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Case Report

Rare presentation of chronic myeloid leukemia in a HIV patient: A coincidence or an association with a genetic basis? Review of literature

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ABSTRACT

Human immunodeficiency virus (HIV) infected individuals are always at an increased risk of malignancy. This goes well with regard to AIDS (Acquired Immunodeficiency Deficiency Syndrome) defining malignancies such as Kaposi's sarcoma, Non-Hodgkin lymphoma and invasive carcinoma of the cervix, and non-AIDS defining/AIDS-associated malignancies like Hodgkin's lymphoma anal carcinoma and squamous cell carcinoma.

Usually solid malignancies are noted in HIV patients. Among hematological malignancies, chronic myeloid leukemia (CML) has rarely been described in association with HIV-infection. Till date, less than 50 cases have been reported in literature. Majority of these reported cases are from African continent. Our patient was a 45-year old female with this dual pathology and presented with pain abdomen, hepatosplenomegaly and high-grade fever.

CML can be considered as a rare AIDS defined hematological malignancy. Timely diagnosis can help in initiating dual treatment for HIV & CML, thereby preventing grave complications in such patients. This paper is an attempt to review the pathogenesis behind this association.

1. Introduction

Hematological complications are common and diverse in people living with HIV/AIDS (PWHA). The usual abnormalities encountered are anemia, leukopenia, thrombocytopenia, coagulation disorders and malignancies.[1–5] These complications can be the first manifestation of HIV infection. These hematological derangement are often multi-factorial with opportunistic infections, drugs, malignancy, and HIV infection itself contributing to the clinical presentation.[5–11] All these conditions should be kept in my mind while making a diagnosis.

PLWH are commonly predisposed to opportunistic infections and hematological malignancies with increased risk for lymphomas.[12–18] Even after treatment with ART, HIV patients are more prone for developing these hematological malignancies. Presence of tuberculosis in HIV patients, delay the diagnosis of these lymphomas due to similar clinical presentations. Other hematological diseases associated with HIV/AIDS include are myeloma, peripheral-T cell lymphoma, natural killer cell lymphoma.[17–21] Among solid malignancies, commonly seen are cervical cancer, hepatocellular and lung carcinoma.[12–21]

In the present case, an unusual association of myeloproliferative lesion (Chronic myeloid leukemia-chronic phase) was seen in a 42-year old HIV patient. This paper aims at discussing this rare association along

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with its pathogenesis and also reviewing the handful cases published in the medical literature.

2. Case Report

A 42-year old HIV positive, female patient presented to hospital with chief complaints of pain abdomen & high-grade fever. The patient had noted an abdominal mass on left upper part. The mass has progressed gradually to increase in size towards the umbilical region. The patient had history of headache, dizziness. There was no history of heart burn, difficulty in swallowing, diarrhea or constipation, yellowish discoloration of eyes, swelling of legs or joints.

On examination, vital signs were normal. She had hepatosplenomegaly. X-ray chest did not reveal any abnormality. Her routine blood investigations were sent. Mild derangement was noted in liver function test with elevated liver enzymes (AST & ALT). The patient had been on ART for last 2 years. Complete blood count revealed marked leukocytosis with total leukocyte count of approximately 1.5 lac/cumm with marked shift to left showing presence of more immature forms. Differential leukocyte count showed predominantly myelocytes & metamyelocytes along with promyelocytes, band forms, polymorphs [Figure 1]. Occasional blast cells were seen (3%). Basophils were <1%. Red blood cells showed moderate anisopoikilocytosis with microcytic hypochromic RBCs. Platelets were adequate on smear.

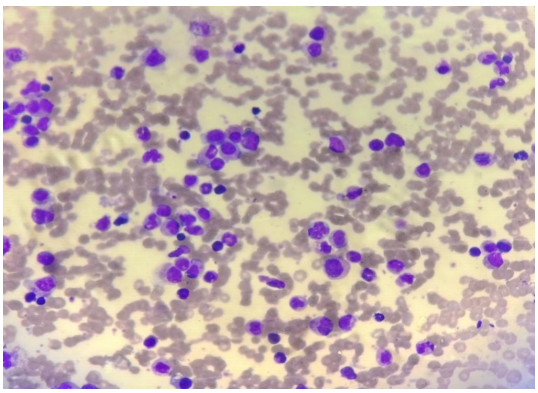

Figure 1: Peripheral smear showing marked increase in total leukocyte count & myeloid series cells in different stages of maturation with immature forms

Based on peripheral smear findings, a diagnosis of Chronic myeloid leukemia [chronic phase] was made. The finding of CML was by chance on her admission to hospital this time. For a definitive diagnosis, blood sample was sent for molecular analysis and detection of Philadelphia chromosome. The sample tested positive for major complex, BCR-ABL positive.

