Fatal Cerebral Leucostasis in Acute Leukaemia with Hyperleucocytosis

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Introduction

Acute leukaemia may present with extremely high blast counts, a phenomenon known as hyperleucocytosis. It is blood blast count greater than 100,000/cmm and occurs occasionally in Acute Myelogenous Leukaemias [1]. The risk of death is disproportionately high (20% to 40%) when acute hyperleucocytosis is present. Respiratory failure, intracranial haemorrhage and severe metabolic abnormalities occur frequently and are the primary determinants of high mortality. Risk of death due to haemorrhage in the central nervous system is higher in acute myeloblastic leukaemia, lymphoblastic leukaemia and blastic phase of chronic myelogenous leukaemia when thrombocytopenia and hyperleucocytosis are simultaneously present [2]. The management involves vigorous supportive measures and reducing the number of circulating leukaemic blast cells. Red cell transfusions should be minimized initially to avoid increasing viscosity. However platelet transfusions are needed to decrease risk of haemorrhage.

Case Report

A sixteen year-old boy reported to OPD with complaints of pain epigastric region, fever, nausea and vomiting of three days duration. Clinical examination admission revealed pulse=86/min, BP 140/106 mm Hg, Respiratory rate = 22/min, pallor present, axillary lymph nodes just palpable, no petechial haemorrhages or ecchymosis seen. Systemic examination revealed tenderness in epigastric region, spleen tip palpable and hepatomegaly of 3cm. Laboratory reported a very high WBC count of 4,20,000/cmm predominantly with myeloblasts suggestive of AML (Fig 1). USG abdomen showed hepatomegaly with RMD grade I. Peripheral Blood smear-RBCs showed mild anisopoikilocytosis, predominantly microcytic hypochromic, No schistocytes seen, myeloblasts 83%, promyelocytes 06%, myelocytes 03%, metamyelocytes 02%, stab forms 1%, lymphocytes 5%, granulocytes nil, Auer

rods seen in some myeloblasts, myeloperoxidase negative, non-specific esterase negative, PAS faint staining positive in blast cells. Severe thrombocytopenia with platelet count of 30,000/cmm present. Diagnosis of Acute Myeloid Leukemia – FAB-M1 was made.

Patient was treated with transfusion of one unit of packed red cells, two units of platelet concentrate and fresh frozen plasma was demanded. The same evening the patient became semiconscious, poorly responded to commands and passed urine in bed, plantars were extensors bilaterally. Urgent CT scan showed multiple intracranial haemorrhages, ventricular effacement, midline shift and cerebral oedema. Leukaemic infiltration due to cerebral leucostasis was suspected. Patient was treated with intravenous steroids, mannitol, lasix, antibiotics and metrogyl but his condition deteriorated and he succumbed the same day.

Discussion

Hyperleucocytosis is more common in acute than in chronic leukaemias. Its incidence ranges from 5% to 13% in adult acute myeloid leukaemias. Risk factors for hyperleucocytosis include younger age, certain types of leukaemias (microgranular variant AML-M4, AML-M5, T-cell ALL) and cytogenetic abnormalities (11q23 translocations or presence of Philadelphia chromosome) [3].

Symptoms of hyperleucocytosis are primarily due to leucostasis, a clinicopathologic syndrome caused by the sludging and overcrowding of circulating leukaemic blasts in tissue microvasculature. It is now becoming increasingly evident that leucostasis results from the adhesive interactions between leukaemic blasts and the endothelium; a mechanism that none of the current therapies directly addresses [4]. The endothelial damage associated with leucostasis is likely to be mediated by cytokines released in situ and by subsequent migration of leukaemic blasts in the perivascular space. A difference in the expression of adhesion molecules on

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Fig. 1 : Photomicrograph showing Hyperleucocytosis due to blast cells in peripheral blood (x 10)

lymphoblast surfaces may explain the higher incidence of leucocytosis in AML vs. ALL.

Although leucostasis can affect any organ system, symptoms usually arise from the involvement of the pulmonary and cerebral microvasculature and early deaths are due to respiratory failure and intracranial haemorrhage. Patients can present with exertional dyspnoea due to severe respiratory distress [5]. Neurological manifestations range from mild confusion to stupor and coma. Focal central nervous system deficits may herald intracranial haemorrhage. Fatal intracerebral haemorrhage may occur [6]. Priapism, enlarged kidneys, hyperuricaemia and renal failure are features of genitourinary involvement. Vascular symptoms include DIC, retinal haemorrhage, myocardial infarction and renal vein thrombosis.

Laboratory evaluation should include assessment for thrombocytopenia, coagulopathy and tumour lysis syndrome. Platelets have to be counted manually, since a spurious elevation of the automated platelet count can occur due to the presence of fragments of white and red cells [7]. Adverse indicators are white cell counts of more than 250,000/cmm or neurologic compromise. Onset of leucostasis may be abrupt and once initiated, it may be fulminant and irreversible.

This condition is a medical emergency which needs prompt recognition and therapy. Initial management includes aggressive hydration with intravenous fluids, use of allupurinol and hydroxyurea; correction of abnormalities of metabolism, coagulation and electrolytes and prevention of tumour lysis syndrome. Definitive treatment consists of leucoreduction (via cytotoxic chemotherapy), hydroxyurea and leukapheresis.

Transfusions should be avoided unless the patient has symptoms of anaemia and the haemoglobin is less than 7-8 g/dl. Increasing the erythrocrit and consequently,

the whole blood viscosity can lead to the development and worsening of leucostasis when the leukocrit is already high in patients with acute hyperleucocytosis. However platelet transfusion is needed to decrease the risk of fatal haemorrhage.

Prompt reduction in the number of circulating blast cells (leucoreduction) is essential to prevent leucostasis in patients with acute hyperleucocytosis and to treat or halt the progression of established leucostasis [8]. Leucoreduction can be achieved by induction chemotherapy, hydroxyurea and leukapheresis. Leukapheresis involves the removal of circulating blasts cells with re-infusion of leukocyte-poor plasma and is started in patients of AML with leucostasis irrespective of the blast count [9,10].

Conflicts of Interest

None identified

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