

**CHRONIC MYELOID LEUKAEMIA PRESENTING WITH MASSIVE ASCITES:  
A CASE REPORT****YUGUDA SALEH<sup>1</sup>, GIREI I. AHMED<sup>1</sup>, SAIDU ABUBAKAR<sup>2</sup>, LAWAN I. ALIYU<sup>3</sup>****ABSTRACT**

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Chronic Myelogenous Leukemia (CML) is a clonal disorder of the pluripotential stem cell characterized by anaemia, extreme blood granulocytosis and granulocytic immaturity, basophilia, often thrombocytosis, and splenomegaly. Only a few cases of extramedullary manifestation have so far been reported in CML. We present a case of CML in accelerated phase with massive ascites who responded well to combination chemotherapy and oral hydroxyurea.

**KEYWORDS:** Chronic Myeloid Leukemia, extramedullary blast, ascites.

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**INTRODUCTION**

Chronic Myelogenous Leukemia (CML) is a clonal disorder of the pluripotential stem cells characterized by anaemia, extreme blood granulocytosis and granulocytic immaturity, basophilia, often thrombocytosis, and splenomegaly. It is caused by a balanced genetic translocation, t(9;22)(q34;q11.2), involving fusion of the Abelson oncogene (ABL) from chromosome 9q34 with the breakpoint cluster region (BCR) gene on chromosome 22q11.2 thus resulting in the formation of Philadelphia chromosome. The molecular consequence of this translocation is the generation of a BCR-ABL fusion oncogene, which in turn translates into a BCR-Abloncoprotein.

Worldwide, CML has an annual incidence of one to two per 100,000 population and accounts for about 15% of adult leukaemias. It is rarely seen below the age of 20 years and the median age of onset is 50–60 years. The incidence is slightly higher in males than in females. The median age in Nigeria is 38 years with a range of 20–75 years. Clinically, CML is a biphasic or triphasic disease that is usually diagnosed in the initial 'chronic', 'indolent' or 'stable' phase and then spontaneously evolves after some years into an advanced phase, which can sometimes be subdivided into an earlier accelerated phase and a later acute or blastic phase.

The chronic phase lasts several years and is characterized by accumulation of myeloid precursors and mature cells in the bone marrow, peripheral blood, and extramedullary sites. The accelerated phase lasts 4 to 6 months and is characterized by an increase in disease burden and in the frequency of progenitor/precursor cells rather than terminally differentiated cells. The blast crisis lasts only a few months and is characterized by the rapid expansion of a population of myeloid or lymphoid differentiation-arrested blast cells. Extramedullary manifestation though rare in CML,

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can occur in any organ in approximately 10% of CML patients. We report a case of CML in a lady who presented with massive ascites.

### CASE REPORT

A 40 year old full time housewife who was referred to our centre from a general hospital, with a year history of progressive abdominal distension associated with dragging sensation, early satiety and marked loss of appetite and weight loss. There was no history of swelling on the other parts of the body, no dyspepsia or change in bowel habit. There was also history of low-grade intermittent fever. Other systems were apparently within normal limits. While at the source of referral, she was transfused with four units of blood within the last 6 months; the last two units were transfused six (6) weeks prior to presentation. On examination, we found a chronically ill-looking middle aged woman, wasted, afebrile (temp-36.9°C), pale, anicteric with no significant peripheral lymphadenopathy and no pedal oedema. The abdomen was uniformly distended, non-tender, liver was enlarged 10 cm below the right costal margin and the spleen was also enlarged 14 cm below the left costal margin. Both were smooth, firm and non-tender. There was massive ascites demonstrable by fluid thrills.

Laboratory investigations done revealed: Hb - 8 g/dl, WBC -  $115.5 \times 10^9/L$  (differential counts: Myeloblasts - 6%, Promyelocytes - 12%, Myelocytes - 16%, Metamyelocytes - 18%, Band forms - 20%, Neutrophils - 26%, Eosinophils - 2%), Platelets -  $142 \times 10^9/L$ . Peripheral blood film and bone marrow cytology are in consistent with CML in accelerated phase as shown in figure 1.

