Acute Lymphoblastic Leukemia Complicated by Acute Severe Asthma - A Rare Finding: A Case Report

Abstract

Introduction : The leukaemias are a group of disorders characterized by the accumulation of malignant white cells in the bone marrow and blood. These abnormal cells cause symptoms because of bone marrow failure and infiltration of organs; but acute severe asthma has not been reported as one of the manifestations/complications of acute lymphoblastic leukemia.

Objective: The aim of this paper is to briefly review the literature on acute lymphoblastic leukemia and its clinicopathologic relationship with asthma. A case of Acute Lymphoid leukemia being complicated by acute severe asthma is also reported.

Method/Result: I present a 36-year old male welder who came to the hospital with anaemic heart failure, leucocytosis and thrombocytopenia. Final diagnosis of acute lymphoblastic leukemia was made following bone marrow aspiration cytology and was subsequently commenced on chemotherapy. After successful Induction and Consolidation therapy, the patient had Acute Severe Asthmatic attack during the maintenance therapy and subsequently died in the hospital.

Conclusion: Acute Lymphoblastic Leukemia can be complicated by acute severe asthma. Early diagnosis and use of genuine cytotoxic drugs will go a long way to ameliorate the complications of Acute leukemia.gs gave variable results. Local injections with lidocaine were also successful. Refractory cases had surgical decompression.

Conclusion: Entrapment neuropathies were common conditions prevented by early identification and treatment.

Keywords: *Acute Lymphoblastic Leukemia Acute Severe Asthma*

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Introduction

Acute Lymphoblastic Leukemia (ALL) is a neoplastic disease that results from multistep somatic mutation in a single lymphoid progenitor cell at one of several stages of development[1]. Leukemic cells accumulate relentlessly because of their altered response to growth and death signals[2]. They compete with normal haematopoietic cells, resulting in anaemia, thrombocytopenia and neutropenia. At diagnosis, leukemic cells not only have replaced normal marrow cells but also have disseminated to various extramedullary sites such as the liver, spleen, lymph nodes, meninges, gonads and thymus[3].

The presenting features reflect the degree of marrow failure and the extent of marrow spread[4-6]. About 50% of patients present with fever which is often induced by pyrogenic cytokines (such as IL-1, IL-6 and TNF) released from leukemic cells[7,8]. Clinicopathological relationship between asthma and ALL is not extensively documented in literature. The two major components of asthma are chronic airway inflammation and bronchial hyper-responsiveness where inflammatory cytokines play major roles[9]. Many mediator cytokines have been implicated in the asthmatic response. The cytokines (released by lymphoblasts in ALL) provoke acute bronchoconstriction through central and local reflexes together with increased vascular permeability, oedema and mucus secretion. The cytokines are also known to cause influx of eosinophils whose major basic protein cause epithelial damage[10] and airway constriction[11]. This results in coughing, wheezing, chest tightness and shortness of breath. In some patients, the bronchial wall may lead to irresversible obstruction of airflow.

Case Report:

EE is a 36year old welder who presented to the Haematology clinic of Delta State University Teaching Hospital (DELSUTH) on 10/12/2010 with complaints of recurrent fever, cough, abdominal and leg swellings for one month duration. The cough was productive of frothy/whitish sputum, worse at night, distressing and not associated with chest pains. There was high grade intermittent fever associated with throbbing headache and blurring of vision. The abdominal swelling was associated with easy satiety. There was no vomiting and no change in bowel movements. The leg swelling were progressive, associated with orthopnea but no leg pains. There was no bleeding diathesis. He was not a known asthmatic. The essential findings on physical examination were that of a young man in respiratory distress, febrile and severely pale. There was axillary lymphadenopathy and bilateral pitting pedal oedema. The respiratory rate was 48 cycles per minute and there was bilateral coarse crepitations affecting the lower lung zones. The pulse rate was 116 beats per minute and there was hepatosplenomegaly.

