DOI: 10.7860/JCDR/2015/14318.6172

Case Report

Internal Medicine Section

Spontaneous Soft Tissue Haematomas- A Rare Presentation of Chronic Myeloid Leukemia (CML)

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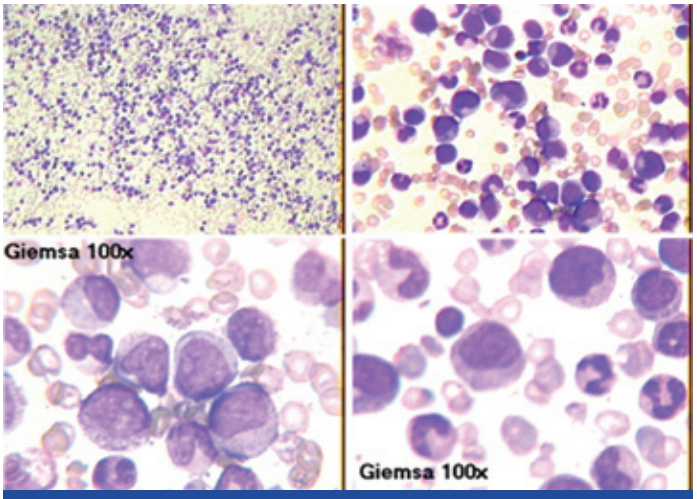
ABSTRACT

Spontaneous soft tissue haematomas are rarely found in haematological malignancies. Chronic myeloid leukemia (CML) is a myeloproliferative disorder which rarely present with thrombo-haemorrhagic phenomenon. It is a malignant clonal disorder of pleuripotent stem cells that results in increase in myeloid, erythroid and platelets cells in peripheral blood and marked myeloid hyperplasia in bone marrow. It is characterized by the presence of Philadelphia chromosome (Ph) with BCR – ABL 1 fusion gene. This gene is responsible for the formation of 210 KDa chimeric proteins with enhanced tyrosine kinase activity which leads to the abnormal bone marrow cell proliferation and to the clinical and morphologic manifestations of leukemia. Cutaneous and mucous membrane bleeding is common in CML whereas bleeding in deep soft tissue is rarely found because of qualitative and quantitative platelet abnormalities. Here, we report a case of CML (BCR-ABL rearrangement positive) who presented with large haematoma in the anterior as well as posterior compartment of left thigh and treated successfully with hydroxyurea and imatinib.

