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Visual and Auditory Complications of Chronic Myeloid Leukemia: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. All the authors were involved in the management of the patient discussed, authors HEO and CI managed the literature searches and all the authors were involved in the review and correction of the final manuscript. All authors read and approved the final manuscript.

Case Report

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ABSTRACT

Hearing loss and visual impairment are not common presentations of Chronic Myeloid Leukemia (CML). We report such a case who presented in the chronic phase with profound hearing loss, visual impairment, progressively enlarging spleen, anaemia, and weight loss.

Laboratory evaluation showed Packed Cell Volume – 10%, Total White Cell Count – 1,343 x 10^9/ L, Platelets – 589 x 10^9/ L. Blood chemistry showed Uric Acid level of 530mmol/L. Karyotyping showed the Philadelphia chromosome.

Chemotherapy was instituted and she improved remarkably with minimal improvement in perception of sound.

Keywords: Chronic myeloid leukaemia; visual impairment; hearing loss.

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1. INTRODUCTION

Chronic Myelogenous Leukaemia (CML) is a haematological malignancy which occurs as a result of clonal expansion of haemopoietic progenitor cells and it is characterized clinically by myeloid hyperplasia, leucocytosis with basophilia, and splenomegaly. There is usually the characteristic Philadelphia chromosome translocation, t(9;22)(q34;p11), which juxtaposes the c-abl oncogene from chromosome 9 with the Breakpoint Cluster Region (BCR) on chromosome 22, resulting in the generation of aberrant bcr/abl transcripts. The abnormal protein produced, causes uncontrolled production of myeloid cells in the bone marrow. These cells crowd out the other normal haemopoietic cells, spill over into the peripheral blood and also infiltrate organs and cause some of the presenting symptoms of CML.

CML can cause hyperleucocytosis with its attendant complications as in the index case. Hearing loss and visual impairment are not common in patients with leukaemia but have been strongly associated with hyperviscosity syndrome [1]. It was difficult to evaluate the cause of loss of hearing in this patient, but a few workers have associated this neurological finding with the slowing of the circulation through small blood vessels in the brainstem.

2. CASE PRESENTATION

A 24 year old woman was referred from a private clinic in Port Harcourt to the Haematology clinic at University of Port Harcourt Teaching Hospital (UPTH), Nigeria on account of a 20 months history of hearing loss and abdominal swelling. She noticed the swelling about 20 months earlier, while receiving antenatal care at the referring centre. The abdominal swelling steadily increased in size and was associated with a dragging pain in the left flank and easy satiety. The obstetrician had told her that the swelling will reduce in size after childbirth. She had normal delivery at term of a healthy female child and the postnatal period was uneventful. The child had normal developmental milestones and had started nursery school by the time the patient presented to our centre.

The patient was seen one year postpartum, and had had continuous low grade fever for two weeks before presentation. This was associated with sudden hearing loss and cloudiness of vision in both eyes. She also complained of severe weakness and small swellings on both buttocks and the right shin. Her menstrual flow had also increased from 4-5 days to 6-8 days during this period, but she denied any history of clots or dysmenorrhoea. She had been transfused 8 pints of whole blood in 6 weeks period before referral to University of Port Harcourt Teaching Hospital.

On examination we found an acutely ill woman in painful distress. She had moderate weight loss, marked pallor and significant cervical lymphadenopathy. Her abdomen was asymmetrically enlarged, (the left more than the right) with an enlarged smooth, firm, non-tender spleen 18cm below the left costal margin. The liver and kidney were not palpable. She had no ascitis. The swellings on the buttocks and shin were soft, fluctuant, warm and non-tender. She walked with her head down, holding up her face with her hands and had no signs of meningism. She had normal tone, power and reflexes in all the limbs. She obviously could not hear, but could read lips and communicated by reading and responding to what was written to her.

Investigations done included Full blood count (FBC) and Erythrocyte Sedimentation Rate (ESR); Electrolytes, Urea and Creatinine (EUC); Liver Function Test (LFT) and Uric Acid

level. FBC showed a WBC of 1343 x 10^9/L with predominance of myelocytes (40%), neutrophils (35%), eosinophils (5%), metamyelocytes (6%), lymphocytes (4%)and basophilia (10%), platelet count of 589 x 10^9/L and packed Cell volume of 10%, ESR of 1mmHr by Westergren method, Uric Acid level was raised – 530mmol/L(150 – 420mmol/L). Renal function test showed Sodium -136mmol/L (128 – 142mmol/l), Potassium – 5.9mmol/L (3.4 – 4.8mmol/l), bicarbonate - 13mmol/l (24 – 32mmol/l), urea – 8.1(2.4 – 6.0mmol/l), creatinine 70mmol/l (60 – 120mmol/l). The liver function test showed total bilirubin of 8umol/l (7 – 15umol/l), AST 32IU/L (1 – 12IU/L), ALT 9IU/L (1-12IU/L), ALK 1166IU/L(98 – 279IU/L).

