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Case Report

Peripheral gangrene in a child as a result of Primary Thrombocytosis

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ABSTRACT: Essential Thrombocytosis (ET) is a clonal disorder of unknown etiology involving a multipotent hematopoietic progenitor cell and is manifested clinically by the overproduction of platelets without a definable cause. Clinically, ET is most often identified incidentally when a platelet count is obtained during the course of routine evaluation. There are very few case reports in the pediatric age group in which peripheral gangrene is caused by primary thrombocytosis or essential thrombocythemia. This is a case report of a 5 year old male child who presented to us as peripheral gangrene of toes which was caused by ET, one of the Myeloproloferrative disorders.

KEY WORDS: ***Essential thrombocythemia; Gangrene, Myeloproliferative disorder; Primary thrombocytosis***

INTRODUCTION

A platelet count exceeding the upper limit is called thrombocytosis. The physiologic reference range of platelet counts is 150-400 x 10^9/L. Thrombocytosis is classified as either primary or secondary. Primary thrombocytosis (also called essential thrombocythemia, ET) is caused by autonomous production of platelets unregulated by the physiologic feedback mechanism to keep the count within the reference range. It is a subset of myeloproliferative disorder (e.g. essential thrombocythemia, myelofibrosis with myeloid metaplasia, polycythemia vera, chronic myelocytic leukemia [rare]) [1] The incidence of ET is estimated to range from 1-4 cases per 10 million people younger than 20 years.[2]

CASE REPORT

We report a 5 year old boy who presented in the pediatric outpatient department of tertiary care teaching hospital, with complaints of blackening and swelling of four lateral toes excluding great toe of both legs for 1 week along with pain in both legs. There was no history of fever, bleeding from any site or trauma.

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On examination there was blackening of four toes in both lower limbs excluding the hallux (**Figure 1**). There was no restriction of movement and it was not tender. Pulsation of all peripheral pulses--femoral artery, popliteal artery, anterior tibial artery, posterior tibial artery as well as dorsalis pedis artery was palpable. Blood pressure was normal in all four extremities. All the other systems were within normal limits.

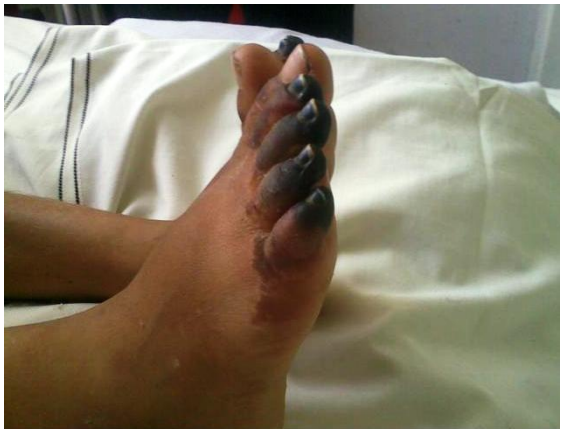

Figure 1: Gangrene of four toes in both lower limbs excluding thumb

Doppler flow study showed normal flow in dorsalis pedis artery bilaterally. The blood investigations showed haemoglobin 11.5 gm/dl, total leucocyte