Laboratory investigations revealed a packed cell volume (PCV) of 16%, white cell count (WBC) of 95, 100 per mm^3 with lymphoblastosis of 69.5%. The platelet count was 100,000 per mm^3. Malaria parasite was positive (+ + +). Leishman stained Peripheral blood film showed normochromic normocytic red blood cells with increased number of lymphocytes most of them were immature. Bone Marrow Aspiration Cytology showed a hypercellular spiculate marrow with lymphoblasts making 90% of marrow cells. Morphologically, the lymphoblasts were homogenous and having thin rim of basophilic agranular cytoplasm and also increased nucleo-cytoplasmic ratio.

Diagnosis: Acute Lymphoblastic Leukemia (ALL) of FAB subtype L_1 and Anaemic heart failure. The patient was transfused with three units of red blood cells (as packed red cells) and one unit of fresh whole blood. The patient was placed on Induction chemotherapy on 29/12/2010 using the COAP-regimen (Cyclophosphamide, Oncovin, Arabinocide

Cytosine and Prednisolone). He was also treated for malaria using Artemisinin-combined therapy (ACT). The patient achieved remission, and consolidation therapy was given using same regimen. He was doing very well and stable clinically, with his blood counts within normal ranges. He commenced maintenance therapy on 16/2/2011 using methotrexate, vincristine and dexamethasone. On 6/10/2011 while still on maintenance therapy, he was rushed to the Accident and Emergency Unit of DELSUTH with clinical features of Acute severe asthma. He was immediately placed on IV aminophylline, IV hydrocortisone, nebulized salbutamol with oxygen and prednisolone. Repeat of WBC was 156,000 per mm^3. Significant finding on Chest radiograph was hyperinflation of the lungs and air trapping extending to the neck. He died on 21/10/11 while still on admission.

Discussion

There is a great variation in the clinical presentation of patients with leukemia depending on the extent of bone marrow involvement and dissemination to other extramedullary sites [4-6]. The initial complaints of productive cough in this patient which was worse at night was not directly due to the effect of leukemic cells, rather, it was due to congestive cardiac failure secondary to anaemia. Prompt and early management of the anaemia with red blood cell transfusion would have prevented degeneration to heart failure. In addition, early diagnosis of leukemia and commencement of chemotherapy would have also significantly reduced the sequelae of anaemia. The anaemia and mild thrombocytopenia were due to the bone marrow suppressive action of malignant lymphoblasts on erythropoeisis and megakaryopoeisis, respectively. The patient benefited from red blood cell transfusion (as packed red cells) and fresh whole blood (within six hours of donation) to correct the anaemia and thrombocytopenia, respectively. Thrombocytopenia is best treated with platelet concentrate. This patient was given fresh whole blood as an alternative because at the time of presentation, the hospital did not have the facility to make blood products. The patient was responding very well to the chemotherapeutic agents. He was on maintenance chemotherapy when he had acute severe asthma, which has not been reported to be a complication of acute lymphoblastic leukemia. Firstly, there is a possibility of development of resistance to the cytotoxic drugs by the malignant cells leading to their increased proliferation and ultimate extramedullary spread/ dissemination to the lungs. Secondly, one would have expected the intake of steroids to ''prophylactically'' protect this patient from asthma, again the genuineness of the medications may be in doubt because the patient procured some of his drugs outside the hospital. Again, various cytokines and proteins released by clones of lymphoblasts such as IL-1, IL-6 and TNF have been shown to play a major role in the pathogenesis of acute severe asthma[10-11]. This calls for research and possible production of medications against these cytokines as a novel approach in management of asthma arising as a sequelae of acute lymphoblastic leukemia.

Conclusion and Recommendation

Acute severe asthmatic attack is a complication of acute leukemia- a call for

vigilance. It is recommended that our hospitals especially the tertiary healthcare centres should keep in stock and make available chemotherapeutic agents to prevent the use of substandard drugs which can lead to development of resistance by malignant cells. There is need for pharmaceutical research into the area of anti-cytokines medications for asthma treatment.

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