The patient was encouraged to take at least 3 litres of fluids by mouth and Intravenous fluid, 4.3% Dextrose saline 1L was slowly given. Tablets of Allopurinol, haematinics and Antibiotics were also commenced. Patient was placed on Capsules of Hydroxyurea 1500mg daily. Input and output charting of fluid was done and electrolytes, urea and creatinine were evaluated closely. Consults were promptly sent to the Otorhinolaryngologist and Ophthalmologist to review her.

The Otorhinolaryngologist's review included pure tone audiometry (Fig. 1). It showed that the patient's ears were normal but she had profound bilateral sensorineural hearing loss and was therefore offered the use of hearing aids or cochlear implants if she could afford them.

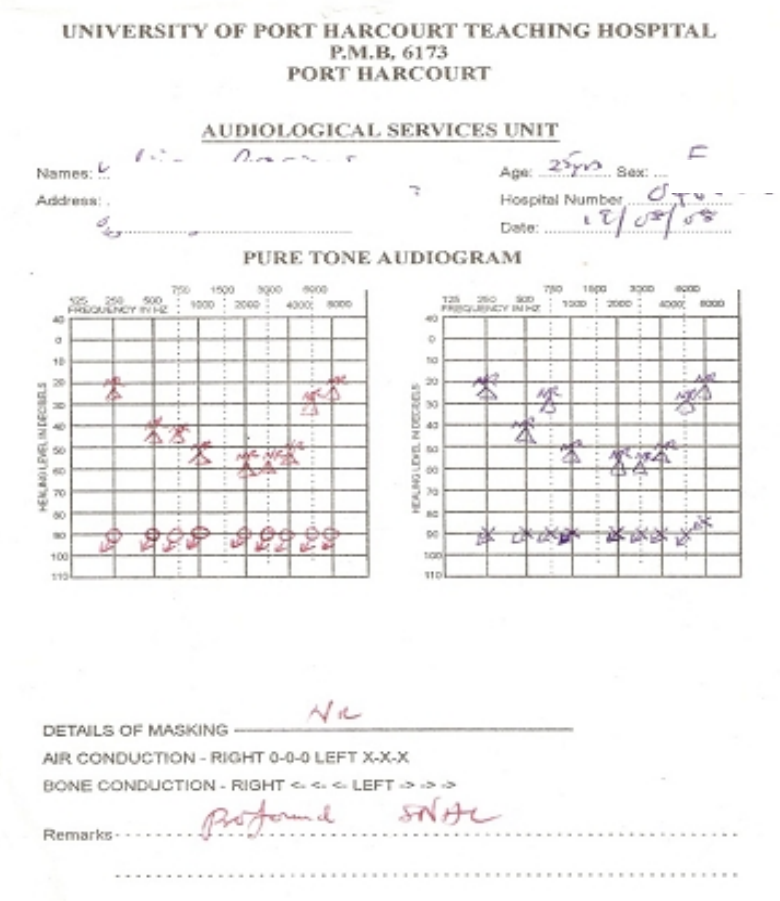

Fig. 1. Audiogram showing profound hearing loss

She responded well to chemotherapy. Hearing improved very slightly as patient could hear a loud knock on the table beside her, though she heard faintly. She was discharged to be seen on outpatient basis on the same dose of chemotherapy having shown satisfactory improvement and cytoreduction.

The Ophthalmologist's review revealed a visual acuity of 6/12 in the right eye and 6/36 in the left eye and this did not improve with pin-hole or refraction. External eye examination and intra-ocular pressures were normal, however funduscopy, revealed plethoric discs with blurred margins, venous engorgement, patchy areas of ischemia and blot haemorrhages, and choroidal folds. The patient was examined at the slit lamp with +78D lens and the macular was normal. Fundus photography and Florescien angiography could not be done due to financial constraint. An impression of optic disc oedema probably secondary to leukemic infiltrates was made.

