*Case report*

Concurrent Chronic Myeloid Leukaemia and Non-Hodgkin Lymphoma at Presentation in a Young Man: A Case Report and Literature Review

abstract

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| Chronic myeloid leukaemia is a haematologic malignancy characterized by increased white cell count triggered by the constitutively expressed tyrosine kinase which is the product of an abnormal oncogene, BCR-ABL1. Non-Hodgkin lymphoma is the commonest of the lymphomas. It is a lymphoid malignancy arising from the acquisition of proliferation advantage either by chromosomal translocations or mutations of genes. Both diseases have overlapping symptoms but are distinct disease entities requiring different drug treatments. Literature shows the development of non-Hodgkin lymphoma in patients who had been on Imatinib treatment, however, the co-occurrence of both diseases in a patient who is chemotherapy naive is rare. This article reports the co-occurrence of chronic myeloid leukaemia and non-Hodgkin lymphoma, and also highlights its poor prognosis, especially when patients do not receive treatments for both diseases. The article also amplifies the need for high index of suspicion for possible non-Hodgkin lymphoma in a chronic myeloid leukaemia patient with significant lymphadenopathy. |

*Keywords: [Chronic myeloid leukaemia, non-Hodgkin lymphoma, advanced stage disease, tyrosine kinase inhibitors, bicytopaenia, bone marrow aspiration, bone marrow biopsy]*

INTRODUCTION

Chronic myeloid leukaemia, CML is a common haematologic malignancy, and a significant number of cases have been reported in Port Harcourt, Nigeria. It is a blood malignancy characterized by the presence of the Philadelphia chromosome, Ph, an abnormal chromosome 22 that results following the reciprocal translocations between chromosomes 9 and 22. This translocation generates a fusion oncogene, BCR-ABL1 usually found in the Ph chromosome, but could be domiciled in another chromosome entirely (Jabbour & Kantarjian, 2020). Proteins produced from by the oncogene has excess tyrosine kinase activity and confers a proliferation advantage on myeloid cells. This causes increased production of the myeloid cells, manifesting as elevation in complete blood count, CBC parameters (Popp et al, 2020). CML is classified into chronic phase (CML-CP), which is the commonest stage at presentation, and the blastic phase (CML-BP). Current treatment standard involves the use of tyrosine kinase inhibitors, TKIs; (Ahmed et al, 2022) if patient is in blastic transformation then treatment is with TKIs in addition to the regimen for acute myeloid leukaemia.

Non-Hodgkin lymphoma, NHL which is the more common type of lymphoma, is a malignancy of lymphocytes that occurs in lymphoid tissues/organs. The excessive proliferation of the lymphocytes in the lymphoid tissues results in the enlargement of the tissues/organs in the absence of a response to infective process, and most times, these lymphocytes are functionally useless predisposing patients to infections (Meng et al, 2020). NHL is due to genetic mutation events and/or other immune dysregulation which could be caused by viral infections or exposure to carcinogens in the environment. Over time, there could be marrow involvement with the accumulation of the malignant lymphocytes in the bone marrow, resulting in marrow failure (Pamungkas, 2025); marrow failure may also be due to antibodies generated against blood cells by the malignant cells (Barcellini et al, 2021).

The pathophysiology of CML and NHL occurring concurrently is not clear but different mechanisms have been suggested and because this simultaneous occurrence is rare, consistent explanations are difficult (Benjamin et al, 2022). CML and NHL are known to occur in young people and the case we report is of a man in the third decade of life.

CASE PRESENTATION

Our patient was a 27 - year - old male who presented to the accident and emergency, A&E unit of our facility on referral from a hospital in a neighbouring State. He gave history of two-months duration of swellings on the body involving the jaw, neck, the axilla, and the upper thighs. These swellings were first noticed in the submental area and initially small but increased in size, subsequently involving the neck, axilla, and groin bilaterally; there was associated difficulty in swallowing and speaking that developed while on admission. He also gave history of abdominal swelling and pain, described as non-radiating, generalized, dragging and mild in intensity, which also started at about the same time as swellings in the neck, axilla and groin. There was also drenching night sweats, episodes of fever described as continuous, and unintended weight loss. Examination showed a young man in mild painful distress, febrile at 38oC, pale, not cyanosed and no scleral jaundice; he had generalized lymphadenopathy with the biggest ones being the axillary nodes and the inguinal nodes, and measuring 8cm x 6cm in the widest diameters respectively; the cervical nodes were about 4cm x 4cm. Remarkable abdominal examination findings were hepatomegaly of 2cm and splenomegaly of 6cm below the costal margins.

