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**Disseminated candidiasis: A rare presentation of acute leukemia****Faheem Arshad\* , Tajamul hussain shah, Waseem Raja dar, Rameez Mohiudin Mir , Shabir Ahmad***Senior resident, Department of internal medicine, Sher-i-kashmir institute of medical sciences, Soura, J&K., India*

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**ABSTRACT**

Disseminated fungal disease most commonly found in patients with hematologic malignancies or immune-compromised state, is rarely seen. Though the reported prevalence ranges from 20% to 40%, most fungal microabscesses occur in leukemic patients and are caused by candida albicans; others include cryptococcosis, mucormycosis and histoplasmosis. Hepatosplenic candidiasis also known as chronic disseminated candidiasis has been described in patients with acute leukemia following recovering from neutropenia, pathogenesis of which is not understood, thought to be due to exacerbated inflammatory reaction resulting in an immune reconstitution inflammatory syndrome. The purpose of presenting this case is to describe variable presentation of disseminated candidiasis which can be presenting feature of acute leukemia even without neutropenia and atypical radiological pattern in hepatosplenic candidiasis.

**Keywords:** candidiasis, leukemia, fungal

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**Case report**

20 year male was referred to our tertiary hospital with 1 month history of high grade fever with rigors and chills associated with rash over anterior chest and lower limbs and loss of appetite. In addition he had history of bleeding from gums 3 episodes for 1 week. His examination revealed normal hemodynamics with a temperature of 101.6 F, severe pallor, icterus and petechial rash over anterior chest and lower limbs with bilateral axillary lymphadenopathy. Liver span was 16 cm and spleen was palpable 3 cm below costal margin. Investigation revealed haemoglobin 4.9 gm/dl, total leucocyte count  $2.64 \times 10^3/\mu\text{l}$  (normal range 4-10) with 38% neutrophils and 44% lymphocytes. and platelet count was only  $13 \times 10^3/\mu\text{l}$ . Peripheral blood film showed 10 % promyelocytes, 6% metamyelocytes and presence of 22% blasts. Absolute neutrophil count was 1000. Bone marrow examination revealed 25% blasts, 30% promyelocytes and 6% metamyelocytes[1].

Renal function tests were normal and liver function tests revealed transaminites, raised alkaline phosphatase and hypoalbuminemia (2.6gm/dl). Lactate dehydrogenase levels were markedly raised. Coagulogram revealed anINR of 1.98.<sup>1</sup> Sonography of abdomen revealed multiple hypoechoic lesions 1-2 cm in size in liver and spleen which was typical of type 3 pattern of hepatosplenic candidiasis on sonography pattern (figure 1). It is the least specific pattern of candidiasis and may mimic metastatic disease or lymphoma. Blood cultures including fungal were sterile. Contrast enhanced CT of abdomen revealed multiple hypo-dense lesions of varying sizes with central hyper-dense foci suggestive of bull's eye appearance in liver and spleen (figure 2). Aspiration of lesion yielded growth of candida albicans ruling out a metastatic disease. Final diagnosis of acute promyelocytic leukemia with hepatosplenic candidiasis was made and treatment with all-transretinoic acid and chemotherapy induction with daunorubicin followed by consolidation was given. Patient also received lipid form of amphotericin followed by oral fluconazole. Repeat sonography and CT abdomen revealed disappearance of lesions in liver and spleen. fever not responsive to wide-spectrum antibiotics, abdominal pain and nausea and raised alkaline phosphatase. Diagnosis is always challenging and requires a high

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index of clinical suspicion. Though Pestalozzi BC *et al* were the first to demonstrate disappearance of lesions during neutropenia and reappearance during recovery,

same was not seen in our case as lesions persisted throughout chemotherapy and disappeared after prolong duration of antifungal drugs[2].



**Fig 1: Ultrasonography of abdomen showing multiple hypochoic lesions 1-2 cm in size in liver and spleen which was typical of type 3 pattern of hepatosplenic candidiasis**

Candidiasis mostly affects acute leukemia patients after chemotherapy but our case presented with hepatosplenic candidiasis which is rare. Clinical features include persistent fever not responsive to wide-spectrum antibiotics, abdominal pain and nausea and raised alkaline phosphatase. Diagnosis is always challenging and requires a high index of clinical

suspicion. Though Pestalozzi BC *et al* were the first to demonstrate disappearance of lesions during neutropenia and reappearance during recovery, same was not seen in our case as lesions persisted throughout chemotherapy and disappeared after prolong duration of antifungal drugs[2].



**Fig 2: Contrast enhanced CT of abdomen showing multiple hypo-dense lesions of varying sizes with central hyper-dense foci suggestive of bull's eye appearance in liver and spleen**

In addition 4 imaging patterns of candidemia have been described which include wheel within wheel, a bull's eye pattern, type 3 and 4; of which type 3 is common and non-specific[3]. Thus biopsy of the lesion in such case is gold standard for differentiating it not only from a metastatic lesion but also infective pathology like tuberculosis which is very common in India. Biopsy would reveal multiple granulomas, yeasts and hyphal forms and negative biopsy does not rule out the diagnosis. Tuberculomas also present with multiple round hypoattenuated lesions which would necessitate aspiration of the lesion. Thus diagnosis of hepatosplenic candidiasis is difficult because of a variable presentation. Incidence ranges between 3 and 29% in previous series of leukemic patients, but it is rarely reported now due to widespread use of antifungal agents as prophylaxis or pre-emptive therapy[4]. though promising Candida antigens or molecular methods have not been validated yet. Candidemia is difficult to treat. A mortality rate of 46% was reported in a recent series[5]. Though fluconazole and amphotericin B are preferred, echinocandins are recommended as alternatives and have provided better results to overcome toxicity of amphotericin. Antifungal treatment should be continued until clinical improvement and resolution of lesions on imaging studies (3–6 months) as in our patient. The lesions can appear and disappear depending on rise and fall of neutrophil count, hence antifungal drugs need to be continued throughout periods of immune-suppression and not stopped based on the imaging findings alone. The use of adjuvant corticosteroids and splenectomy has been shown to be beneficial[6] Our case describes a rare association of acute promyelocytic leukemia and hepatosplenic candidiasis highlighting the importance of aspiration of lesion. To conclude disseminated candidiasis is a rare complication of haematological malignancies, proposed to occur by translocation of candida from gastrointestinal tract. It can often be

confused with other infective pathologies in addition to metastatic disease. We presented a patient who presented with multiple hypoechoic atypical lesions in liver and spleen on sonography and hypo-dense lesions on computed tomography, suggestive of an isolated infective or metastatic pathology but to our surprise patient was subsequently diagnosed to acute promyelocytic leukaemia (APML) with hepatosplenic candidiasis which is a rare association among acute myeloid leukaemias.

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