Keywords: *BCR-ABL*, Haematoma, Imatinib, JAK 2, Philadelphia chromosome

CASE REPORT

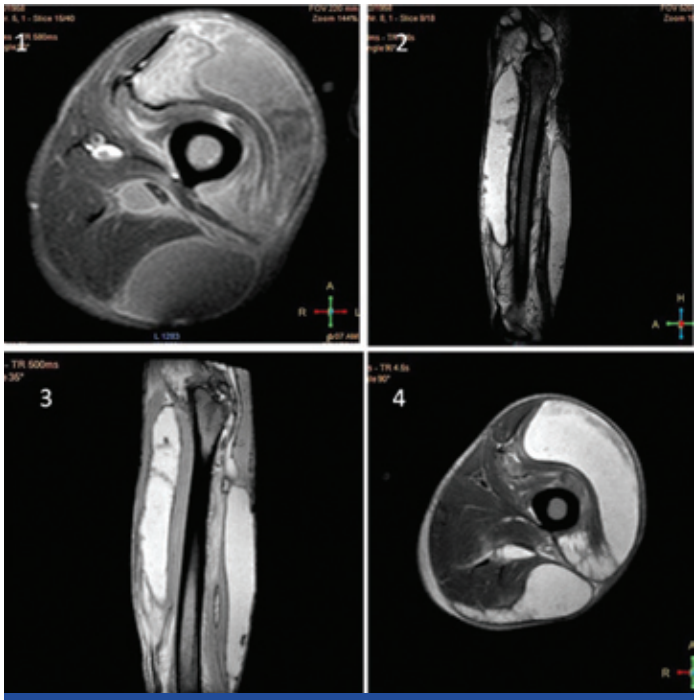
A 55-year-old male presented to us in the Department of General Medicine at Mahatma Gandhi Hospital Jodhpur, India with complaint of pain and swelling of left thigh since 10 days. He denied of trauma in recent past. He had no sternal tenderness, purpurae, petechiae, and ecchymosis on his body. His family history was not significant in relation to haematological disease. He was not suffering from any chronic illness and had no addictions. On examination patient had swelling of the left thigh not extending beyond knee joint. The left mid thigh girth was 70 cm as compare to right that was 57 cm. The swelling was warm to touch, soft, boggy and tender to palpate. Fundoscopy was normal. His vital parameters were within normal limits. Lungs were bilaterally clear and cardiac auscultation was normal. Splenomegaly was found on palpation. Lymph nodes were not palpable. Laboratory investigations revealed a haemoglobin (Hb) of 5.7 g/dL, total leukocyte count (TLC) of 3,20,000/mm^3, and Platelets were 12,24,000/mm^3 with PBF showing normocytic normochromic anaemia with leukocytosis and thrombocytosis with few myelocytes and metamylocyte. The Bone marrow examination showed hypercellular marrow (myeloid hyperplasia) with M:E ratio of 49:1 and 28% myelocytes, 3% myeloblast, 7% promyelocyte , 14% metamyelocyte, 42% neutrophils, and 2% basophils, suggestive of CML [Table/Fig-1]. FISH (Fluoroscent In-Situ Hybridization) analysis on the patient's peripheral blood revealed the presence of the BCR/ABL1 gene rearrangement in 72.8% of nuclei evaluated. Polymerase chain reaction (PCR) analysis of the patient's peripheral blood was negative for JAK2 V617F mutation. Coagulation profile showed bleeding time (BT) 15 min (normal up to 5 min), clotting time (CT) 2.25 min (normal up to 8 min), prothrombin time (PT) 15 sec (Control 14 sec) with INR of 1.05 and thromboplastin time with kaolin (PTTK) 38 sec (control 35 sec). The patient's lactate dehydrogenase level was significantly elevated to 1080 IU/L. Leukocyte alkaline phosphatase (LAP) score was 30. Renal, liver functions, serum electrolytes and urinanalysis were normal. Ultrasonography of the abdomen showed moderate splenomegaly (21cm) and hepatomegaly (14 cm). MRI of left thigh showed lobulated hyperintense lesion in the anterior as well posterior compartment suggestive of haematoma [Table/Fig-2]. After confirming the diagnosis of CML, he was started on hydroxyurea, imatinib and allopurinol. On 15th day of starting imatinib, and hydroxyurea, repeat CBC revealed Hb 8.6 g/dL, TLC 56,000/mm^3 and platelets were 4,50,000/mm^3. Coagulation profile became normal. Haematoma managed conservatively and resolved completely in repeat MRI after 20 days and he became asymptomatic with normal hematologic parameters. He was discharged on imatinib 400mg with advice for further follow up.



[Table/Fig-1]: Bone marrow aspiration showing hypercellular marrow (myeloid hyperplasia) with M:E ratio of 49:1 and 28% myelocytes, 3% myeloblast, 7% promyelocyte , 14% metamyelocyte, 42% neutrophils, and 2% basophils, suggestive of Chronic Myeloid Leukemia

DISCUSSION

CML is a malignant clonal disorder of pleuripotent stem cells that results in increase in myeloid cell, erythroid cell and platelets in peripheral blood and marked myeloid hyperplasia in bone marrow. It is characterized by the presence of Philadelphia chromosome (Ph), which is formed by reciprocal translocation between long arm of chromosomes 9 and chromosomes 22 {t(9;22) (q34;q11)} leading to formation of Philadelphia chromosome with BCR-ABL 1 fusion gene. This gene is responsible for the formation of 210 KDa chimeric protein with enhanced tyrosine kinase activity than normal which prevents apoptosis [1].



[Table/Fig-2]: Image 1-T1W, image 2-T2W, image 3-STIR, image 4-GRE. Intramuscular haemorrhagic collection in anterior and posterior compartment of the most of the length of left thigh. The collection is hyper intense as compare to surrounding musculature. The size is of approximately is >20 cm in length and on axial section width is ~7.5 cm in anterior compartment haematoma. Visible femur is normal