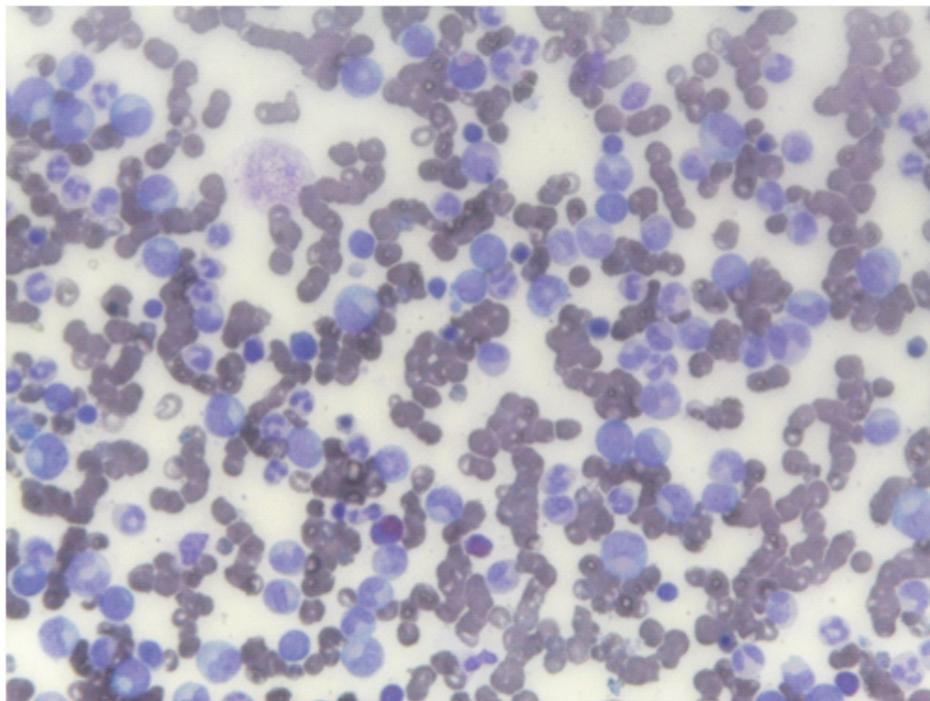
Abdominal ultrasonography shows gross ascites and splenomegaly. No enlarged para-aortic lymph node enlargement. Liver, gall

bladder, pancreatic bed and kidneys were normal. Both liver and renal function tests were within normal limits. Viral screening (hepatitis B & C and HIV I/II) were negative.

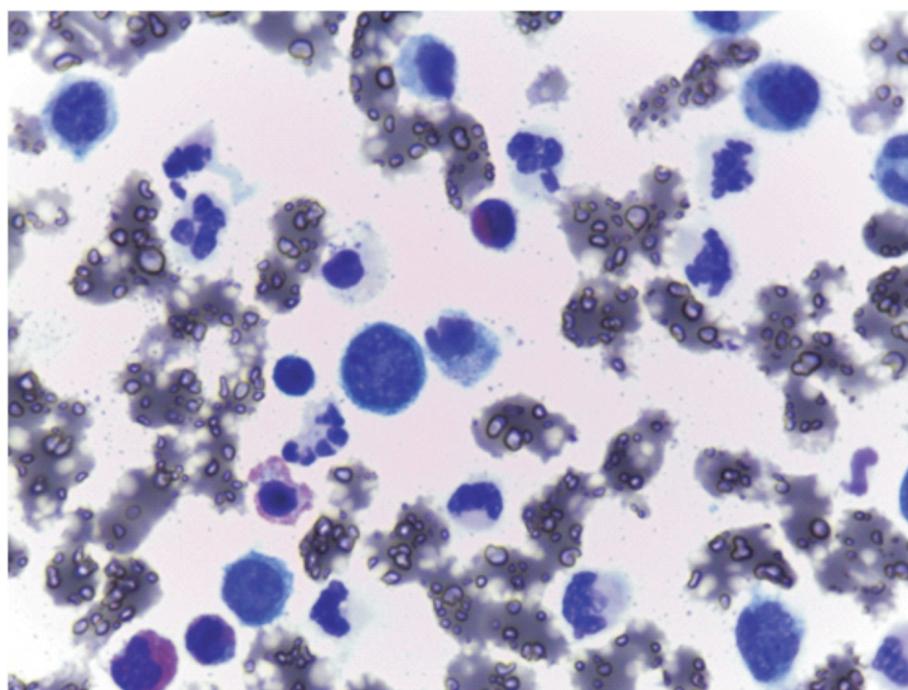
Ascitic fluid tap revealed a haemorrhagic ascitic fluid and chemistry revealed glucose of 4.1 mmol/L, total protein 49 g/L (serum total protein 66 g/L), albumin 33 g/L (serum albumin 37 g/L). Ascitic fluid cytology (figure 2) showed numerous granulocytes at varying stages of maturation (differential count: Myeloblasts - 2%, Promyelocytes - 8%, Myelocytes - 15%, Metamyelocytes - 25%, Band forms - 20%, Neutrophils - 29%, Eosinophils - 1%, Basophils - 0%). A diagnosis of Chronic Myeloid Leukaemia in Accelerated Phase with malignant ascites was made. She was initially placed on combination chemotherapy (cyclophosphamide, vincristine, cytosine arabinoside and prednisolone) which she had one cycle and later maintained on hydroxyurea 2g daily while waiting for the BCR-ABL analysis. There was complete resolution of the ascites and significant reduction in the size of the splenomegaly (from 14cm to 4cm below the left costal margin) after a month of this treatment.