Her FBC was monitored weekly while she was on admission showing good cytoreduction. The FBC showed WBC 32.2 x 10^9/L, PCV – 36%, Platelet count of 128 x 10^9/L, ESR 12mmHr at discharge.

The patient was referred to Obafemi Awolowo University Teaching Hospital where the clinical trial of Imatinib is done. She had karyotyping and was found to be Philadelphia Chromosome positive and Glivec therapy was commenced. She is doing well clinically; her vision however remained the same and still cannot hear clearly but pursued the option of hearing aids.

3. DISCUSSION

Chronic myelogenous leukemia (CML) is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line without the loss of their capacity to differentiate. Consequently, the peripheral blood cell profile shows an increased number of granulocytes and their immature precursors, including occasional blast cells. The Philadelphia Chromosomes is present in about 95% cases by molecular diagnostic analysis [2]. This translocation relocates an oncogene called *abl* from the long arm of chromosome 9 to the long arm of chromosome 22 in the *bcr* region. The presence of *bcr-abl* rearrangement is the hallmark of CML.

CML represents 14% of all leukemias and 20% of adult leukemias [3] with a median age of occurrence being 65 years in western countries [4]. A report from Nigeria puts the age range at 12 – 74yrs and a median age at 38 years [5].

The clinical presentation of CML is varied. It may be asymptomatic in some patients. However neurological complications are usually associated with hyperleucocytosis [6].

Premature deaths in chronic myeloid leukemia (CML) can be directly attributed to hyperleukocytosis and its resultant microcirculatory dysfunction, a phenomenon known as leukostasis. In leukostasis, there is sludging of leukemic blasts in capillary vessels and their adhesive interactions give rise to deleterious effects [7].

The symptoms in the index patient are largely associated with the very high white blood cell count. It is possible that the disease was ongoing in the antenatal period, but it was undiagnosed as her obstetrician did not do a full blood count during the antenatal period. This is very significant, as early diagnosis would have prevented the neurological

complications as we saw in this case. Pregnancy complicated by leukaemia is uncommon in our practice, but poses a very significant health challenge because of the concerns posed for the mother and fetus [8].

Up to 40% of leukemia patients may have otologic symptoms, sudden hearing loss is however thought to be rare[1]. These symptoms can originate from bleeding, infiltration of the tumor, infection, or hyperleukocytosis [9]. It is also postulated that the elevated viscosity causes partial occlusion of the cochlear vessels resulting in ischaemia of the cochlea and subsequent hearing loss [10] as in the index patient. Otologic complications of leukaemia as a first clinical presentation are rare in our practice.

In their retrospective review of 32 cases of CML in Jos, Northern Nigeria, Joseph et al. [11] reported five cases of sensori-neural defect; three of which were bilateral hearing loss. One of the three had both hearing and visual involvement as in the case above. Hearing loss may not be reversible in some patients, but early leukapheresis may help to improve perception of sound [10].

Although ophthalmic involvement in leukaemia is not commonly evaluated in our practice, they have been reported to be a major complication of leukaemia in some centres; especially in acute myeloid leukaemia [12]. A prospective observational study in University of Nigeria Teaching Hospital showed a prevalence of leukaemic ophthalmopathy of 77.8% in 72 subjects, 32.1% being asymptomatic [13]. A report from Benin puts the prevalence at 14.9% [12], but they noted that some of the ocular symptoms were not due to the leukaemia *per say*. The high rates of leukemic ophthalomopathies may be linked to the fact that most of these patients present late.

Some potentially blinding conditions of the eye observed in leukaemia include retinal detachment, orbital disease, retinopathies. This may also result from secondary haematologic changes or complications of treatment modalities employed [12,13].

This makes it important for all patients with leukaemias to have a thorough ophthalmic examination, as this will help in prognosticating and management. It is also essential to state here that the ophthalmologists should get very conversant with the presentation of leukaemic ophthalmopathy, (especially if they work outside the secondary or tertiary centre) so that such cases can be promptly referred for diagnosis and treatment.

4. CONCLUSION

Sudden hearing loss and visual impairment may occur as complications of haematologic malignancies such as Chronic Myeloid Leukemia. This study reported a patient who presented with profound hearing loss, visual impairment, in the chronic phase of chronic myeloid leukemia. After treatment, her underlying disease was controlled but with minimal improvement in hearing and visual acuity.

CONSENT

All authors declare that consent was obtained from approved person for the publication of this case report and accompanying images. The patient's identity has also been kept anonymous for this publication.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

The authors declare that no conflicting financial or personal interest exists.

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