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Case Report: We report a rare case of 49-year-old male with generalized chloromas in chronic myeloid leukemia (CML) associated with multiple cranial nerves deficit suggesting an intracranial involvement. The central nervous system (CNS) is considered to be an uncommon site for chloromas. Treatment with hydroxyurea was unremarkable as the chloroma became more widespread and neurological deficit worsen. This study brings to fore this rare presentation and the apparent limitation of hydroxyurea (cytoreductive therapy) in patient management.

Conclusion: Widespread florid chloromas presenting in chronic phase of CML with associated CNS manifestation is rare. The response to Initial therapy with hydroxyurea was unremarkable. The patient was discharged against medical advice and thus lost to follow-up.



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CASE REPORT

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Introduction: Chloromas or granulocytic sarcomas are extramedullary granulocytic tumors which occur in acute myeloid leukemia (AML), myeloproliferative disorders and myelodysplastic syndromes. They are composed of myeloid blast and herald the onset of systemic relapse. **Case Report:** We report a rare case of 49-year-old male with generalized chloromas in chronic myeloid leukemia (CML) associated with multiple cranial nerves deficit suggesting an intracranial involvement. The central nervous system (CNS) is considered to be an uncommon site for chloromas. Treatment with hydroxyurea was unremarkable as the chloroma became more widespread and neurological deficit worsen. This study brings to fore this rare presentation and the apparent limitation of hydroxyurea (cytoreductive therapy) in patient management. **Conclusion:** Widespread florid chloromas presenting in chronic phase of CML with associated CNS manifestation is rare. The response to Initial therapy with hydroxyurea was unremarkable. The patient was discharged against medical advice and thus lost to follow-up.

Keywords: Chloromas (myeloid sarcoma), Chronic myeloid leukemia, Hydroxyurea, Granulocytic sarcoma

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INTRODUCTION

Chronic myeloid leukemia (CML) is a malignant tumor of the pluripotential hematopoietic stem cell. It is characterized by marked increase in granulocytes and more than 95% of cases are associated with the presence of Philadelphia chromosomes [1]. Chloromas are tumors composed of immature granulocytic cells and reported in 2–5% of cases affected with CML [1]. They are often localized, very rarely generalized and are regarded as an early sign of systemic relapse or blastic transformation [2].

CASE REPORT

A 49-year-old male artisan referred from a private hospital with two months history of left sided abdominal pain, progressive weakness and easy fatigability. He had a persistently low hematocrit ranging from 0.18–0.20 L/L despite repeated transfusion with three units of blood in the private hospital. His physical examination findings were as follows; middle aged man afebrile (temperature 36.8°C), moderately pale, anicteric, not cyanosed, not dehydrated, no significant peripheral lymphadenopathy, no pedal edema, no purpura or ecchymotic lesions. His

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abdomen was asymmetrically distended, moved with respiration. The liver was not palpably enlarged and had a span of 12 cm. The spleen was enlarged and measured 17 cm below the left costal margin, it was firm and smooth with a blunt edge. The kidneys were not ballotable and there was no ascites. Rectal examination was normal; other systems were essentially normal. Hematological investigations of the patient are hematocrit 0.20 L/L, total white blood cell count $135.5 \times 10^9/L$ and platelet count $171 \times 10^9/L$.

Peripheral blood film (PBF) examination showed a complete spectrum of myeloid cells at different stages of differentiation and basophilia- WBC differential: myeloblasts 02%, promyelocytes 05%, myelocytes 22%, metamyelocyte 07%, band forms 20%, neutrophils 33%, eosinophils 03%, basophils 05%, and lymphocyte 03%. Platelets appeared normal on the film (Figure 1A). Bone marrow aspiration (BMA) cytology showed hyperactive myelopoiesis with complete spectrum of myeloid series with peaks at the myelocytes stage of differentiation. Myelogram was as follows: Myeloblast 05%, promyelocytes 6%, myelocytes 24% metamyelocytes 6%, band forms 20%, neutrophils 30%, eosinophils 04%, Basophils 03%, and lymphocytes 02% (Figure 1A). The PBF and BMA examinations were in keeping with chronic myeloid leukemia (CML) in chronic phase. Therefore, patient was counsel on the course of the disease.

Also, 10 mL of EDTA anticoagulated blood sample was used for BCR-ABL transcript quantization. BCR-ABL 1 major (e14a2) transcript type was detected using multiplex PCR method. ABL quantization was 1.20×10^4 copies per micro liter of cDNA, BCR-ABL quantity was 6490 copies per micro liter of cDNA using Real time PCR. BCR-ABL ratio was 54.083%.

