ABSTRACT

Acute Lymphoblastic Leukaemia (ALL) a malignant proliferation of immature lymphoid cells is a biologically heterogeneous disorder with variable outcomes in adults. We present a case report of a 54 year old woman who presented with fever, anaemia and peripheral lymphadenopathy of four weeks duration, and was managed for disseminated tuberculosis initially. Full blood count and bone marrow aspiration cytology constituted part of her initial investigations and were found to be in keeping with acute lymphoblastic leukaemia (ALL-L3). Patient had supportive treatment and managed with Cyclophosphamide, Vincristine (Oncovin), Cytosine Arabinoside and Prednisolone (COAP Regimen), achieved complete clinical and haematologic remission, and has remained disease free after consolidation and maintenance therapy. No evidence of haematologic or clinical relapse at five years and currently in her ninth-year post diagnosis and treatment. With high index of suspicion, timely investigation and referral, satisfactory outcomes are achievable in managing some patients with acute lymphoblastic leukaemia.

Keywords: Acute lymphoblastic leukaemia, Cytotoxic, Chemotherapy, Disease free survival.

INTRODUCTION

Acute leukaemias are a group of clonal malignant disorders of the white blood cells characterised by impaired maturation of the early haemopoietic cells, accumulation of blast cells in the bone marrow, spillage into the peripheral circulation and tissue infiltration. It may be acute myeloblastic leukaemia (AML) or acute lymphoblastic leukaemia (ALL) and less frequently mixed lineage. Acute lymphoblastic leukaemia arises from an early lymphoid progenitor cell that may give rise to cells with either B- or T-cell phenotypes. The aetiology of acute leukaemias are mostly unknown but certain risk factors like chronic exposure to benzene and radiation, previous therapy with some cytotoxic drugs, congenital abnormalities like Down syndrome have been associated...
Acute lymphoblastic leukaemia is the most common form of leukaemia in children but has a bimodal distribution with an age-adjusted incidence of 1.7 per 100,000 persons in the United States affecting 4 to 5 children per 100,000 and half that number around the fifth decade of life. Acute lymphoblastic leukaemia remained relatively high among adults in selected South American, Caribbean, Asian, and African populations as corroborated by Egesie et al in a sixteen years review of haematologic malignancies in Jos, Nigeria.

Clinical features occur as a result of bone marrow failure, organ infiltration, haemopoietic marrow expansion and acquired immunologic deficiency while diagnosis are made from history, physical examination and laboratory investigations that include full blood count, bone marrow aspiration cytology, cytogenetic analysis and Immunophenotyping.

Modalities of treatment of acute lymphoblastic leukaemia include chemotherapy, immunotherapy, radiotherapy and stem cell transplant. However, a number of biological variables affect individual response to all the management strategies thereby determining the chance for long term survival or cure in an individual. Treatment outcomes are much better in children than in adults and also better in females than males.

We are not aware of any record of long term, ALL, post cytotoxic chemotherapy disease free survival in our setting. We report a case of Acute Lymphoblastic Leukaemia in an Elderly Nigerian woman who achieved remission and over five year disease free survival following a first line chemotherapy.

**CASE REPORT**

AL is a 54-year-old female, retired civil servant referred to us on the 21st March, 2011 by the pulmonology unit of the Jos University Teaching Hospital where she initially presented with a four weeks history of recurrent headache, fever and axillary swelling with a two days history of worsening cough and breathlessness. She had no associated mucosal bleeds or bone pain, and no history of ingestion of unpasteurized milk or contact with patients having chronic cough. Patient had six (6) weeks of anti-Koch's for suspected disseminated tuberculosis (DTB) without improvement.

On examination, she was moderately pale, anicteric, acyanosed, febrile (temperature 37.7°C) with a solitary lymph node enlargement in the right axilla. Chest was clinically clear while pulse rate was 100 beats per minute with a blood pressure of 120/60 mm Hg. Abdominal examination showed a full abdomen, moderate epigastric and left side tenderness, liver was 6cm below the right coastal margin while the spleen was 20cm below the left coastal margin.

Packed Cell Volume (PCV) was 0.20, White Blood Cell (WBC) Count of 125 x 10^9/L (Lymphoblast 93.7 x 10^9/L, Lymphocytes 6.3 x 10^9/L, Neutrophils 25.0 x 10^9/L), Platelet 107 x 10^9/L (Fig 1a) ESR 46 millimetres in the first one hour. Bone marrow aspiration (BMA) cytology showed a Hypercellular marrow with vacuolated-lymphoblast infiltration in keeping with Acute Lymphoblastic Leukaemia (ALL), French-British-American (FAB) Class L (Fig 1b). Electrolytes, Urea and Creatinine were within normal range, liver function test was slightly deranged while human immune deficiency, hepatitis B and C viral screenings were negative. Her ABO/Rh blood group was O'Rh positive.