The incidence of CML is reported as between 1-2 cases/100,000/year, without major geographical differences. The mean age at diagnosis is about 60-65 years [2]. In up to 50% of asymptomatic cases the diagnosis is made incidentally from a routine blood count. The common presenting symptoms are weight loss, lassitude, anorexia, night sweats, pallor, dyspnoea, palpitation, abdominal discomfort due to splenic enlargement and gout. Cutaneous and mucous membrane bleeding are common in the form of bruising, purpurae, petechiae, ecchymosis, epistaxis, menorrhagia or haemorrhages from other sites because of abnormal platelet function. Patient may present with infections due to dysfunctional neutrophils and because of leukocytosis there may be features of hyper viscosity syndrome e.g. veno-occlusive disease, cerebrovascular accident, myocardial infarction, priapism, visual disturbances and pulmonary infarction [3,4]. Haematomas in soft tissue is a very rare presenting symptoms of CML. A case of mediastinal haematoma and haemothorax as a presenting manifestation of CML has been reported in the literature [5].

Thrombotic and haemorrhagic complications are common in myeloproliferative disorders. In the patients with myeloproliferative disorder including CML who have bleeding complications, qualitative platelet abnormalities are frequently observed. Cutaneous and mucous membrane bleeding are common but deep bleeding is rare. The role of thrombocytosis in haemostatic dysfunction is controversial. Thrombocytosis is found in one third of CML patients and one sixth patients have dysfunctional platelets. Platelet dysfunction in chronic myeloproliferative disorders is multi-factorial [3]. Abnormal platelets morphology, storage pool defect, platelets membrane abnormalities and arachidonic acid metabolism defect are observed in the patients of myeloproliferative disorders. Most frequently found platelets abnormalities are reduced responsiveness of platelets to epinephrine, while the response to collagen and ADP are less common [3,6]. This is found to be due to a reduction in α-adrenergic receptors on the platelet membrane. There is relatively lower incidence of haemorrhage in patients with CML, compared to other myeloproliferative disorders [7].

Vignal CV et al., [8] found strong correlation between bleeding time (BT) and prediction of bleeding in myeloproliferative disorders. The platelet aggregation pattern was not found to predict the occurrence of bleeding in patients with myeloproliferative disorders, as observed in a study [9]. Bleeding was more common as compare to thrombosis in CML. Most of the CML patients have BCR-ABL rearrangements in megakaryocytes. It has been found that there occurs reduction in the number of BCR-ABL+ megakaryocytes in the cases of CML after therapy to reduce CML blasts cells. A variable degree of bone marrow fibrosis can be found in CML. Interferon or busulfan therapy may exaggerate the fibrosis [10]. In a study done by Beham Schmid et al., [11] found that there was significant regression of bone marrow fibrosis with marked reduction in the number of megakaryocytes, normalization of megakaryocytopoiesis and reappearance of normal-sized forms during treatment of bcr-abl+ CML with the tyrosine kinase inhibitor STI571. Fibrosis is reduced because megakaryocytes are the principal mediators of fibrogenesis in myeloproliferative disorders, acting through the abnormal release of transforming growth factor-β, and platelet derived growth factor (PDGF). Hence tyrosine kinase inhibitor STI571 can exert anti PDGF activity and reduces bone marrow fibrosis which improves the survival of CML patients [12,13]. Atypical micro-megakaryocytes were also found in Ph+ CML and their number significantly decreased and replaced by large, normally appearing cells of this lineage after imatinib therapy. These small megakaryocytes are characteristic of CML [14].

Our patient presented with haematoma in left thigh having thrombocytosis and leukocytosis. Bleeding time (BT) was prolonged. BT was normalised after 20 day of therapy with imatinib and hydroxyurea with normalisation of platelets and WBC. We assume that thrombocytosis and dysfunction platelets in a case of CML were the cause of haematoma in our patient which resolved after imatinib therapy.

CONCLUSION

In a patients presenting with soft tissue haematoma, after exclusion of surgical and traumatic causes, hematological disorder should be keep in mind. If haemogram and peripheral blood film showing atypical cells then looked for hematological malignancies. In a case of CML, soft tissue haematoma is explained because of dysfunctional platelets. Thus proper treatment with tyrosine kinase inhibitors according to standard guideline can resolve haematomas timely and improve the quality of life.

ACKNOWLEDGMENT

Special thanks to Dr Jainapur Ravi Sangappa, and Dr Prakash kumar Choudhary Resident, department of medicine, Dr. SNMC Jodhpur Rajasthan, India.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Apr 04, 2015**
Date of Peer Review: **May 05, 2015**
Date of Acceptance: **May 20, 2015**
Date of Publishing: **Jul 01, 2015**