The patient was given appropriate counseling on the disease with assistance from Social and Counseling unit of the hospital. Supportive treatments including; optimization of hematocrit, hydration and allopurinol to prevent tumor lysis syndrome were instituted prior to commencement of hydroxyurea at a dose of 1 g daily. On day-3 of admission, patient complained of difficulty in swallowing, hoarseness of voice, slurred speech and facial deviation to the left. There was no headache or limb weakness. He was reviewed by the neurologist who made an impression of multiple cranial nerve palsies secondary to infiltration of cranial nerves V, VI, VII, IX and XII. On day-6 of admission a repeat hemogram was done which showed a hematocrit of 0.29L/L, white blood cell count $191.7 \times 10^9/L$ and platelet count of $415 \times 10^9/L$. Myelogram were: Myeloblast 18%, Promyelocyte 10%, Myelocyte 20%, metamyelocyte 15%, Band form 10%, Neutrophils 15%, Lymphocyte 03%, Eosinophils 02% and Basophils 07% (Figure 1B). Also, multiple subcutaneous nodules involving the scalp, face, trunk and extremities were noticed (Figure 2). The following differential diagnoses were considered; Non-Hodgkin's lymphomas of the lymphoblastic type, large-cell lymphoma and small round cell tumors.

Excision biopsy of a subcutaneous nodule was done. The histologic sections showed diffuse infiltration of fibro connective tissue by sheets of rounds to oval immature cells (blasts) with scant cytoplasm, vesicular to hyperchromatic nuclei and frequent mitotic figures. In many foci, there was also numerous tingible body macrophages scattered within the lesion (Figure 3A–B). Based on this a histological diagnosis of granulocytic sarcoma (chloroma) was made. The dose of hydroxyurea was increased to 2 g daily, however, response both clinical and hematological were minimal. The chloromas became more widespread and the neurological deficits worsen. The patient insisted on being discharged, declining further treatment and referral to another tertiary health facility in South-West Nigeria for further treatment with Imatinib. This chemotherapeutic agent is given free to patients through the support of an international donor agency in this centre. Since then, the patient was lost to follow-up.

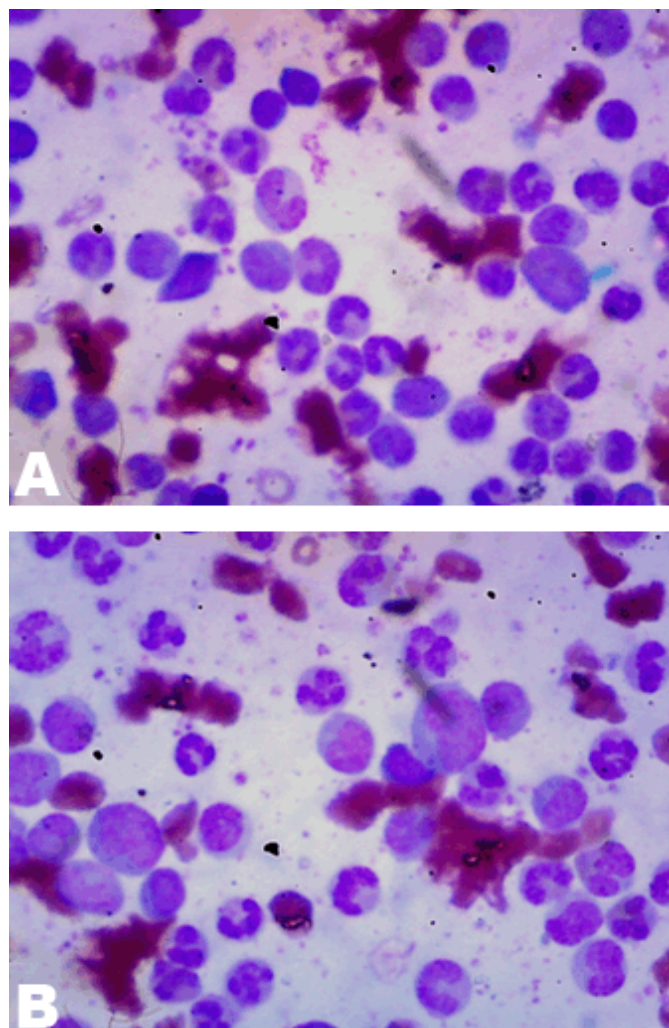


Figure 1: (A) Peripheral blood film of subject, showing complete spectrum of the myeloid cells at different stages of maturation (Leishman stain, x100). (B) Peripheral blood film showing increasing number of blasts (Leishman stain, x100).



Figure 2: Generalized chloromas on different parts of the body of the index patients.

