



SUCCESSFUL TREATMENT OF INVAZIVE MUCORMYCOSIS FOLLOWING CHEMOTHERAPY IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA

Dr. Abdulkerim Yıldız*¹, Murat Albayrak¹, Osman Şahin¹, Güleser Saylam², Gürsel Güneş¹,
F. Aybala Altay³

¹Diskapi Yildirim Beyazit Education and Research Hospital, Department of Hematology, ANKARA.

²Diskapi Yildirim Beyazit Education and Research Hospital, Department of Otolaryngology, ANKARA.

³Diskapi Yildirim Beyazit Education and Research Hospital, Department of Infectious Disease and Microbiology, ANKARA.

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Corresponding Author: Dr. Abdulkerim Yıldız

Diskapi Yildirim Beyazit Education and Research Hospital, Department of Hematology, ANKARA.

ABSTRACT

Mucormycosis is a fungal infection mainly affects immunocompromised patients especially with malignant hematologic diseases. Fludarabine is commonly used chemotherapeutic agent in Chronic Lymphocytic Leukemia (CLL) which causes severe immunosuppression and has been suggested to increase risk of invasive fungal infections. A 70-year old man with CLL developed severe mucormycosis after the first cycle of Fludarabine-Cyclophosphamide chemotherapy. He was treated successfully with extensive surgical debridement and intravenous liposomal Amphotericin-B. This case highlighted that fludarabine-based regimens can cause severe immunosuppression and fungal infections even after first cycle of chemotherapy.

KEYWORDS: Mucormycosis, chronic lymphocytic leukemia, fludarabine.

INTRODUCTION

Mucormycosis is a fungal infection mainly affects immunocompromised patients with diabetes mellitus or malignant hematologic diseases.^[1] Fludarabine causes T-helper cell depletion which is important in defending against invasive fungal infection and has been suggested to increase risk of invasive fungal infections in leukemia patients.^[2] We herein report a Chronic lymphocytic leukemia (CLL) patient with invasive fungal sinusitis which was successfully treated.

CASE PRESENTATION

A 70-year old man admitted to our hematology department of hospital with the complaint of fullness in the left upper abdomen and severe fatigue. His radiological investigations revealed that he had multiple enlarged lymphadenopathies and splenomegaly 25 cm in diameter. We performed left axillary lymph node excisional biopsy resulted as small lymphocytic leukemia (SLL). He had severe B symptoms, anemia and thrombocytopenia on laboratory tests (Hb: 8.5 gr/dl, Plt: 47000x10³/ml, WBC: 17100x10³/ml, Lymph: 14700x10³/ml). Flow cytometry was compatible with chronic lymphocytic leukemia (CLL). Bone marrow biopsy

showed involvement of atypical lymphoid cell infiltration. We diagnosed patient as CLL/SLL stage 4 (RAI), stage C (Binet). His performance was fit. Genetic analysis of 17p deletion has not been resulted yet. We gave dosage adjusted Fludarabine and Cyclophosphamide chemotherapy as first cycle. Two weeks after chemotherapy he was admitted to emergency department with neutropenic fever. We hospitalized the patient and started empirical antibiotic treatment and G-CSF. On the seventh day of hospital stay, he had headache, left eyelid swelling and periorbital edema. He had still neutropenia despite G-CSF usage. Paranasal sinus computerized tomography (PNCT) revealed soft tissue lesion on left nasal cavity that obliterates nasal passage and borders can not clearly be distinguished from middle concha. Cranial MRI showed lesion 23x33 mm in diameter on the level of left anterior ethmoidal cell, lamina propria, left bulbous oculi which is adjacent to medial rectus muscle, left half of nasal bone involves left nasolacrimal gland and also has air spaces and no contrast enhancement. We performed soft tissue biopsy from that lesion and immediately started on empirical liposomal amphotericin-B treatment for opportunistic fungal infections. But his eye swelling, periorbital edema and headache progressed so that surgical resection was

performed by otolaryngologists due to consideration of invasive fungal infection spreading from paranasal cavity to orbital region. Lesion biopsy resulted as mucormycosis and we continued Amphotericin-B and G-CSF treatment. His neutropenia recovered on the 14th day of hospital stay and his other complaints improved

day by day. Cranial MRI scan also showed significant improvement on the 30th day of stay and we stopped Amphotericin-B treatment. The patient then was discharged and referred to follow-up in outpatient clinic for further chemotherapy cycles.



A. Pretreatment appearance of eyeball

B. Posttreatment appearance of eyeball

Figure 1: Pre-post appearance of external orbital region of the patient.

DISCUSSION

Mucormycosis (MCM) is the third most common invasive fungal infection (after candidiasis and aspergillosis) in hematological malignancy.^[3] It is a life-threatening infection that causes high mortality despite recent advances in diagnosis and treatment. A retrospective analysis of 14 MCM cases revealed that 6 patients had underlying hematological malignancy. The mortality rate was reported to be 50%.^[4] It was also reported before in CLL patients.^[5,6] Rituximab-fludarabine-cyclophosphamide therapy is first line treatment in fit CLL patients. Our patient had invasive fungal infection within 21 days of receiving fludarabine in spite of taking only one cycle of chemotherapy regimen. A study including 13 mucor cases with underlying hematological malignancy showed that majority of cases occurred post-chemotherapy period and all the patients are neutropenic.^[3] Our patient was also neutropenic after first cycle of chemotherapy and hospitalized with the initial diagnosis of neutropenic fever.

Clinical suspicion is the most important factor for the diagnosis of MCM. Because it may progress leading mortality if not treated.^[5] We firstly hospitalized the current patient with the diagnosis of neutropenic fever and started empirical antibacterial agents. We have waited for recovery but the patient condition deteriorated and swelling on left eye occurred. Fever and neutropenia continued for a long time. PNCT imaging noticed us for MCM. In a large case series, about 25% of patients was

not treated because fungal infection was not suspected.^[3] In neutropenic hematologic patients MCM is rarely suspected. Gold standard treatment includes antifungal agent, reversal of underlying immunosuppression, if possible, and most importantly aggressive surgical debridement.^[5]

The current patient was treated successfully with extensive surgical debridement and intravenous liposomal Amphotericin-B. This case showed us that fludarabine-based regimens can cause severe immunosuppression and fungal infections even after first cycle of chemotherapy. Mortality is better than past in mucormycosis if we start antifungal antibiotics and perform surgical resection as soon as possible.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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