At presentation, complete blood count CBC, done showed hyperleukocytosis with white cell count (WBC) of 148 x 109/L, absolute neutrophil count (ANC) of 64.6 x 109/L, absolute monocytes count of 56.7 x 109/L, absolute lymphocytes count (ALC) of 27.2 x 109/L, platelets count of 41.0 x 109/L and haemoglobin concentration (Hb) of 8.1g/dL. The peripheral blood film, PBF showed complete spectrum of the myeloid series from myeloblasts to mature granulocytes, with a myeloid blast percentage of 20% and significant basophilia, summarizing the diagnosis to chronic myeloid leukaemia in blastic phase, CML-BP. Immunophenotyping, IPT requested was not done due to financial constraint. Bone marrow aspiration and biopsy - BMA/BMB done using the posterior superior iliac spine, PSIS, showed hypercellularity as seen in Fig. *1*. Also seen were hyperactive myelopoiesis showing increased myeloblasts of up to 25% of marrow nucleated elements as captured in Fig. *2*, significant marrow eosinophilia as seen in Fig. *3* and increased lymphopoiesis; megakaryopoiesis was present but reduced as seen in Fig. *4*.

   

Figure1 Figure2 Figure3 Figure4

Figure 1 shows 2 hypercellular marrow fragments.

Figure 2 shows sequential maturation of the myeloid cells with increased myeloblast count

Figure 3 shows significant marrow eosinophilia

Figure 4 shows a mature megakaryocyte in the marrow

The BMB showed myeloblast population of 30% - 40% of the granulocytes. Lymph node biopsy done reported NHL, however patient could not afford immunohistochemistry - CD20, CD19, CD22, CD79a, BCL6, CD10. A BCR-ABL1 transcript analysis was done though outsourced to a laboratory outside of the state and results showed major transcripts -e14a2- of about 1907 copies/uL of BCR-ABL1 proteins, with a BCR-ABL1/ABL1 ratio of 10.5%. Other investigations done were serology for HIV 1&2, HBsAg, HCV, and VDRL, which were non-reactive; chest X-ray, CXR was normal and echocardiography showed normal echocardiogram for height. On presentation, he was commenced on empiric broad spectrum antibiotics and antipyretics, while cytoreduction with caps hydroxyurea 2g daily and prednisolone 60mg daily, while allopurinol 300mg daily was initiated by the haematologist on to prevent tumour lysis syndrome and to reduce the dysphagia he developed while on admission. He was also started on IV fluids and received a unit of fresh whole blood (FWB) on account of the reduced Hb and platelets count as blood component therapy was unavailable. He had significant reduction in WBC count but with attendant further reduction in platelets count, the lowest platelet count recorded being 7 x 109/L; for these reasons, another unit of FWB was given, the dose of hydroxyurea was reduced to 1g daily and then subsequently to 500mg daily, and tabs elthrombopag were added at 50mg daily which was subsequently increased to 100mg daily. Afterwards, the platelets count slowly improved to 12.0 x 109/L and then to 25.0 x 109/L. Following these measures, compression symptoms were relieved, followed by a significant but not complete regression of the cervical lymphadenopathy and hepatomegaly after patient received the first cycle of chemotherapy comprising cyclophosphamide, oncovin, hydroxydaunorubicin, and prednisolone, CHOP. Complicating hyperglycaemic episodes were treated on different occasions with subcutaneous insulin 10IU at bedtime and tabs metformin 1g daily. A repeat CBC after chemotherapy showed a Hb of 11.4g/dL, WBC of 63.0 x 109/L, ANC of 21.3 x 109/L, ALC of 47.0 x 109/L and platelets count of 25.0 x 109/L. With his clinical improvement, patient requested discharge; he was to see the haematology daycare in 5 days to follow up his optimization for second cycle of chemotherapy, however, he was rushed to the A&E 4 days later. He succumbed to his disease before he arrived.

