Acute myeloblastic leukemia in a patient with primary antiphospholipid syndrome

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ABSTRACT

Antiphospholipid syndrome is characterized by venous and arterial thrombosis, recurrent pregnancy loss and the presence of the lupus anticoagulant, anticardiolipin antibodies or both. Antiphospholipid syndrome may occur as a primary disease or in patients with systemic lupus erythematosus or other autoimmune, infectious or neoplastic disorders. In this paper we report a 29-year-old Saudi female, a known case of antiphospholipid syndrome, presented with complaints of fever, breathlessness and generalized fatigue. Further investigations confirmed her as a case of myeloblastic leukemia (M1, French-American-British classification). Acute myeloblastic leukemia is not described to be associated with primary antiphospholipid syndrome in the literature to date. This is the first case report of such association.

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Leukemias are rarely associated with antiphospholipid syndrome (APLS). However, occasionally they can develop during follow up of patients with APLS. Thus, the possibility of hematological neoplastic disease should be borne in mind in the initial evaluation and follow up of patients.[1] We report a case of acute myeloblastic leukemia associated with APLS. Such association is not reported in the literature to date.

Case Report. Twenty-nine year old Saudi female, a known case of APLS, presented to the King Fahd National Guard Hospital, Riyadh, Kingdom of Saudi Arabia in August 2002 with complaint of fever, severe shortness of breath and generalized fatigue of 2 weeks duration. Patient was a known case of primary antiphospholipid syndrome with history of 8 abortions and one still birth in the past. Diagnosis of APLS was made in 1999, while being investigated for recurrent abortions by obstetrician. Anticardiolipin antibody titre was significantly raised 34.20 GPL/U (normal <12.4). Test for antinuclear antibody, antibody specific for systemic lupus erythematosus, rheumatoid factor were negative. Serum C3, C4 and 50% hemolyzing dose of complement were normal. As there was no obvious cause for presence of antiphospholipid antibodies, she was diagnosed as a case of primary antiphospholipid syndrome. In October 2001 patient developed breathlessness with bilateral basal pulmonary crepitations. Chest x-ray and high resolution computerized tomography (CT) was suggestive of bilateral pulmonary fibrosis. Transbronchial biopsy revealed non-caseating granuloma and no acid-fast bacillus (AFB) were detected. Keeping into consideration possibility of pulmonary tuberculosis or sarcoid, patient was given a therapeutic trial of antituberculous treatment (isoniazid, rifampicin, ethambutol) and oral prednisolone. Since there was no

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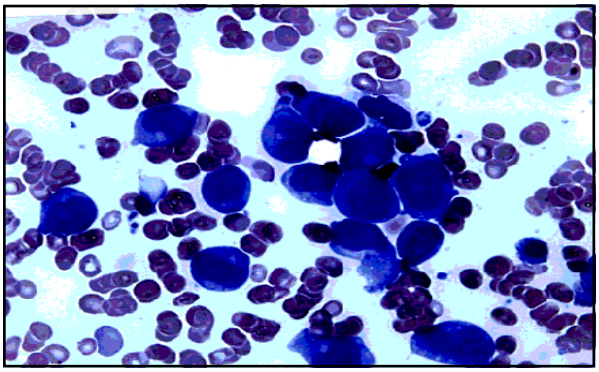

Figure 1 - Bone marrow aspirate with May-Gruwald-Giemsa stain, showing myeloblasts with fine azurophilic granules.

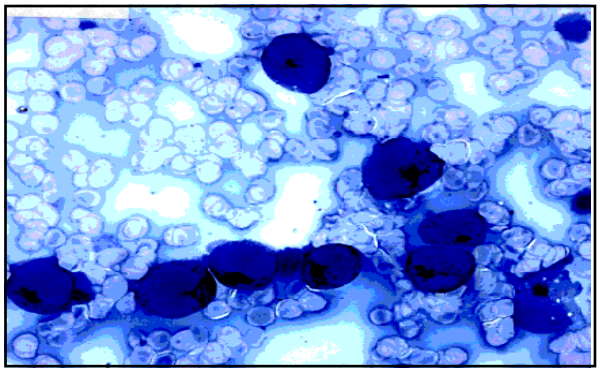

Figure 2 - Bone marrow aspirate demonstrating blast cells strongly positive for Sudan black B stain.

