetation, and intestines of most animals. In humans, they cause chronic skin and subcutaneous infections usually following abrasions or insect bites.[1] While infections had been geographically restricted to tropical Asia and Africa, however recently its epidemiology has evolved about geographical location, host susceptibility and involvement of deeper tissues.[2,3] Diagnosing Basidiobolus is difficult and can only be reliably made with both culture and histopathology. On histopathology, the infection is characterized by necrotizing granulomatous inflammation with predominant eosinophils and fungal element (hyphae).[1] Failure to detect hyphae due to presence of rare or degenerated fungal elements or inappropriate staining often lead to other diagnoses including soft tissue tumors, autoimmune disorders and tuberculosis.[4]

Here we present one such case of a 25-year-old female with Rhinofacial Basidiobolus, initially misdiagnosed as Granulomatosis with Polyangitis (GPA).

Case History
A 25-year-old female from Iran, presented to outpatient clinic at the Aga Khan University, Karachi, Pakistan with complaints of right facial swelling for the past 3 months. On examination, the right side of her face was hyperemic, swollen with proptosis. Endoscopic nasal examination revealed necrotic tissue with purulent discharge. Her extraocular movements and visual acuity were intact. The rest of the systemic examination was unremarkable.

Computed Tomography (CT) of Paranasal sinuses revealed an extensive 50 x 39 mm soft tissue mass in the right maxillary sinus with subcutaneous infiltration into the right orbit and the skin anteriorly. The mass extended into the ethmoid sinuses with bony erosion however, there was no intracranial extension.

She had undergone endoscopic sinus surgery 3 months ago in Iran with tissue histopathology report suggesting GPA (Wegener's granulomatosis), unfortunately the slides from that time were not available for reviewing. The patient had not undergone any therapy or work-up for the presumed GPA and travelled to Pakistan for further management.

Initial investigations showed a leucocyte count of 15.4 x 109 cells/liter, with neutrophilia, an ESR of 55 mm/hour and normal chest radiography. Given the scenario, a presumptive diagnosis

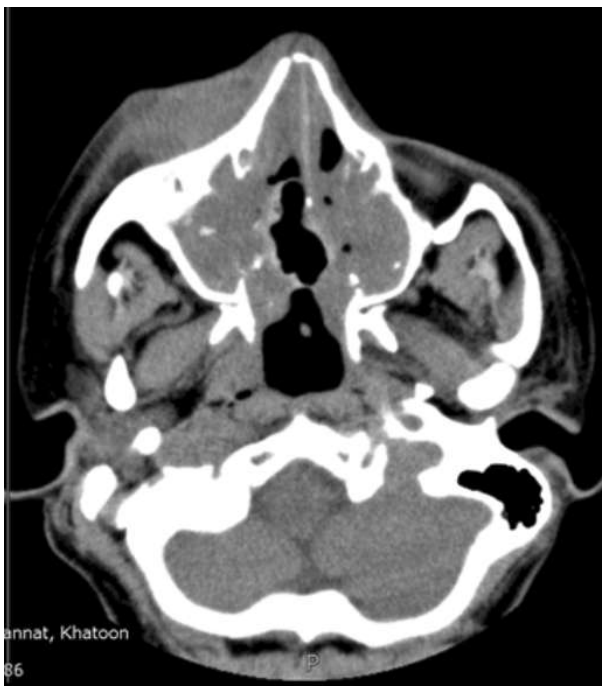

Figure showing CT Scan image of the patient.

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of GPA with superimposed bacterial infection was made and Piperacillin-Tazobactam was empirically started. Later, her serum anti-nuclear cytoplasmic antibodies (ANCA) was reported negative. She had to undergo endoscopic debridement and hence tissue was resent for histopathology along with cultures. Potassium hydroxide (KOH) smear of the tissue showed broad hyphae with rare septation. Based on this Amphotericin B at 1mg/kg/day was added to cover Mucormycosis. Forty-eight hours later fungi had grown on all primary plates. A Lactophenol cotton blue preparation of the colonies showed broad hyphae with occasional septae and thick-walled intercalary zygospore with beak like projections; appearance typical of Basidiobolus species. Histopathological examination of the excised tissue showed mixed acute and chronic granulomatous inflammation with histiocytes and multinucleated giant cells with abscess formation with no evidence of vasculitis or necrosis to suggest a diagnosis of GPA. Periodic Acid Schiff stain also highlighted broad aseptate hyphae. Further clinical correlation of these findings with a negative ANCA helped exclude the possibility of GPA with secondary fungal infection.

