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SEVERE SUBCONJUCTIVAL HAEMORRHAGE IN A CHRONIC MYELOID LEUKAEMIA PATIENT FOLLOWING LOW-DOSE ASPIRIN THERAPY FOR THROMBOCYTOSIS.

AUTHORS

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Introduction

CML is an acquired clonal myeloproliferative neoplasm characterized by a unique cytogenetic abnormality, reciprocal translocation between the long arms of chromosomes *9* and *22, t(9;22)(q34;q11)* in over 95% of patients, leading to generation of the Philadelphia (Ph) chromosome and a highly oncogenic *fusion gene, the BCR-ABL1 fusion gene, which encodes for the Bcr-abl1 fusion protein* with a very high tyrosine kinase activity. It has an aannual incidence of 1-2/100,000 worldwide with a male to female ratio of 1.8:1. The median age of presentation is 38 years in Nigeria and 67 years in Western World. The disease is a triphasic neoplasm: **Chronic phase (CP)** in over 85% of patients **(duration 3-6 yrs, med 4 yrs)**, which progresses to **the aggressive accelerated phase (AP), and finally the terminal blastic phase (BP).**

Bleeding and thrombosis are frequent complications in myeloproliferative disorders and are associated with severe organ damage and high mortality. These are usually related to abnormalities in platelet number and functions.

We report a case of severe subconjuctival haemorrhage in a CML patient with thrombocytosis following low-dose aspirin therapy.

Case Report

A sixty-one year old lady who presented with a six month history of right-sided abdominal swelling and pain. The spleen and liver were 15 cm and 12 cm enlarged below the costal margin respectively. The full blood count showed haematocrit of 29%, leucocytosis of 228 x 10^9/L and thrombocytosis of 716 x 10^9/L. The blood film and bone marrow reviews were in keeping with CML in accelerated phase. She was initially treated with hydroxurea with poor

response, but there was dramatic decrease in the leucocyte and platelet counts when she wa placed on COAP (cyclophosphamide, vincristine, cytarabine and prednisolone). The PCF results showed Ph chromosome positivity with BCR-ABL 1 major transcript typ (e14a2/e13a2), BCR-ABL quantity 2000 copies/3 µl of cDNA, ABL quantity 2.2 x 10 copies/3 µl of cDNA and BCR-ABL ratio of 9.091%.

She was then commenced on Gleevec 400 mg daily. She was also commenced on low-dos aspirin, 75 mg daily on account of thrombocytosis, 550 x 10^9/L. She developed sever headache, dyspepsia and redness of both eyes on day 8 of Aspirin, her Hct was 29% and ha bilateral subconjunctival haemorrhage more florid on the left (figures 1 & 2). There was n associated bleeding from any other site. PT/aPTT was normal. The cause of the haemorrhag was possibly due to aspirin-induced thrombocytopathy. The aspirin was immediatel discontinued and there was a complete resolution of the subconjuctival haemorrhage by th third week (figure 3).

DISCUSSION

CML is an acquired clonal myeloproliferative neoplasm characterized by a uniqu cytogenetic abnormality, reciprocal translocation between the long arms of chromosomes 9 and 22, *t(9;22)(q34;q11)* in over 95% of patients, leading to generation of the Philadelphi (Ph) chromosome and a highly oncogenic *fusion gene, the BCR-ABL1 fusion gene, whic encodes for the Bcr-abl1 fusion protein* with a very high tyrosine kinase activity.

Thrombohaemorrhagic complications are common in MPDs with bleeding being mor common in CML. One study reported bleeding in 20% and thrombosis in 6% of CMI patients (Wehmeier *et al,* 1991). In another study, 28% of CML had bleeding abnormalitie (Vignal *et al,* 1997).

The mechanism of abnormal bleeding in CML is multifactorial ranging fron thrombocytopenia to abnormal platelets function. Specific platelet defects in CML include abnormal platelet morphology, acquired storage pool disease, platele membrane/aggregation abnormalities (Murphy *et al,* 1978) and abnormal arachidonic aci metabolism (Schafer, 1982).

It is believed that in CML the platelet dysfunction originated from a clonal expansion o dysfunctional megakaryocytes. These are possibly derived from the identical stem cell fron which the CML blasts had originated. Therefore, treatment targeting BCR-ABL would b equally effective in reducing the CML blasts and dysfunctional megakaryocytes. This i validated by observation that using tyrosine kinase inhibitors in patients with CML woul improve the platelet dysfunction (Alexander S-V *et al,* 2011).

Conclusion

Even though some CML patients present with thrombocytosis, they are still at risk o bleeding because of thrombocytopathy, which may be compounded by the use of antiplatele drugs.

References

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6 Vignal CV, Lourenço DM, Noguti MA, Chauffaille Mde L, Kerbauy J. Hemorrhagic and thrombotic complications in patients with myeloproliferative diseases. *Sao Paulo Med J.* 1997 Nov-Dec;115(6):1575-9.

Figure 1: Day 8 of Low-Dose Aspirin

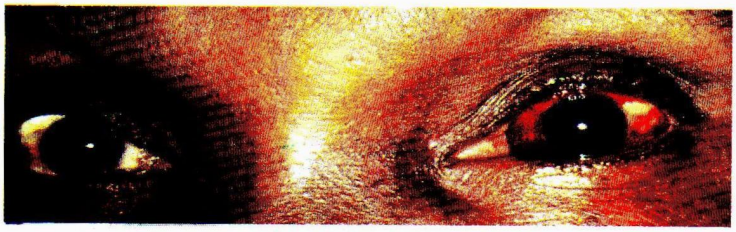

Figure 2: Day 2 Post-Low-Dose Aspirin

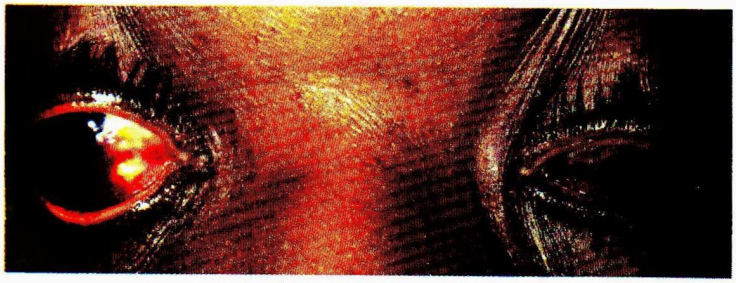

Figure 3: Third Week After Discontinuation of Aspirin