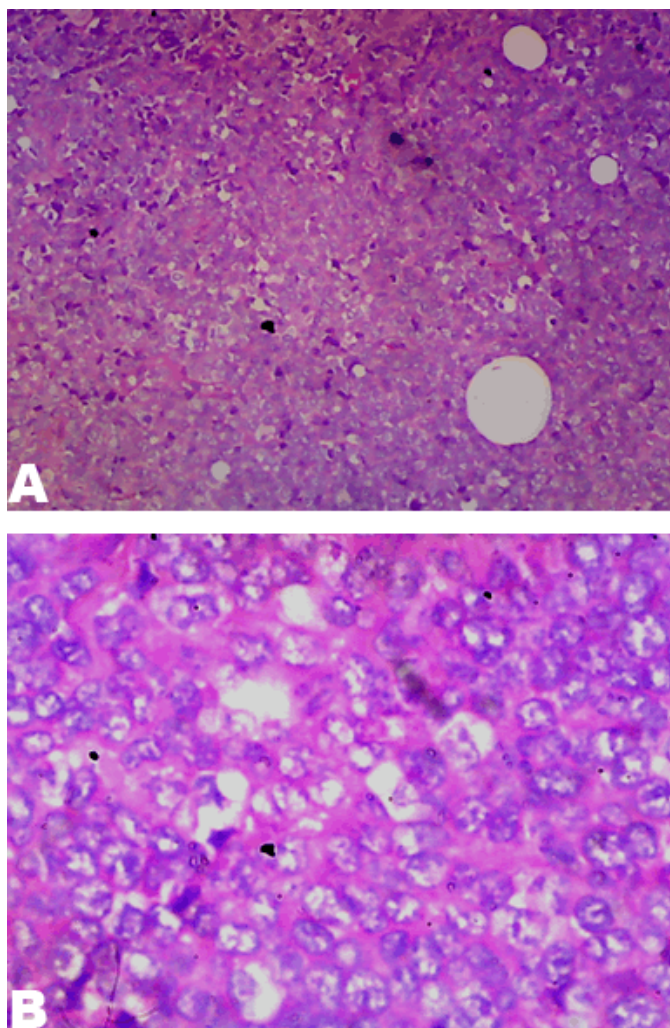


Figure 3: (A & B) Photomicrographs of fibro-connective tissue showed chloroma consisting of round-to-oval immature tumor cells (blasts) with vesicular to hyperchromatic nuclei and scanty cytoplasm admixture with numerous tangible body macrophages (H&E stain, x100, x400 respectively).

DISCUSSION

Granulocytic sarcomas or chloromas are rare extramedullary tumors [3], they are localized tumor

masses usually arising de novo or associated with other hematologic disorders such as acute myeloid leukemia, myeloproliferative disorders or myelodysplastic syndromes [3].

The incidence of chloromas in patients with CML ranges from 2–4% [3–5]. They can present in various organs or tissues. The commonest sites of involvement in CML patients are bone (57%), lymph nodes (29%) and skin or soft tissue (21%) [6]. Involvement of the central nervous system is rare [7]. Both solitary [6] and multiple lesions have been reported [8]. Commonly, chloromas presents in the late stage of the disease or during a relapse and its occurrence is associated with a poor disease outcome [5, 6].

In our index case, the patient developed chloromas while on hydroxyurea, a cytoreductive chemotherapy. Also, the associated neurological deficit involving some cranial nerves may suggests intracranial deposits of these malignant myeloid cells. Intracranial chloromas are seen more commonly in AML or following a relapse case of AML. In CML, it is associated with the onset of blastic crisis [2]. Smidt et al., reported a case of intracranial chloroma which was initially missed-diagnosed as chronic subdural hematoma in a 45 years male with relapsing AML [9]. The diagnosis was, however, made radiologically using gadolinium enhanced magnetic resonance imaging (MRI) scan of the brain and confirmed by biopsy and histology examination of the biopsied tissue. This imaging technique is able to determine the identity of an intracranial mass, particularly when differentiating between intracranial chloromas and hematoma in patients with hematologic malignancies [9]. However, the intracranial involvement in this patient could not be diagnosed radiologically because of financial constraint as the patient was unable to afford the cost of MRI scan of the brain. Healthcare cost is largely out of pocket payment borne entirely by patients in our environment.

Currently, no therapeutic strategies including; chemotherapy, radiotherapy and/or hemopoietic stem cell transplantation have been considered best in the management of this condition [10]. The initial therapy with hydroxyurea used in this case was apparently ineffective as the chloroma persisted and the neurological deficit worsened. Perhaps early introduction of imatinib may have slowed down the progression of the disease. The agent was not available to us and also the patient could not afford it. Hence, the need to refer him to another health facility where he could access the drugs free, but patient declined. Unfortunately, the final outcome of the patient is unknown as he requested to be discharged against medical advice.

CONCLUSION

Widespread florid chloromas presenting in chronic phase of chronic myeloid leukemia (CML) with associated central nervous system manifestation is rare. The patient

response to hydroxyurea was unremarkable. However, the final outcome of this case is unknown as patient was discharged against medical advice and thus lost to follow-up.

Author Contributions

Mabel Ino-Ekanem – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Timothy Amos Ekwere – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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