LETTER TO EDITOR (VIEWERS CHOICE)

RENAL AND DISSEMINATED ASPERGILLOSIS IN A CHILD WITH FEBRILE NEUTROPENIA

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A 12 year old boy, suffering from acute lymphoid leukemia (ALL) on Berlin-Frankfurt-Muenster (BFM) high-risk protocol had fever up to 101-102 °F along with neutropenia [absolute neutrophil count (ANC): 300 cells/cumm]. Initially, he was treated as febrile neutropenia and was started on cefoperazone-sulbactum and amikacin as per institute protocol. He continued to have fever and low ANC. Blood culture initially did not grow any organism. After 96 hours, liposomal amphotericin B at 5mg/kg/day was started and work-up was done to rule out fungal infections. Workup on day 4 of hospitalization showed hemoglobin of 9.6 gm/dl, total leucocyte count of 400 cells/cumm, ANC of zero and platelets of 48000 cells/cumm. Chest x-ray and contrast-enhanced computerized tomography (CECT) chest showed consolidation along with a ground glass pattern in the right upper zone suggestive of fungal infection. Ultrasound abdomen was also done to look for deep tissue infiltration which showed a fungal ball in left kidney 3.6 x 3 cm in size in the pelvicalyceal system; however, there was no obstruction in urinary drainage. Fine needle aspiration cytology (FNAC) was done under USG guidance on day 3 of amphotericin B which showed Aspergilluslus flavus. Galactomannan antigen index done in blood was positive [> 6 (≥ 0.5 is considered positive)]. Blood culture and sputum smear examination and urine culture showed Aspergillusus flavus. Liposomal Amphotericin B was stopped after 5 days once we got report of blood culture and he was given intravenous voriconazole (6 mg/kg q12hr for first 24 hours, then 4 mg/kg q12hr). Fever subsided after 2 days of voriconazole and ANC improved significantly (300 and 1000 cells/mm3 on day 4 and 7 after voriconazole respectively). Serial galactomannan antigen index at day 4, 7 and 10 after voriconazole were 2.5, 1.1 and 0.4 respectively. He received voriconazole for 14 days and ultrasound at the end of therapy showed resolution of the fungal ball. Currently, the child is continuing on chemotherapy for his ALL.

Invasive fungal infections are gaining more importance and are increasing in incidence in immunocompromised hosts like hematological malignancy. Also, in neutropenic patients with acute leukemia, there is an increase in the incidence of invasive mold infections. (1) If children with acute myeloid leukemia (AML) receiving highly myelosuppressive chemotherapy have prolonged neutropenia and persistent fever despite prolonged (≥ 96 hours) use of broad-spectrum antibiotic therapy, then, they are considered high-risk candidates for invasive fungal disease and should receive empirical antifungal therapy. If, despite antifungal therapy, there is persistent fever and neutropenia then search for a definitive etiological agent along with deep tissue involvement should be done. (2) According to various studies incidence of invasive fungal infection varies from 2 to 36.5% out of which 40-50% are caused by aspergillus. (3,4) In largest reported series, aspergillosis is found in around 0.7% of cancer children of which renal aspergillosis was seen in 1.5% of total aspergillosis infections. (5) Invasive aspergillosis occurs when the infection travels from the lungs into the bloodstream. Immunocompromised children get it more commonly because of poor cellular defense and leucopenia. Fungal infections of the urinary tract tend to occur more in the pelvicalyceal structures than in renal parenchyma. In patients with systemic mycosis, the kidney is vulnerable to the formation of fungal masses, usually at the ureteropelvic junction. (6) Initial management of renal aspergillosis "fungal ball" is medical with antifungal therapy. For aspergillosis voriconazole is the drug of choice however, amphotericin B or itraconazole are also effective. (7) As per Infectious Diseases Society of America (IDSA) guidelines, (8) voriconazole is drug of choice for invasive aspergillosis and in our case, the child was not responding to Amphotericin B so we switched to voriconazole. Regarding duration of therapy there are no clear cut evidence based guidelines. In absence of evidence based guidelines most experts recommend to treat infection until resolution or stabilization of all clinical and radiographic manifestations of aspergillosis. (8) The response to these antifungal agents is usually good. In cases with incomplete obstruction, treatment with antifungal alone may cause resolution of the lesion and hence obviate the need for surgical intervention. (9)

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