The patient was initially started on Hydroxyurea followed by Imatinib mesylate. At her last follow up, her counts were decreased, total leukocyte count being 45,000/cmm. The patient is kept on regular follow up with medications, ART & imatinib mesylate and their side effects if any. This combination of two ailments is rarely reported in literature.

3. Discussion

Currently, India contributes to a major portion of population of people living with HIV/AIDS. Still the data from our country of presence of hematological malignancies in PLWH is not accurate, it can account to more percentage. This is due to under-reporting of cases or improper maintainance of records. In western countries, one-third of HIV patients suffer from various cancers. This can be attributed to the fact that in developing countries focus is more on tuberculosis and other common ailments which are usually the major threats in PWHA.

In a study by Sharma et al,[2] among 135 patients of PWHA, tuberculosis was found in 71% patients. Dhir et al[3] found non-hodgkin lymphoma to be the most common type of cancer followed by anal cancer and hodgkin lymphoma. Another study from south India showed similar findings.[4]

There are very few Indian studies on hematologic malignancies in PWHA. Agarwal et al[5] in their study from Tata Memorial Hospital, Mumbai noted 35 patients with hematological malignancies [24 NHL, 7 HL, 4 plasmacytomas]. A tertiary care center in North India reported 7 patients of NHL in PWHA.[6] Only 14 patients had hematological malignancies among 5100 PWHA in a retrospective study by Sachdeva et al.[7] The crux of this low incidence of hematological malignancies in our country is due to the lack of systematic recording of such data and under-reporting of cases.

CML has rarely been described in association with HIV infection. Less than 50 cases have been reported in medical literature, mentioning CML in PWHA. CML is a myeloproliferative neoplasm with marked increase in total leukocyte count and presence of more immature forms. Cytogenetically, it is characterized by presence of bcr-abl fusion gene, noted in 90-95% of the patients. CML is diveided into 3 phases as per the percentage of blasts. Our patient was HIV positive and was diagnosed with a hematological malignancy, CML- chronic phase, which has rarely been reported in literature. Similar to our case, Reddy et al[1] reported only 1 case of CML in blast crisis among total of 13 cases of hematological malignancies in PWHA. 12 of 13 patients had NHL. This explains the rarity of this association.

HIV and zidovudine (antiretroviral agent), both are known to cause derangement in myeloid series cells.[7–11] But no such typical case has been reported in literature till date where side effects of these drugs in particular led to development of CML. Our patient was already HIV positive and on ART when the diagnosis of CML was made. This association could be coincidental. In a large study, done

between 1991 to 2011 by Patel et al,[9] 18 patients with HIV and co-existing CML were found. Among these 18 patients, 72% of them were newly diagnosed cases of both diseases simultaneously. 89% of these patients presented with advanced CML compared to HIV negative patients and 44% of patients had an accelerated phase and blast phase. It can be considered that HIV enhances the occurrence of CML. In a study from 2011-2014, few more such cases of HIV & CML were added in literature.[9,11–21]

The patients diagnosed with both HIV and CML are given combination of ART and Tyrosine kinase inhibitors to increase survival of the patients. Data has been published for six patients diagnosed with both CML & HIV who were treated with both ART & TKIs had better outcome than other patients who were not given Imatinib.[9,20,21] Our patient was on ART, hydroxyurea followed by Imatinib. On last follow up after 6 months of diagnosis of CML, the patient was stable with decrease in total count.

4. Conclusion

Combination of HIV & CML is rare finding. Diagnosing both gives an edge in management of these patients, thereby preventing further complications. Association of CML & HIV can be coincidental or HIV infection can cause CML in patients. However, the exact pathogenesis cannot be established with few of the cases reported in literature. An extensive study and systematic data review is required to validate this association. CML can be considered as one of the AIDS related malignancy. Combined treatment with ART & TKIs give provide better survival rates in these patients with dual infection.

5. Source of Funding

None.

6. Conflict of Interest

None.

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