The BCR-ABL analysis done by RT-PCR was positive. (BCR-ABL Quantity - 112,200 copies/reaction; ABL Quantity - 7,929,000 copies/reaction; BCR-ABL/ABL Ratio - 1.41). Due to financial constraints, she could not access OAUTHC (Obafemi Awolowo University Teaching Hospital) Ile Ife for commencement of Tyrosine Kinase Inhibitors (TKIs). Her full blood count also improved; PCV - 28%; WBC -  $22.9 \times 10^9/L$ ; Platelets -  $936 \times 10^9/L$ . She was discharged on hydroxyurea 1g daily and still maintained on this cytoreductive agent as at the time of this report.





**Figure 1:** Bone marrow aspiration cytology film showing hypercellular marrow with granulocytosis (differential count: Myeloblasts – 4%, Promyelocytes – 10%, Myelocytes – 18%, Metamyelocytes – 20%, Band forms – 23%, Neutrophils – 20%, Eosinophils – 2%, Lymphocytes – 3%)



**Figure 2:** Ascitic fluid cytology showing all the cells of myeloid series

## DISCUSSION

Generally, extramedullary blast crisis in CML is considered as a poor prognostic factor with a median time to progression to blastic phase of five months. It is the first manifestation of accelerated phase in approximately 10% of patients with CML with the lymph nodes, serosal surfaces, skin and soft tissue, breast, gastrointestinal or genitourinary tract, bone, and central nervous system among the principal areas involved. Several mechanisms for the development of extramedullary blast crisis in CML have been proposed. These include infiltration of tissues by blast cells, extramedullary haematopoiesis, bleeding into cavities due to thrombocytopenia or thrombocytopathy and non-malignant causes such as infection.

Infiltration of tissues by leukaemic cells usually present with diffused swelling and the composition of the cells have the same picture as the peripheral blood. Extramedullary haematopoiesis on the other hand present as a discrete mass and can occur in almost any organ, including the liver, spleen, breasts, lymph nodes, kidneys, thyroid, pancreas, endometrium, and mediastinum, or in the serous effusion. Unlike leukaemic blast infiltration, extramedullary haematopoiesis includes haematopoietic cells of the erythroid, myeloid, and megakaryocytic cells, although one lineage can predominate.

The first choice of treatment CML is the use of tyrosine kinase inhibitors (TKI). These drugs act via competitive inhibition at the ATP-binding site of the BCR-ABL protein, which results in the inhibition of phosphorylation of proteins involved in cell signal transduction. They efficiently inhibit the BCR-ABL kinase, and also block the platelet-derived growth factor receptor (PDGFR), as well as the C-KIT tyrosine kinase.

Only few cases of extramedullary blast crisis presenting as ascites in CML have so far been

reported worldwide. All the reported cases showed good response to Imatinib (Glivec) and one showed poor clinical response to hydroxyurea.

To the best of our knowledge, there has been no reported case of CML presenting with massive ascites in Nigeria. Our patient presented with massive ascites that was initially thought to be due to chronic liver disease, however, hepatitis B & C screening, liver function test and abdominal ultrasonography does not support this diagnosis. Based on the review of the literature and the clinical presentation as well as the laboratory results, our patient most likely had leukaemic infiltration of the peritoneal cavity by the leukaemic cells as the cause of the massive ascites. She could not be placed on TKIs due to financial constraints and lack of easy accessibility to the only Glivec Trial Centre in the country at OAUTHC Ife, Nigeria. She was therefore commenced initially on combination chemotherapy (cyclophosphamide, vincristine, cytosine arabinoside and prednisolone; which she had one cycle) and later maintained on oral hydroxyurea at 2g daily. There was complete resolution of the ascites and a significant reduction in the white blood cells count (from  $115.5 \times 10^9/L$  to  $45 \times 10^9/L$ ) after one cycle of the treatment. In conclusion, we have presented a case of CML in accelerated phase with massive ascites who responded well with combination chemotherapy and oral hydroxyurea.



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