discussion

While there are documented cases of secondary malignancies from chemotherapy treatment of primary malignancies, neoplasms occurring concurrently is an uncommon phenomenon. Though more cases of CML present in the chronic phase, presentation in the blastic phase is not uncommon. Males show slight predominance for all CML cases (Ahmed et al., 2022; Zammoeva et al., 2024; Aslam et al., 2024) with the median age at presentation being in the late 30s (Durosinmi et al., 2023). Though our patient was in his late 20s, he falls within the age range that most CML patients in Nigeria present (Boma et al, 2006). Lymphadenopathy is an uncommon feature of CML-CP but it has been reported in advanced stage CML (accelerated phase or blastic phase), representing a worse prognosis (Prasanna et al, 2019). Significant lymphadenopathy is also seen in up to 2/3 of cases of NHL (Sapkota & Shaikh, 2023). Our patient presented with lymphadenopathy (the cervical lymph nodes likely causing oropharyngeal compression) and hepatosplenomegaly, features which are suggestive of advanced phase CML, and accounts for 15% of newly diagnosed CML, and can pose a therapeutic challenge (Fu et al., 2018). Lymphadenopathy on both sides of the diaphragm, and hepatosplenomegaly are also in keeping with at least stage III NHL. Our patient had features of CML and NHL at the time of presentation, evidenced by results of the CBC, PBF, BMA, BMB, BCR-ABL1 transcripts and histology of lymph node. Our patient was unable to afford IHC and so it was not possible to characterize his NHL, but the fact that he presented in Ann Arbor stage III, and with the rapid progression of lymphadenopathy, it is obvious his disease was of an aggressive nature; Ann Arbor stage of at least III seems to be the commonest stage patients in these parts present with (Madu et al., 2020).

Most patients with CML and NHL developed secondary NHL following TKIs therapy (Gajendra et al., 2019; Paczkowska et al., 2021), our patient only had cytoreduction with hydroxyurea and prednisolone just a few days before histology confirmed NHL, and was yet to commence TKIs as his BCR-ABL1 transcripts results were being awaited. Though, concurrent CML and NHL has very poor prognosis, as evidenced by mortality in our patient, combined treatment with TKIs and the CHOP for NHL is known to prolong survival (Fu et al., 2018).

A study among NHL patients across 3 tertiary health facilities in Nigeria from data collected in a space of 4 years showed that the mean age at presentation of NHL is about 50 years (Madu et al., 2020). Our patient was younger than this mean age but falls within the range of 16 – 81 years stated in this study; he was also seronegative to HIV 1&2, in keeping with the finding that most NHL patients are seronegative.

Few reports of coexisting CML and NHL have been reported. Fu et al, 2018 reported similar cases involving two patients who had both malignancies at the time of presentation; while one was in CML-AP, the other was in CML-CP. Both had lymphadenopathy and histology plus IHC of cervical node confirmed T-cell NHL. The patient in CML-AP went into remission for years after treatment with TKI, chemotherapy and subsequent bone marrow transplant while the second case delayed treatment for months before commencing TKIs, only to default in treatment and succumbed to the disease few months after. There is also the case of a much older male patient of 73 years, who had CML-CP with follicular lymphoma and was treated with TKI alone; because his NHL was an indolent one and for age considerations, a watch-and-wait course of action was necessary. This patient achieved a partial cytogenetic remission and was alive years after the therapy (Starr et al., 2018). Benjamin et al, 2022 reported a case of a man who had presenting complaints and clinical features which were strikingly similar to our patient. This patient was in CML-CP and progressed through accelerated phase to blastic phase unlike our patient who presented in blastic phase. Both had cytoreduction with hydroxyurea and while our patient got just one cycle of chemotherapy with CHOP, theirs received 2 cycles of chemotherapy; in both cases, IHC could not be done due to financial challenges. These two cases highlight the fact that significant lymphadenopathy in a patient with CML is a poor prognostic factor (Abuelgasim et al., 2016), suggesting an advanced disease and necessitating lymph node biopsy for histology, as lymphadenopathy just might be a pointer to the development of NHL. Blood parameters were also similar in both cases but while our patient presented with thrombocytopaenia not due to therapy, this patient had thrombocytosis. Both were unable to start TKIs therapy before they succumbed to the diseases.

Conclusion

There are more reports of NHL developing in CML patients who have been on TKIs for a while; it is a rare occurrence for CML and NHL to be seen in same patient at time of presentation, and the prognosis is poor, especially in situations wherein patient does not get to receive TKIs together with treatment regimen for NHL. While this co-occurrence is rare, our case has shown it is possible and so clinicians must maintain a high index of suspicion for coexisting NHL in CML patients in advanced disease, and in those with significant lymphadenopathy.

Consent

All authors declare that written informed consent was obtained from the patient’s mother for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

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