Case Report

Digital Gangrene in chronic myeloid leukaemia

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SUMMARY

Digital necrosis is an uncommon presentation of chronic myeloid leukaemia.

A male Nigerian with chronic myeloid leukaemia, in accelerated phase with hyperleucocytosis, leucostatic symptoms and gangrene of the right third toe is presented. He had conservative management consisting of combination chemotherapy with partial exchange blood transfusion; having rejected digit disarticulation. Patient achieved full digit recovery on conservative management alone.

This case suggests that digit gangrene in chronic myeloid leukaemia may respond to conservative management with combination chemotherapy and other supportive treatment.

Keywords: Gangrene; Leukemia, Chronic Myeloid; Leukocytosis; Leukemia, Myeloid, Accelerated Phase; Hydroxyurea; Interferon-alpha.

INTRODUCTION

Chronic myeloid leukaemia (CML) generally presents with elevated white blood cell (WBC) count, however WBC count in the hyper leucocytotic range is not as commonly seen as in acute leukaemias.[1] Exaggerated WBC count is as a result of the aberrant proliferation and expansion of myeloid precursors in the bone marrow, a consequence of the dysregulated tyrosine kinase of the BCR-ABL chimeric gene, the molecular hallmark of this disease. Marked elevation in the WBC count causes leucostasis, a condition that results from the sludging of the microvasculature by circulating blasts which have been shown to produce cytokines and adhesion receptors which enable them to activate and bind to endothelial cells and therefore block the microvasculature, leading to leucostatic symptoms. Consequently, it has been suggested that cytokine inhibitors and adhesion molecule antagonists may prevent these symptoms.[2]

Leucostatic symptoms include that of blood hyperviscosity and may include headaches, respiratory insufficiency, cerebrovascular accidents, dizziness, fever, priapism, altered sensorium, blurred vision and digital necrosis.[3] Leucocytosis induced hyperviscosity is a medical emergency and responds to leukapheresis (rapid cytoreduction) and less rapidly to chemotherapy.

In this report, we present a CML patient with digit gangrene who responded to conservative management with combination chemotherapy and other supportive treatment.

CASE REPORT

A 35 year old Nigerian male was referred to our facility with a three month history of left sided abdominal swelling, tiredness, anorexia and jaundice of two weeks duration. There were no swellings elsewhere on the body. He was not a known hypertensive or diabetic patient and not on any chronic medication. His profession was trading; he did not smoke, but took alcohol beverages occasionally.

Examination revealed a young man with moderate

conjuctival icterus and mild mucosal pallor, lymph nodes were not enlarged. Abdominal examination revealed splenomegaly of 19 cm below the left costal margin, mid clavicular line, smooth surface, non tender. Blood pressure was 120/60 mmHg.

Full blood count (FBC) showed a haematocrit of 0.34/L, WBC count of 141 × 10^9/L and a normal platelet count. Differential counts, peripheral blood film (Figure 1) and bone marrow aspirates confirmed chronic myeloid leukaemia, CML, in chronic phase. He was commenced on Hydroxyurea (HU) alongside other supportive medications. Patient's WBC count normalized three months following therapy and spleen size regressed to 5 cm below the left costal margin. He however absconded from treatment for three months and represented with generalized body weakness, left-sided hemiparesis, priapism, dizziness, loss of consciousness, fever, and blackness of the tip of the right third toe, associated with pains, massive splenomegaly and generalized peripheral lymphadenopathy. Examination showed splenomegaly of 16 cm below the left costal margin and darkening of the tip of the right third toe with associated loss of sensation.

Haemogram showed a WBC count of 218 × 10^9/L and an accelerated phase differential picture. A diagnosis of CML in accelerated phase with dry gangrene of the right third toe secondary to leucocytosis was made (Figure 2A).

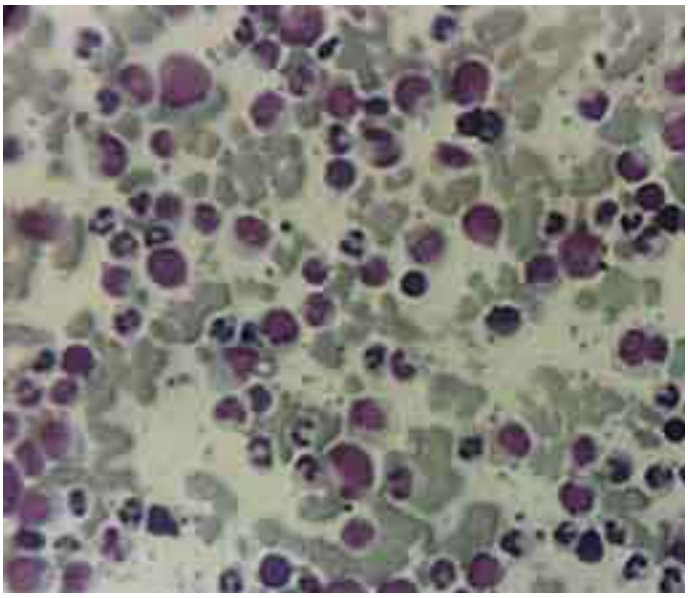

Figure 1. Peripheral blood film showing elevated white blood cell count with a left shift in granulocyte maturation and increased myelocytes.