counts 7700/mm^3, differential counts (polymorphs 56%, lymphocytes 33%, eosinophils 7%, monocytes 4%), mean corpuscular volume (MCV) 94.6fl, mean corpuscular haemoglobin (MCH) 31pg and mean corpuscular haemoglobin concentration (MCHC) 30.5%. Perpheral blood smear showed normocytic normochromic RBCs, no evidence of immature cells and increased platelets. Antiphospholipid antibody syndrome panel was negative i.e. prothrombin time 14 seconds (INR ratio-1.1), APTT 31.3 seconds (control-18-32 seconds), anticardiolipin antibody IgA 2.65 APL U/ml, anticardiolipin antibody IgM 3.24 MPL U/ml, anticardiolipin antibody IgG 6.62 GPL U/ml and antiphospholipid antibody IgG 3.8 GPL U/ml (reference value of all antibodies 0.5-10). As the general blood picture showed increased platelets, platelet count was done, which was 800 x 10^9/L. To exclude infection as a cause of thrombocytosis, C reactive protein (CRP) and D dimer assay were done which were fould as 6.2mg/dl (upper 95th percentile 11.0mg/dl) and116.0ng/ml (reference-57-495.5 ng/ml) respectively. As by the above investigations, iron deficiency anemia and infection which can produce thrombocytosis were excluded and it was presumed to be primary thrombocytosis. To confirm the diagnosis bone marrow aspiration was done. It showed hypercellularity, megakaryocytic hyperplasia and giant megakaryocytes. Bone marrow aspiration confirmed the diagnosis of primary thrombocytosis. The patient was put on aspirin for 3 months. After 3 months platelets came down to 300 x 10^9/L with spontaneous resolution of the gangrene.

DISCUSSION

Thrombotic or hemorrhagic complications caused by reactive or secondary thrombocytosis are described only anecdotally and must be regarded as extremely rare. However, in children with autoimmune disease or vasculitis, such as Kawasaki syndrome, thromboses do develop. In Kawasaki syndrome, this occurs particularly in the coronary arteries. In patients with primary nonfamilial thrombocytosis, which is a myeloproliferative disorder, the frequency of thrombosis and/or hemorrhage widely varies among various reports (20-84% for thrombotic complications and 4-41% for bleeding complications). However, these statistics are for adult patients, and incidences of hemorrhagic and thrombotic complications in primary thrombocytosis of children are not known.[1] In one study, 0.5% of hospitalized children had a platelet count more than 800 x 10^9/L.[3] On the basis of experiences in young adults with primary thrombocytosis, these complications may occur less often in children than in adults.[4] Teofili et al[4] reported no thrombosis in children with essential thrombocytosis, as opposed to 10 of 32 patients in a study of adults. On the other hand, Dame and Sutor[5] reported that about 30% of children with essential thrombocytosis had thromboembolic or hemorrhagic complications at the time of diagnosis or later, and that about 20% of initially asymptomatic children had these complications later. These figures are similar to those of adults. Bleeding mainly involves the mucous membranes and skin (e.g. GI hemorrhage, hemoptysis, post surgical bleeding, bruises, epistaxis). Thrombosis involves the veins and arteries.

Preston[6] published a case series of six adult patients in which peripheral gangrene was caused by ET. Papadonikolakis et al[7] also published a case report of 34 year old male who had Raynaud's phenomenon presented with peripheral gangrene. Cecil[8] published the single institutional experience of 39 cases of adult patients with mean age of 55.5$\pm$14.5 years, of which 14 had thrombosis as a complication. They concluded that the identification of Janus kinase 2 mutation (JAK 2) probably defines a sub entity in ET with aggressive behaviour as evidenced by splenomegaly, higher total counts and transformation to polycythemia rubra vera.

Use of pharmacologic agents to prevent thrombotic complications in primary or ET is controversial, even in the internal medicine literature, because no laboratory studies offer predictive value in terms of the risk of thrombosis or hemorrhage. Tefferi et al[9] recommend their use only in patients older than 60 years, individuals with a history of thrombosis, or persons with cardiovascular risk factors, virtually eliminating pediatric patients.

Symptomatic patients with essential thrombocytosis (ET) should receive treatment to lower their platelet count. For pediatric use, anagrelide or hydroxyurea is recommended. In a study by Harrison et al[10], adult patients (median age, about 60 y) were randomly assigned to receive low-dose aspirin plus hydroxyurea or anagrelide.

Significantly more patients in the anagrelide arm than in the hydroxyurea arm reached the study endpoint. The authors concluded that hydroxyurea plus aspirin was more effective than anagrelide plus aspirin in preventing complications in adults with ET.

We report this case because a rare cause for reversible peripheral dry gangrene in the pediatric population was diagnosed. We have given aspirin, by which the platelet counts came down to normal with no recurrence of thrombosis.

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