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Central Nervous System Fungal Infections in Children with Leukemia, Risk Factors and Outcome: A Multicentric Study

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Abstract

Introduction: Invasive fungal infections, including central nervous system fungal infections (CNSFI), cause significant morbidity and mortality in children with leukemia,necessitating early diagnosis and treatment.

Material and Method: In this retrospective study, the demographic features, diagnostic approach, treatment and outcome of CNSFI in 32 children with leukemia treated in 12 centers in Turkey were evaluated.

Results: Of the 32 patients,12 were female,20 were male.The diagnosis was ALL in 23, recurrent ALL in 5, CML in 1, AML in 1; two others had underwent allogeneic bone marrow transplantation. Most (22/32-68,7%) CNSFI episodes occurred during the remission induction phase of the treatment. All recieved broad-spectrum antibiotics for prolonged neutropenic fever. Twenty two had seizures. Six patient had headache, two patient had double vision and headache, one patient had loss of vision and one patient had fascial paralysis. Radiologic imaging was performed for neurologic symptoms and/or prolonged fever in patients with febrile neutropenia after a median of seven days (1-22). Twenty three had multiple and 9 single brain lesions in magnetic resonance imaging. In 15/23 patients, invasive pulmonary fungal infection; in two patients, hepatosplenic fungal infection were detected concurrently. On blood cultures, one patient had geotrichum capitatum fungemia and one had candida albicans fungemia.Galactomannan was positive in 15 (46%) patients. Fourteen patients underwent surgery, in ten microbiological evidence of fungi was confirmed; four aspergillus flavus, one aspergillus niger, one candida, one mucormycosis and one trichoderma longibrachiatum. Hemophagocytosis was observed in three patients. Nine received granulocyte transfusions. Fifteen were transferred to the ICU. Extracorporeal Membrane Oxygenation (ECMO) was used in one patient. Eleven patients (34%) died due to CNSFI at a median of 30 (15-42) days from the beginning of the episode. Out of 21 survivors, seven have permanent neurological sequela. Eighteen patients were recieving antifungal prophylaxis (Fluconazole (16), voriconazole(1) and itraconazole(1), before the CNSFI diagnosis. Thirteen patients received a single antifungal agent, 19 were treated with a combination of antifungals. Median duration of antifungal treatment was 186 (20-730)days. Liposomal amphoterisin-B and voriconazole were the two mostly used agents. Six of the 12 centers participating in the study had a construction going on near their ward at the time of diagnosis.

Conclusion: CNSFI is a major cause of mortality and morbidity in children with leukemia and prolonged neutropenic fever. The evaluation of children with leukemia and prolonged neutropenic fever for invasive

fungal infections and the addition of empirical antifungal treatment to antimicrobial treatment is important. Cranial imaging in children with leukemia and prolonged neutropenic fever, even in the absence of local sign and symptoms may lead to earlier diagnosis of CNSFI.

Disclosures

No relevant conflicts of interest to declare.

Author notes

* Asterisk with author names denotes non-ASH members.