The patient and care givers were counselled on the diagnosis, treatment options, side effects and prognosis. Supportive treatment was commenced using intravenous fluid, allopurinol, blood transfusion, and prophylactic antibiotic administration. Patients estimated body surface area was 1.3 meter square (m²). She was commenced on remission induction with intravenous (IV) Cyclophosphamide 1gram on days 1 and 8, Vincristine-2mg weekly for four weeks, Cytosine Arabinoside-100mg daily for ten days and tabs Prednisolone-20mg twelve hourly for twenty-eight days (COAP Regimen). She was transfused one unit of packed red blood cells daily for 3 days. Full blood count on the 5th day post induction was; PCV 0.29, WBC 20 x 10^9/L (Lymphoblast 12.0 x 10^9/L, Lymphocytes 4.0 x 10^9/L, Neutrophil 4.0 x 10^9/L) Platelet 50 x 10^9/L. Patient had her fourth unit of packed red cells...
on the 6th day of chemotherapy and subsequently certified fit for discharge to continue chemotherapy on outpatient bases. She was assessed for remission in our day-ward after the 28th day of the first cycle of COAP and was assessed to have improved clinically but had lymphoblast of 10% on peripheral blood film. Re-induction with COAP regimen was then instituted and completed four weeks later. Assessment of remission after re-induction was confirmed favourable with PCV of 0.34, WBC 3.12 x 10^9/L (Lymphocytes 2.1 x 10^9/L, Neutrophil 1.02 x 10^9/L), Platelet 186 x 10^9/L. Electrolyte, Urea, Creatinine, fasting blood glucose and liver function test were assessed to be normal except a slightly raised alanine and aspartate transferase. Two cycles of the COAP regimen was used for consolidation of remission.

Patient remained stable after the consolidation of remission and maintenance regimen of Tabs 6-Mercaptopurine 100mg daily, Tabs Methotrexate 20mg weekly, IV Vincristine 2mg monthly and Tabs Prednisolone 20mg twice daily, days 1-5 monthly was prescribed. All medications prescribed for maintenance were procured and administered except 6-mercaptopurine which was not readily available. She commenced the maintenance therapy after completion of consolidation therapy. Five days after commencement of the maintenance therapy, she presented at the haematology day ward with complaints of progressively increasing jaundice and body itching. Abdominal ultra-sound showed enlarged spleen with a normal liver architecture while liver function test was deranged with total bilirubin-305 mmol/L, Conjugated bilirubin-259 mmol/L, alkaline phosphatase-179 IU/L, alanine and aspartate transaminase of 1,392 and 2,420 IU/L respectively. A diagnosis of Methotrexate induced hepatitis was made and it was withdrawn from her treatment regimen. In the absence of 6-mercaptopurine, the patient was maintained on monthly 2mg of intravenous Vincristine and oral prednisolone for five days every month. Her follow up continued with monthly FBC and fasting blood glucose (FBG). Patient completed her maintenance therapy on the 29th November, 2013 with a PCV of 0.39, WBC 3.9 x 10^9/L (Lymphocytes 1.8 x 10^9/L, Neutrophil 1.9 x 10^9/L, Monocytes 0.2 x 10^9/L), Platelet 148 x 10^9/L. She continued her uneventful routine medical check and at five (5) years after achieving remission on the 7th October, 2016 she had a PCV of 0.35, WBC 6.77 x 10^9/L (Lymphocytes 1.7 x 10^9/L, Neutrophil 4.5 x 10^9/L, Monocyte 0.4 x 10^9/L, Eosinophil 0.2 x 10^9/L), Platelet 206 x 10^9/L(Fig 2a) with a normal bone marrow cytology (Fig 2b) while the last FBC on the 6th February, 2020 showed a PCV of 0.30, WBC 6.33 x 10^9/L (Lymphocytes 1.7 x 10^9/L, Neutrophil 4.0 x 10^9/L, Monocyte 0.4 x 10^9/L, Eosinophil 0.1 x 10^9/L, Basophil 0.1 x 10^9/L), Platelet 277 x 10^9/L(Fig 3).