He was commenced on HU (5g in divided doses initially, gradually reduced to 3g daily over a period of 2 months), α-Interferon (3 mega units daily), low molecular weight heparin (40mg daily) and had partial exchange blood transfusion. Partial exchange blood transfusion was done by performing a phlebotomy and letting out a unit of whole blood, followed by packed red cell transfusion from a compatible donor. Disarticulation was suggested following orthopaedic review where a diagnosis of gangrene of the tip of the right third toe was made. Patient however persistently refused disarticulation despite due counseling. Six weeks on the above regimen, the WBC count normalized, splenomegaly decreased to 9 cm below the left costal margin and the gangrenous area of the right toe showed signs of healing, becoming well demarcated with separation from the healthy area. In addition, other symptoms of blood hyperviscosity, including left sided hemiparesis and priapism resolved completely within this period. He was discharged home on HU, α-Interferon and haematinics. Gangrene resolved completely on the above management (Figure 2B) and patient was followed up for 5 years when he finally absconded from the clinic.

DISCUSSION

In this report, the patient presented in chronic phase and showed a fairly good response following initiation of chemotherapy, he absconded from care for three months and re-presented in accelerated phase with associated hyperleucocytosis and hyperviscosity symptoms. This observation further drives home the place of uninterrupted care in the management of haematological malignancies. Indeed progression to more aggressive tumour biology has been noted in other malignant conditions; following disruption of treatment protocols.[3] As such it is imperative that patients are extensively counseled along this line.

This patient should have had leukapheresis as a way to achieve rapid cytoreduction, this being the standard of care.[3] There were however no facilities for such in our hospital at the time he was seen,

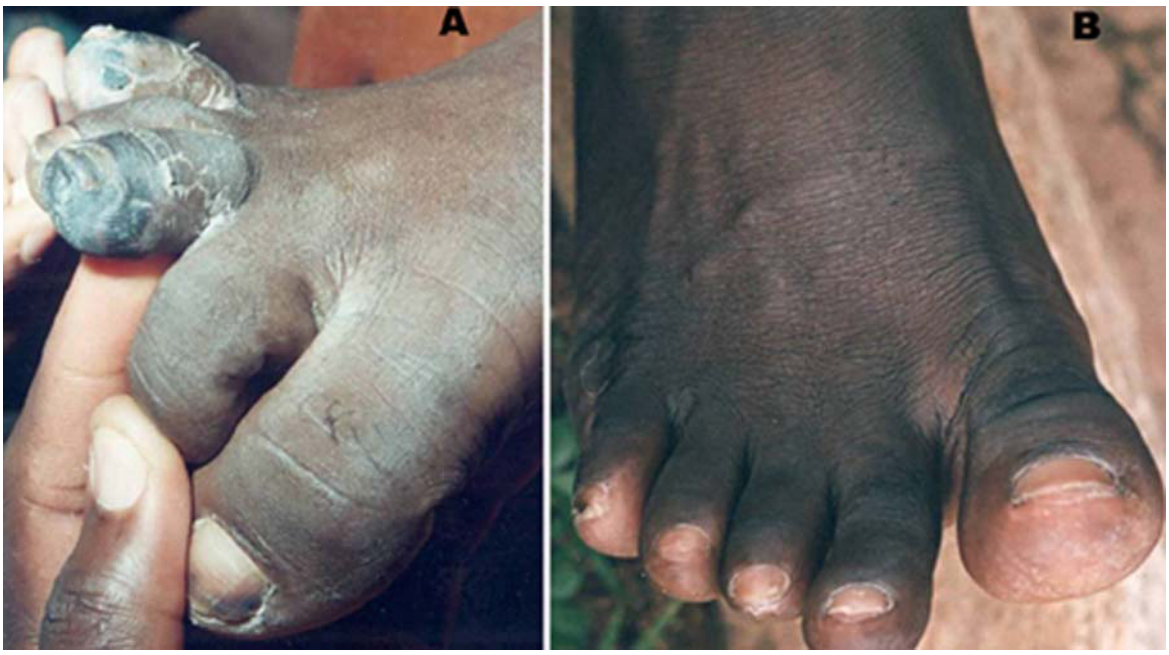

Figure 2. Dry gangrene of the right third toe secondary to leucocytosis (A). Right third toe showing complete resolution of gangrene (B).

consequently chemotherapy was commenced immediately and partial exchange blood transfusion was given as well. Combination chemotherapy may be used for CML patients with progressive disease. Indeed patients in blastic crises may receive combination chemotherapy analogous to that used for de-novo acute leukaemias or tyrosine kinase inhibitors (TKIs) in escalated doses, singly or in combination with other agents.[4,5] Our patient re-presented in accelerated phase and received combination of high dose HU and α-Interferon. He was not offered any of the TKIs because not only were these not available but importantly, the diagnostic facility/manpower for assessing Philadelphia chromosome or the BCR-ABL molecular transcript were all lacking in our facility then.

Interestingly, this patient declined digit disarticulation suggested by the orthopaedic team that co-managed him. This became a significant landmark in his management as he achieved full digit recovery on conservative management alone.

Digital necrosis occurring in the setting of Hepatitis A and Human Immunodeficiency Virus, (HIV) infections have been reported in literature.[6,7] Vasculitis or vasospastic phenomenon is thought to underlie the development of gangrene in these settings. Our patient tested seronegative to HIV1 and 2, however he was not screened for Hepatitis A virus. Other causes of digit gangrene such as trauma, tobacco and drug use were not identified in this patient.

Osteonecrosis of the femoral head as well as digital gangrene have been reported in CML patients, all had hyperviscosity-induced leucostasis.[8,9] Both conditions improved markedly with conservative management which suggests that preventing or quickly reversing the interaction between blasts and endothelial cells may prevent or reverse leucostatic features such as digital necrosis and cerebrovascular accidents. As long as tissue ischaemia is not widespread, there seems to be a place for conservative management bringing about complete restoration.

It thus appears that cytoreduction with opening up of the microvasculature may be superior to invasive (surgical interventions) in cases of gangrene and other conditions that may occur as a result of blood hyperviscosity induced by leucostasis.

FOOTNOTES

Competing interests. Authors declare no competing interests

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