

# Reactive Thrombocytosis with Digital Gangrene

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## Abstract

Patients with reactive thrombocytosis are generally asymptomatic and platelet counts of up to 1000, 000/ $\mu$ L are seen in this disorder. However, in a small proportion of cases platelet counts may be in the range generally seen in Clonal Thrombocytosis (CT). In elderly patients or those with symptomatic atherosclerosis or thrombotic disease or immobility, thrombosis may occur even with reactive thrombocytosis. We report a case of a rare presentation of Reactive Thrombocytosis with digital gangrene in an elderly lady. She was evaluated for thrombocytosis and was given supportive treatment after which she clinically improved.

## Introduction

Thrombocytosis can be attributed to many causes. Platelet counts can be elevated as a result of abnormal proliferation of megakaryocytes. This is known as primary, essential or clonal thrombocytosis or thrombocythemia and is part of the spectrum of myeloproliferative disorders.<sup>1</sup> However, most cases of thrombocytosis are reactive, or secondary resulting from the effects of other diseases such as chronic infectious or inflammatory states, malignancy, iron deficiency anaemia, and postsplenectomy states.<sup>2</sup> It is important to differentiate clinically aggressive clonal or primary thrombocytosis from reactive thrombocytosis because clonal thrombocytosis (CT) may require cytotoxic therapy while in reactive thrombocytosis the cause has to be resolved.<sup>3</sup>

## Case Report

An 80 year old lady with no prior comorbidities presented to our department with a history of paraesthesias in hands and feet for three months followed by gangrene of multiple digits of hands and feet for 6 weeks which was painful and progressively increasing. There was no history of oral ulcers, arthralgia, rash, Raynauds phenomenon or intermittent claudication.

She was referred from Civil Hospital Sukkur with a platelet count of 2250 X 10<sup>9</sup>/L. On examination she was alert, conscious and oriented with a pulse of 100/min B.P of 120/70mmHg and temp was 101°F. She was mildly anaemic with no jugular venous distention, lymphadenopathy or bone tenderness. Local examination

revealed gangrene of right index and little finger and left index finger with well formed line of demarcation. Radial pulses were palpable bilaterally. Examination of feet revealed gangrene and auto amputation of 2nd, 3rd and 4th toes on right side and 4th and 5th toes on left side. Dorsalis pedis and posterior tibial were palpable but feeble bilaterally. Her lungs were clear to auscultation, and she had a regular heart rhythm and normal heart sounds. Her abdomen was soft, and her liver edge was palpable 2 cm below the costal margin and was soft and nontender. Rest of systemic examination was unremarkable. On investigations her Hb was 10.9g/dl with Haematocrit of 33.3%, WBC 15x 10<sup>3</sup>/ $\mu$ L with 80% granulocytes, platelet count 2250x 10<sup>3</sup>/ $\mu$ L and ESR of 125mm/1st hour. Her urea, creatinine, electrolytes and calcium were all within normal limit. Her ANA, AMA, ASMA were also negative. Serum albumin was low at 2.6g/dl and globulin was elevated at 4.6g/dl. Mycoplasma antibody, Anti HCV and cryoglobulins were negative. The blood culture showed no growth.

Her protein electrophoresis revealed polyclonal gammopathy. Bone marrow trephine reports clearly revealed myeloid hyperplasia with plentiful megakaryocytes suggestive of Reactive Thrombocytosis. There was no justification for pursuing flow cytometry, cytogenetic and molecular analysis, as these are fairly expensive tests for a patient admitted in a public sector hospital.

During her hospital stay, her platelet counts were decreasing with treatment of infection without any specific treatment for clonal thrombocytosis. This is also again suggestive of Reactive Thrombocytosis. Her platelet count at the time of discharge had fallen to 538 X10<sup>3</sup>/ $\mu$ L.

Her bone marrow revealed myeloid hyperplasia with plentiful megakaryocytes suggestive of Reactive thrombocytosis. Doppler Ultrasound showed Biphasic flow in radial and ulnar arteries and monophasic flow in dorsalis pedis arteries.

She was managed with amoxicillin/clavulanic acid, aspirin, clopidogrel, nifedipine, analgesics and carbamazepine. She improved clinically and intensity of pain decreased.

She was discharged after a hospital stay of one

month with WBC count of  $4.0 \times 10^9/L$  and Platelet count of  $538 \times 10^9/L$ . Digital gangrene did not progress beyond the affected areas at the time of admission.

## Discussion

Clonal thrombocytosis was excluded as a cause of thrombocytosis by the bone marrow examination in this patient. Besides infection of gangrenous digits, no other site of infection was identified and as she had received antibiotics prior to being admitted in the hospital, no infective organism could therefore be isolated. However with the institution of antibiotics, hydration and antiplatelet therapy, the patient improved systemically and the digital gangrene stabilized without local infection and with progressive delineation of viable and gangrenous parts of digits.

Although the exact mechanism for reactive thrombocytosis is unknown, it may result from persistent overproduction of one or more thrombopoietic factors that act on megakaryocytes or their precursors in addition to principal factor thrombopoietin (TPO) which is expressed primarily in liver but is also found in bonemarrow, spleen and kidney.<sup>4,5</sup> This would indicate an endocrine as well as paracrine role of TPO action in regulating thrombopoiesis.

It may be due to the overproduction of pro-inflammatory cytokines, such as interleukins IL-1, IL-6, IL-11 and TNF that occurs in chronic inflammatory, infective and malignant states. The presence of elevated levels of IL-1, IL-6, C-reactive protein, granulocyte colony-stimulating

factor (G-CSF), and granulocyte-macrophage colony-stimulating factor (GM-CSF) in individuals with this condition suggests that these cytokines may be involved in reactive thrombocytosis states. IL-6 is mainly produced by monocytes, but it can also be produced by lymphocytes, endothelial cells and fibroblasts. Infusion of IL-6 have shown an increase in platelet numbers.<sup>6,7</sup> More than 80% of platelets with reactive thrombocytosis have raised IL-6 levels.<sup>8,9</sup>

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