Figure 1a: Peripheral Blood Film at Diagnosis showing some vacuolated lymphoblast (Leishman Stain x 100)

Figure 1b: Bone marrow film at diagnosis (Leishman Stain x 40)
DISCUSSION

Acute lymphoblastic leukaemia (ALL) is a haematologic disorder characterise by the malignant transformation and proliferation of the lymphoid progenitor cells in the bone marrow, peripheral blood and extramedullary sites. Eighty percent of ALL occurs in children with a more devastating outcome when diagnosed in adults. An estimated 6,590 were diagnosed in the United States with over 1,400 deaths due to ALL. Significant improvements in treatment outcome have been recorded in paediatric patients with the dose intensification strategies but its prognosis has remained very poor among the elderly hence this report of rare outcome observed in our patient.

At the onset of the management of this patient there was what seem to be a diagnostic dilemma obviously due to her clinical presentation necessitating a clinical trial with anti-Koch's until a full blood count was done. This then brings to bear the need to closely look at differential diagnosis at the onset of managing any patient with a view of carrying out every necessary investigation to narrow down to specific diagnosis for the purpose of early institution of specific treatment for better outcomes. Practitioners in developing countries could invite haematologists early to review and evaluate patients presenting with fever, anaemia and lymphadenopathy as was the case in this patient. Other known features of leukaemia such as mucosal bleeds, bone pains, pruritus and palpable organomegaly should raise suspicion.

The treatment of this patient required supportive antibiotic administration and blood transfusion to manage anaemia, neutropenia and thrombocytopenia. The reliance on fresh whole blood for the care of this patient calls for commitment to improve blood transfusion service with provision of blood component in developing Countries like ours. The inclusion of malignancies under the coverage of the national health insurance scheme would provide the needed opportunity to properly care for increasing number of patients being diagnosed with leukaemia.

Accurate assessment of prognostic factors is central to the management of ALL. The age of our patient, her race, leucocyte count, FAB class, period within which remission

Figure 2a: Peripheral blood film 5 years post chemotherapy (Leishman Stain x40)

Figure 2b: Bone marrow film 5 years post chemotherapy (Leishman Stain x 40)

Figure 5: Peripheral blood film as at 6th February, 2020 (Leishman Stain x 40)
was achieved coupled with her economic status and our resource poor settings were identified pointers to bad prognosis. The availability of cytochemistry, Immunophenotyping and genetic studies would have strengthened the diagnosis, appropriate indebt classification, prognostication and molecular follow up of the patients. Total dependence on morphologic studies in addition to clinical features remains a major limitation in the management of patients with suspected or diagnosed leukaemia in Nigeria.

The COAP regimen used for the induction of remission enable us to achieve remission after two cycles. Worthy of note is the fact that, though central nervous system (CNS) prophylaxis is recommended in the management of ALL, but this was not administered in this case to minimize complications associated with lumbar puncture in such patients. The patient improved remarkably and never showed signs of CNS involvement throughout the course of treatment affirming the need to personalise treatment regimen for each patient. Daily 6-mercaptopurine and weekly Methotrexate are drugs required for maintenance therapy but these were not used in our patient because of financial constraints and unavailability. Her maintenance therapy was carried out using only Vincristine and prednisolone.

Treatment outcome of ALL have significantly improve in the past two decades with 80% of treated children recovering compared to 30-40% cure rate in adults. Achieving first remission has regrettably been difficult in Nigeria with early death still a typical outcome. This poor outcome may be as a result of poverty, poor supportive care in terms of blood and blood products, absent standard infection control strategies at the phase of chemotherapy induce myelosuppression as well as lack of standard chemotherapy supply either because patient could not afford and sustain supply or substandard agents in circulation.

CONCLUSION

We conclude that successful management of patients with poorest prognosis ALL could be achieved in resource limited setting like ours. The index patient has been disease free for more than five years now, confirming the possibility of cure in ALL using cytotoxic chemotherapy.

Limitations

Absence of diagnostic tools for cytochemistry, cytogentic analysis, Immunophenotyping, were limitations to our diagnosis and follow up.

Recommendation

There is a global advancement in the treatment of ALL with 80% curability rate for treated ALL, authorities should support policy implementation aimed at improved management protocols that will enable us carry out Immunophenotyping, cytogentic analysis and other molecular studies to support our diagnosis and enhance treatment, prognostication and follow up. Avenues for enhanced human resource development, facility upgrade, adequate transfusion support and supply of chemotherapeutic agents at subsidized rates is also advocated.

Acknowledgment

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Declaration of Patient Consent

Appropriate patient consent was obtained. Patient gave consent for clinical information to be reported in journal. The patient understands that effort will be made to conceal her identity though anonymity cannot be guaranteed.

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