clinical or radiological response, antitubercular drugs and steroids were discontinued in April 2002. Her course was further complicated by inferior venacava thrombosis in October 2001. She was anticoagulated, initially by heparin followed by warfarin. Patient was on warfarin at the time of present admission in August 2002. Clinical examination revealed a cachectic lady, breathless on rest, no cyanosis, respiratory rate 30/mt, temperature 38.5^{0}C, pulse 120/mt, blood pressure 100/70 mm Hg. Marked clubbing of the nails was present. Chest examination revealed bilateral crepitations. Relevant laboratory results revealed hemoglobin 6.4Gm/dl, platelets 24 x 10^{9}/l, white blood counts 31.6 x 10^{9}/l, blood urea nitrogen, serum creatinine, aspartate transaminase, alanine aminotransferase were with in normal limits, and no growth blood culture. Chest x-ray, bilateral diffuse reticulonodular markings, same as seen in October 2001. Peripheral blood showed >95% blast cells, few of them with fine azurophilic granules (**Figure 1**) and strongly positive for Sudan black B (100%) (**Figure 2**). Immunophenotyping by flow cytometry was positive for CD45, CD33, CD34 (>90% positivity), and cytoplamic myeloperoxidase (76% positivity). It was negative for CD2, CD19, CD13, CD7, CD20 and human leucocyte antigen type DR. These results are consistent with acute myeloblastic leukemia (M1, French-American-British [FAB] classification). Patient was planned for bone marrow examination for further detail evaluation of leukemia. She was treated by broad spectrum antibiotics, IV steroids, packed red blood counts transfusion and other supportive measures. Patient was desaturating and exhausting, therefore she was intubated and ventilated. She had rapid deterioration of her conditions and died one week after admission.

Discussion. The clinical features of APLS include the major manifestations as arterial and venous thrombotic events, recurrent pregnancy loss and thrombocytopenia.[2-6] Other minor clinical presentations of APLS include cardiac, hepatic, pulmonary, renal, neurological, hematological and adrenal disorders.[7-8] Syndrome is characterized by presence of anticardiolipin antibodies, the lupus anticoagulant and false positive syphilis serology.[9-11] Most of the clinical manifestations are mediated by vascular thrombo-embolic occlusions. Antiphospholipid syndrome can be found in patients with no clinical or laboratory evidence of any definable condition (primary APLS), or associated with another disease(secondary APLS).[12-13] The case discussed in this article falls in the category of primary APLS. Thrombocytopenia is the most common hematological manifestation of APLS.[9-11,14-17] It is usually mild and occurs in 40% of patients. Hemolytic anemia, Evan's syndrome and neutropenia have also occasionally been found.[15-17] Extensive medical literature has not revealed any association of APLS with acute myeloblastic leukemia (M1, FAB classification). This may be the first reported case of acute myeloblastic leukemia developed in a case of primary APLS. Literature review including Medline search and King Abdul-Aziz City For Science and Technology (KACST), have revealed 2 case reports of chronic myelomonocytic leukemias in patients of APLS.[18-19] Al-Abdulla et al[20] have described a case of chronic myelogenous leukemia associated with anticardiolipin antibodies and bilateral central retinal vein thrombosis. Antiphospholipid syndrome associated with chronic lymphatic leukemia has been reported in a single patient by Ghirarduzzi et al.[21] Acute lymphoblastic leukemia associated with antiphospholipid syndrome, complicated with cerebral infarction has been reported by Donner et al.[22] One case of APLs in a patient of acute monocytic leukemia (M5, FAB classification) has been reported by Mouas et al.[23] Association of APLS with myeloblastic leukemia has yet not been reported. This may be the first case report of such association. This case highlight that the possibility of hematological malignancies should be kept in mind during initial workup, as well as during follow up of APLS patients.

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