A diagnosis of Rhinofacial Basidiobolus was made and Amphotericin B was changed to oral Itraconazole (400mg/day) and Potassium Iodide. The Potassium Iodide dose was gradually increased from 1 mg every eight hourly to 3 mg every eight hourly over a period of six days. She responded well to therapy and was discharged on Itraconazole and Potassium Iodide.

On follow-up her facial edema and erythema had substantially reduced, and she returned to Iran shortly thereafter. Unfortunately, due to non-availability of Potassium Iodide in Iran, Itraconazole monotherapy was continued. Periodic follow ups assured compliance and improvement. She received Itraconazole for six months with complete resolution of radiological findings and clinical symptoms. She remained symptoms free till her last follow i.e. six months after stopping Itraconazole.

Discussion

We describe a case of Rhinofacial Basidiobolus that was initially misdiagnosed as Granulomatosis with Polyangiitis (GPA). On review of literature search we found 85 cases of Basidiobolus. Most cases were reported from South Asia especially from India, Iran and Saudi Arabia with occasional cases from Bangladesh, Oman, Qatar, Thailand, Maldives and Pakistan.[2] The fungus is usually inoculated after trauma contaminated by soil which may also explain the male preponderance (M: F, 3:1).[4] The disease is mostly seen in the younger population (22 out of 66 cases) with median age of less than 25 years.[4] Visceral infections have more commonly been reported (54 of 85 cases) mostly involving GI tract (54.8%).[2] Infection of liver, lung and spleen have also been described. The skin and subcutaneous tissue infections are the second most common type of infection (22 out of 85 cases). Lower extremities are more commonly affected.[4] Unlike Mucormycosis, rhinocerebral involvement with Basidiobolus is rather uncommon (n=5). Basidiobolus skin lesion is described as firm, non-tender nodules; presentation that overlaps with many other inflammatory and infectious processes.[4]

While our patient denied any trauma, she did use homemade "Balochi Surma". This is a traditional mascara made by grinding lead sulfide and other ingredients (including herbs). As the fungus is endemic to the region and ubiquitous, we suspect this to be a possible source of inoculation.

Basidiobolus can easily be misconstrued, hence fungal cultures remain the gold standard for diagnosis. Our case was initially confused with PGA due to the similar clinical and histopathological presentation, but a high index of suspicion and tissue cultures led us to the diagnosis. Interestingly, Basidiobolus has been reported to cause superimposed infections in patients with PGA on steroid therapy, mimicking as disease relapse.[5] However in our patient a negative ANCA, biopsy suggestive of Basidiobolus, improvement without steroids and response to antifungal therapy effectively rules out PGA.

While overall outcomes with Basidiobolus appear to be good, because of the rarity, treatment is not well defined. Surgical debridement with systemic antifungal has been the mainstay of therapy though the optimal antifungal; its dose and duration remain unclear. Azoles are most effective (Itraconazole, Posaconazole, Voriconazole); monotherapy with Amphotericin B was associated with poor outcomes.[1,2] Combination of Azoles with Terbinafine, Amphotericin B, Potassium Iodide and Cotrimoxazole also seems effective, although with handful of cases generalization is difficult.[2] Our patient briefly received Amphotericin B initially suspecting Mucormycosis, but largely remained on Itraconazole monotherapy with good outcome.

To conclude, in contrast to Mucormycosis, Basidiobolus mainly causes visceral disease in children[1,4] with rather good prognosis. As histopathological findings overlap in various chronic infectious and inflammatory processes, biopsy samples should be cultured in clinically relevant settings.

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