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An Unusual Cause of Central Nervous System Infection During Acute Myeloid Leukemia Induction Chemotherapy: *Acanthamoeba* Brain Abscess

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A 19-year old young adult male was admitted with complaints of low-grade fever of two months duration with multiple petechial rashes all over the body for one week. On routine investigation, hemoglobin was 6.7 g/dl, total white blood cell count was 3200 cells/dl and differential count of 58% polymorphs, 30% lymphocytes and 12% blasts. Bone marrow biopsy with flow cytometry revealed 36% myeloid blasts in bone marrow, confirming diagnosis of acute myeloid leukemia (AML). Cytogenetic study from bone marrow aspirate was normal and FISH studies revealed Inv(16) positive. Patient was started 7 + 3 induction chemotherapy with Cytarabine (100 mg/m² 24-h infusion) and Daunorubicin (90 mg/m²). Day 28 bone marrow revealed normocellular marrow with 6% blasts. Patient was given repeat induction chemotherapy with HAM protocol which included Cytarabine (3 g/m² on D1,

3, 5) with Mitoxantrone (12 mg/m² D4, 5, 6). On day 10 post chemotherapy, patient developed high-grade fever associated with severe holocranial headache. There was no neck rigidity or any focal neurological deficits or papilloedema on examination. Absolute neutrophil count at onset of fever was 128 cells/dl. A diagnosis of febrile neutropenia was kept and patient started on Imipenem + Cilastatin along with Vancomycin. Contrast enhanced computerized tomogram (CECT) of the head was done which was suggestive of peripherally enhancing hypodense lesion in the right parietal region suggestive of an abscess (Fig. 1a). Cerebrospinal fluid (CSF) study did not show any cells with 45 mg/dl of protein (Normal 15–50 mg/dl) and sugar levels of 46 mg/dl (Normal 40–70 mg/dl). CSF bacterial culture was sterile. Polymerase Chain Reaction (PCR) done for TB bacilli, HSV and Toxoplasma was negative. A contrast enhanced magnetic resonance imaging (CEMRI) of the brain was done which was suggestive of a hemorrhagic ring enhancing parietal lobe lesion suggestive of brain abscess—possibly fungal etiology. Hence liposomal amphotericin 5 mg/kg/day was added. Patient became afebrile within a week of therapy and his headache resolved. Day 28 bone marrow aspiration and biopsy showed no excess blasts. Repeat CEMRI brain revealed an increase in the size as well as number of abscesses (Fig. 1b). A stereotactic biopsy was done along with excision of the right parietal abscess. Smear of the abscess fluid showed multiple cysts suggestive of *Acanthamoeba* spp. (Fig. 2a). Culture on non nutrient agar showed the presence of *Acanthamoeba* trophozoites and cysts and were confirmed by PCR (Fig. 2b). Histopathology of the lesion also confirmed multiple cysts with morphology suggestive of *Acanthamoeba* in the abscess cavity wall. Diagnosis of *Acanthamoeba* brain abscess was kept and patient started on combination of ketoconazole, rifampicin, trimethoprim-

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Fig. 1 **a** Non contrast computerized tomography image of the head showing hypodensity in the parieto-occipital region (arrow). **b** T1 weighted CEMRI of brain showing ring enhancing hypointense lesion in the parieto-occipital region (arrow) suggestive of abscess

Fig. 2 **a** Photomicrograph of smear of the abscess fluid from stereotactic biopsy showing multiple cysts (arrows) suggestive of *Acanthamoeba* spp. (H&E; $\times 40$). **b** Image of PCR done on the abscess fluid (Lane 2) obtained from stereotactic biopsy showing positive 500 bp band in par with laboratory control of *Acanthamoeba castellanii* spp. (Lane 4) confirming the diagnosis

sulfamethoxazole and azithromycin. CSF for PCR taken before starting of definitive treatment was negative for *Acanthamoeba* species. Patient is now asymptomatic without any complaints of fever, headache, neurological deficits or papilledema. The treatment will further be continued for 4–6 weeks, followed by a repeat MRI at the end of therapy.

Free living amoebae i.e. *Acanthamoeba*, *Balamuthia*, *Sappinia* and *Naegleria* are pathogenic and can cause CNS infections. The immunocompromised conditions reported to predispose to amoebic encephalitis are organ transplants,

human immunodeficiency virus infections, post-bone marrow transplant, older age with severe debilitating conditions and malnutrition etc. [1]. The occurrence of this sub-acute to chronic infection has not yet been described in AML even though these patients have prolonged period of neutropenia. Confirmatory diagnosis is by demonstrating the pathogen in infected tissues including the cerebrospinal fluid (CSF) or by a positive growth of the pathogen in culture media or by PCR/serologic tests [2]. The case fatality ratio of *Acanthamoeba* encephalitis is more than 90%. The Infectious Diseases Society of America (IDSA)

have a level III(C) recommendation for treatment of *Acanthamoeba* CNS infection with either trimethoprim/sulfamethoxazole along with rifampin, ketoconazole or fluconazole and sulfadoxine/pyrimethamine [3]. The Center for Disease Control and Prevention (CDC) has proposed miltefosine as an investigational drug to treat amoebic CNS infection [4]. This report points out that free living amoebic infections should be considered the differential diagnosis of patients presenting with sub-acute or chronic encephalitis so that the patient can be diagnosed and treated at the earliest.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest between the authors.

Informed Consent Informed signed written consent was taken from the patient involved.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of

the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Human and Animals Rights No animals were involved in the study.

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