Invasive Fungal Infection of The Eye Thought to Be Tuberculosis: A Case Report

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Abstract
Invasive fungal infections are rare in children and are even more rare in immunocompetent children. Invasive fungal infections can masquerade as other granulomatous diseases like Tuberculosis, which is highly prevalent in India. We herewith report one such case of a 6-year-old boy with swelling over the right orbit diagnosed as Extra-Pulmonary Tuberculosis of the right orbit and started on ATT (anti-tubercular treatment) for the same. However repeat analysis of the biopsy sample with appropriate staining techniques and high degree of suspicion was diagnosed to have invasive fungal infection, which responded well with use of IV and Oral antifungals. Clinicians should always keep invasive fungal infections as a differential diagnosis with any immunocompetent or immunocompromised child presenting with granulomatous inflammation and proper staining techniques used on the biopsy sample.

Keywords: Invasive fungal infection; Immunocompetent; Staining techniques

Introduction
Invasive fungal infections (IFIs) have become more common and are a leading cause of illness and death in immunocompromised pediatric patients, such as preterm infants, children and adolescents with hematologic malignancies, and those receiving hematopoietic stem cell transplantation (HSCT) and due to COVID[1-3]. While both adults and children are susceptible to Invasive fungal infections, there are important differences between the two diagnostic categories that must be noted. The closest differential will be Tuberculosis (pulmonary and extra pulmonary) due to its high prevalence rate, and as per the Global TB Report 2021, the estimated incidence of all forms of TB in India for the year 2020 was 188 per 100,000 population (129-257 per 100,000 population). The total number of incident TB patients (new & relapse) notified during 2021 was 19,33,381 which was 19% higher than that of 2020 (16,28,161)[4].
Case presentation

A 6-year-old male child was presented with complaint of swelling of right eye near the nasal bridge for 3-4 months. Child also had history of traumatic penetrating injury to right eye near the nasal bridge while playing. Parents noticed swelling at the site of injury for 3 months which was small to start with and gradually increased in size. The child was appropriately immunized for his age. His weight was 23kgs (>97th centile for age and sex) and height 130cm (75th-90th centile).

CECT done 1.5 months after the onset of swelling showed ill-defined heterogeneously enhancing soft tissue lesion in right superior and inferior orbito-nasal region abutting the medial border of eye ball, predominantly in the preseptal plane- likely neoplastic lesion. MRI (T1 and T2) done 2.5 months later -showed ill-defined diffusion restricting soft tissue thickening/lesion in right superior and inferior orbito-nasal region involving upper and lower eye lids and abutting the medial border of eye ball-s/o possible neoplastic lesion. Child underwent incision biopsy for the same on 22/10/21 and histopathology examination done showed eosinophilic inflammatory lesion, GMS staining showed presence of fungal hyphae -s/o secondary to fungal aetiology.

Wide Excision of Right Naso-Orbital Mass done under general anesthesia was done on 3/11/21 showed caseating granulomatous inflammation suggestive of tuberculosis, and was started on ATT. AFB (acid fast bacilli) and CBNAAT (cartridge-based nucleic acid amplification test) of the specimen was negative. As child did not have any risk factors for Tuberculosis like family history, recent significant weight loss, chronic cough, sample was sent to another laboratory for retesting and confirmation. Histopathology report, reviewed on 12/11/21 in view of strong suspicion of invasive fungal infection showed fungal granulomatous inflammation, PAS (Periodic acid-Schiff) staining done showed slender septate fungal hyphae and few retractile spores. The necrotic area shows numerous fungal elements which are broad non-septate with irregular branching consistent with fungal infection. (Figure 1)

Figure 1: Histopathological slides of the specimen.
Hence child was admitted to rule out any underlying immunodeficiency state. At admission child was stable, Pallor+, no lymphadenopathy, bilateral tonsils seen, No mucocutaneous candidiasis+. Local examination-Right eye- Surgical wound seen over the right medial aspect of the eye near the nasal bridge, no discharge or signs of wound infection. Bluish discoloration seen over the inferior orbit. Left eye showed swelling present over the medial side near the nasal bridge which was firm, non-tender and no local rise of temperature or redness. Vision of right eye-Fairly normal-can count fingers from distance of 6 feet. Range of movement in all directions normal with vision 6/6. In view of suspected invasive fungal infection of the adnexa of the right eye relevant test to rule out immunosuppression were sent and child was started on IV Liposomal amphotericin B(7.5mg/kg/day) and other supportive care. Investigations done showed CBC- neutrophilic leucocytosis, CRP negative, LFT and RFT were within normal limits, serology for HIV, HbSAg and HCV was non-reactive. Reports of immunological workup were also normal. COVID IgG antibodies were significantly elevated.

With above evidence and histopathological examination report - A diagnosis of Invasive Mucor mycosis of right orbital adnexa was made. He was started on Liposomal amphotericin B at a dose of 7.5 mg/kg/d. The child tolerated amphotericin B well. He was continued on amphotericin B for 4 weeks. He continues to thrive well and has normal weight for age. After amphotericin-B he was continued on Oral Posaconazole for next 2 weeks. He did not have any recurrence of symptoms or any other opportunistic infection. (Figure 2)

**Figure 2:** Series of pictures showing the course of disease from diagnosis till the completion of treatment. (Clock wise).
Discussion

Invasive fungal infections are opportunistic infection usually affecting patients with debilitating diseases such as cancer, transplant recipients, inherited and acquired immunodeficiencies, diabetes mellitus, diabetic ketoacidosis, malnutrition, and penetrating wounds to the skin. [5] It has also been seen in individuals on deferoxamine medication, injectable drug users and people who don’t seem to have any apparent immune problems. Our patient did not have any of the recognized risk factors. But serology for COVID IgG was significantly elevated. Due to rarity of incidence of fungal infections in children they tend to be missed out and as seen in our case report, children undergo unwanted delay in detection and treatment. These infections need to be considered in all children not responding to antibiotics and specimen should be sent for proper fungal staining techniques. Any child with a caseating granulomatous inflammation should undergo CBNAAT testing for Tuberculosis, if negative should undergo staining for fungal elements and proper culture techniques. Use of adequate staining techniques and high degree of suspicion are required. Serological evidence of history of Covid infection should be considered in all such cases.

Conclusion

India being a developing country with high case load of Tuberculosis, most Chronic granulomatous diseases are suspected to be Tuberculosis unless proven otherwise. When treatment for the same is initiated and there is no improvement, a strong suspicion of other causes like invasive fungal infections is to be considered. Since the child was immunocompetent and had no other underlying chronic diseases, the diagnosis got delayed. Hence the message to all practicing clinicians is to send all histopathological samples to appropriate staining techniques like PAS, GMS (Grocott methenamine silver) and PCR (polymerase chain reaction) for fungal elements and not be biased with tuberculosis alone. However, Tuberculosis falls first in the list of the differentials, but not to miss the fungal infections.

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References