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Case Report

Chronic Myeloid Leukemia (CML) Complicated by Mixed Malaria Infection- An Unusual Presentation

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Abstract

Objective: To report an unusual case of Chronic Myeloid Leukemia (CML) undergoing chemotherapy complicated by co- infection with Plasmodium vivax and Plasmodium falciparum.

Case presentation: A 31 years Kashmiri male who was a known case of Philadelphia positive Chronic Myeloid Leukemia and on chemotherapy for last1 year, presented with high grade fever, left flank pain, vomiting and one episode of epistaxis. The oncologist suspected CML progressing to Accelerated phase or chemotherapeutic drug (Tasigna) associated adverse effects leading to thrombocytopenia. He was diagnosed with mixed malarial infection based on positive blood smear and bone marrow aspirate showing gametocytes of both Plasmodium Vivax and Plasmodium Falciparum. Patient was treated successfully with anti malarial drugs and showed marked improvement in platelet count.

Conclusion: It is suggested that malaria should be considered as a complicating factor in the patients of hematological malignancies or those on chemotherapy in form of fever or thrombocytopenia, especially in malaria- endemic areas.

Keywords: Chronic Myeloid Leukemia (CML), Plasmodium vivax, Plasmodium falciparum, Thrombocytopenia.

Introduction

Malaria continues to be a cause of high mortality and morbidity throughout the developing world1. It is also called Poor man's disease and affect 0.5 million Pakistanis every year 2. Though this region is endemic for malaria but a co- infection with Plasmodium Vivax and Plasmodium Falciparum complicating a hematological malignancy is very unusual. Nirmala et al3 reported multiple cases of leukemias (n = 24) and lymphomas (n = 7) in children complicated by drug resistant Plasmodium falciparum malaria. Tapper and Amstrong4 reported two cases of neoplastic diseases which had transfusion-induced malaria. Rapoport and Uys5 reported three cases (one with Hodgkin's disease and other two with acute lymphoblastic leukemia) undergoing chemotherapy, developed febrile neutropenia and malaria infection concurrently.

Case Presentation: A31 year male resident of Azad Jammu Kashmir (AJK) Pakistan, diagnosed case of Philadelphia positive Chronic Myeloid Leukemia (CML) presented with high grade fever, left flank pain, vomiting and single episode of epistaxis.

Chronic Myeloid Leukemia (CML) was diagnosed by bone marrow biopsy in some other institute one year ago. PCR confirmed the BCR-ABL fusion gene. Chemotherapy was started in January 2013 and he was on Tasigna (Nilotinib) a Tyrosine Kinase Inhibitor for almost 2 months.

On admission, he was having high grade fever of 104 °F with a pulse rate of 115 beats/min, blood pressure of 100/80 mmHg and was well oriented and alert. General physical examination revealed marked pallor and yellow discoloration of sclera. There was no rash, petechiae or bruises and no lymphadenopathy. Patient had a hemoglobin of 10.1 g/dL with hemotocrit of 27.0%, TLC- 4,700/uL and platelet count of 24,000/uL. Antibiotic cover of Tazocin & Vancomycin was given along with Steroids (Deltacortril) and I/V fluids. Multiple transfusions of red cell concentrates and Platelets were also given but platelets continued to drop. Finally Tasigna was with held. A provisional diagnosis of Tasigna associated adverse effects or Chronic Myeloid Leukemia (CML) progressing to

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accelerated phase was made and bone marrow biopsy was ordered.

At time of biopsy patient had a hemoglobin of 9.2 g/dL with hemotocrit of 25.6%, TLC 3,300/uL and platelet count of 19,000/uL. DLC revealed slight neutropenia with neutrophils; 38 % , Lymphocytes; 43 %, Monocytes; 13 %, Myelocytes; 02% Metamyelocytes; 01 %, Basophils; 03 %, NRBC; 02 NRBC/100 WBC.

Peripheral blood film revealed Anisocytosis ++, Poikilocytosis ++, Microcytosis +, Hypochromia +, Target cells ++. Trophozoites and Shizonts of Plasmodium vivax and few Gametocytes of Plasmodium falciparum were also seen. (Figure. 1, 2, 3)

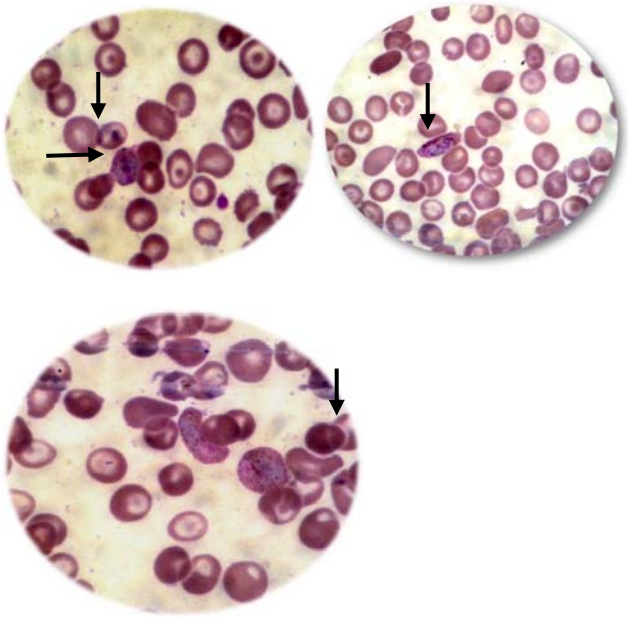

Figure. 1, 2, 3. Peripheral film showing Trophozoites and Schizonts of P.vivax and Gametocyte of P.falciparum

Bone marrow aspirate from posterior superior iliac spine revealed a hypocellular smear with low erthropoietic and myelopoietic activity and decreased megakaryocytes. Platelets were also decreased on smear. Lymphocytes, plasma cells and histiocytes were not increased and no atypical cells seen. Trophozoites and Schizonts of P.vivax and Gametocyte of P.falciparum were seen in the aspirate. (Figure. 4, 5, 6)

A diagnosis of Chronic Myeloid Leukemia with mixed malaria infection was made and the patient was treated with anti malarial drugs, his fever subsided and counts became normal. Steroids were tapered off, Tasigna was started again and patient was discharged after one week.

Discussion

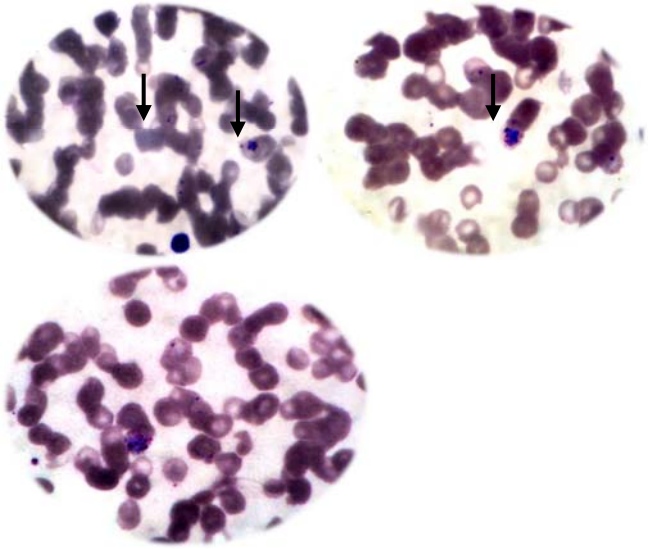

Figure. 4, 5, 6. Bone marrow aspirate showing Trophozoites and Schizonts of P.vivax and Gametocyte of P.falciparum

Bone marrow trephine revealed hypocellular bone marrow fragments with decrease in Erythroid , Myeloid and Megakaryocytic cells series along with marked fibrosis. (Figure. 7, 8)

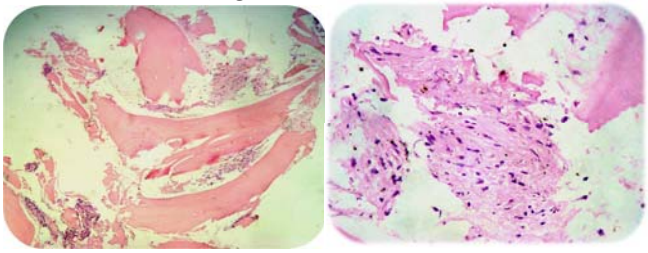

Figure. 7, 8. Bone marrow trephine showing hypocellular marrow and fibrosis.

Malaria remains one of the major health problems in tropical and subtropical countries6. Despite the intensive worldwide efforts to reduce its transmission, it is the most serious and widespread protozoal infection of humans7. Over 40% of world population lives in malaria endemic area. Pakistan being a part of endemic belt has an incidence of one case per thousand persons8. Malaria is caused by four species of plasmodium parasites which spread through the bites of infected Anopheles mosquitoes as a vector". These speceies include: Plasmodium falciparum, vivax, malariae and ovale. P. falciparum and vivax are

the most common and P. falciparum is the most deadly9.

The clinical features of malaria can be misinterpreted in patients with a hematological malignancy especially when the patient is on chemotherapeutic drugs and presents with persistent fever and thrombocytopenia. Malaria is accompanied by various hematological changes which are more pronounced in P. falciparum infection, most likely due to higher levels of parasitemia. These changes include anemia, thrombocytopenia, splenomegaly, and mild-to-moderate atypical lymphocytosis and rarely disseminated intravascular coagulation (DIC). There have also been reports of leucopenia and leucocytosis. Other hematological reactions that have been reported include neutropenia, eosinophilia, neutrophilia and monocytosis8. Thrombocytopenia being the most common of these with incidence ranging from 40.5-85%. It is thought to be caused by increased spleenic sequestration, immune mediated destruction, and a shortened platelet survival1.

Tasigna (nilotinib) is a Tyrosine kinase inhibitor indicated for the treatment of newly diagnosed adult patients with Philadelphia chromosome positive Chronic Myeloid Leukemia (Ph+ CML) in chronic phase10. Its hematologic side effects include thrombocytopenia (up to 37%), neutropenia (up to 37%), anemia (up to 23%), febrile neutropenia, pancytopenia, thrombocytosis, and leukocytosis 11.

In this case bone marrow of the patient revealed a WBC count of 3,300/uL with no blasts in the peripheral blood film and in bone marrow, ruling out the provisional diagnosis of Chronic Myeloid Leukemia (CML) progressing to accelerated phase (associated with leukocytosis, thrombocytosis or thrombocytopenia, persistent fever & bone pain). The only differential of Tasigns (nilotinib) associated adverse effects was left, which include thrombocytopenia and febrile neutropenia. However the presence of Trophozoites and Schizonts of P.vivax and Gametocytes of P.falciparum not only in peripheral blood film but also in bone marrow aspirate ruled out any other possible differential and mixed malaria infection is established as a root cause.

Conclusion

In the patients of hematological malignancies and those who are on chemotherapy presenting with persistent fever and thrombocytopenia, malaria should be considered as a differential especially in malaria endemic areas.

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Contribution of authors

Kanwal Zahra conception and study design and planning and manuscript writing

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