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Thrombocytosis in adults: analysis of 777 patients

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Abstract. Santhosh-Kumar CR, Yohannan MD, Higgy KE, Al-Mashhadani SA (Department of Medicine, Department of Pediatrics and Department of Haematology, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia). Thrombocytosis in adults: analysis of 777 patients. *Journal of Internal Medicine* 1991; 229: 493–495.

A total of 777 patients with thrombocytosis, defined as a platelet count of $\geq 500 \times 10^9\,l^{-1}$, seen in a University hospital over a 1-year period, were studied prospectively for aetiology. The most frequent causes of thrombocytosis were infection (21.9%), rebound thrombocytosis (19.4%), tissue damage (17.9%), chronic inflammatory disorders (13.1%) and malignancy (5.9%). Thrombocytosis associated with multiple causative factors, occurring simultaneously, was seen in 6.1% of cases. Thrombocytosis of ≥ 1 million $\times 10^9\,l^{-1}$ was found most frequently in patients with multiple aetiological factors occurring at the same time, in myeloproliferative disorders, or in postsplenectomy patients.

Keywords: adults, aetiology, platelets, thrombocytosis.

Introduction

Thrombocytosis, defined as an abnormally high platelet count, has been attributed to various pathological and physiological processes [1–3]. With the widespread use of electronic cell counters, an accurate platelet count is now available as part of the routine haemogram in most laboratories. This has inevitably led to a higher incidence of observed thrombocytosis. We here describe a prospective study on the aetiology of thrombocytosis in adults who were seen over a 1-year period in a University teaching hospital.

Patients and methods

For the purposes of this study, thrombocytosis was defined as a platelet count of $\geq 500 \times 10^9\,l^{-1}$. All blood counts performed between 1 January 1989 and 31 December 1989, on both out-patients and in-patients, at King Khalid University Hospital, Riyadh, were screened for instances of platelet counts of $\geq 500 \times 10^9\,l^{-1}$. All counts were performed on Coulter counter S Plus IV (Coulter Electronics, Hialeah, Florida, USA) using EDTA anticoagulated fresh blood, and high counts were confirmed by repeat examinations and peripheral smear examination. The normal range of platelet counts for this machine is $150–400 \times 10^9\,l^{-1}$. In instances where patients exhibited multiple episodes of thrombocytosis during the year, only the episodes with the highest counts were included in the analysis.

A list of possible causes of thrombocytosis, based on potential mechanisms, was compiled from previous publications, and patients were classified into eleven major categories and further subdivisions.

Results

A total of 777 adults with thrombocytosis were observed during the study period. The major causes of thrombocytosis are listed in Table 1. Platelet counts ranged from $500–2475 \times 10^9\,l^{-1}$. Forty-five (5.8%) patients had platelet counts of $\geq 999 \times 10^9\,l^{-1}$. Platelet counts of $\geq 999 \times 10^9\,l^{-1}$ were most frequently observed in patients with multiple causative factors (35.5%), myeloproliferative disorders (26.7%) or postsplenectomy (22.2%).

Table 1. Aetiology of thrombocytosis in 777 patients

Diagnosis	n (%)
Infections	170 (21.9)
Rebound thrombocytosis	151 (19.4)
Tissue damage	139 (17.9)
Chronic inflammatory disorders	102 (13.1)
Malignancy	46 (5.9)
Renal disorders	36 (4.6)
Haemolytic anaemia	28 (3.6)
Myeloproliferative disorders	26 (3.3)
Splenectomy	15 (1.9)
Multiple causes	47 (6.1)
Miscellaneous	17 (2.2)

Total = 777 (100).
Median age = 52 years.
Age range = 16–90 years.
Male : female ratio = 42.2 : 57.8

Infections were the most common cause of thrombocytosis, occurring in 163 patients. It was found that 84% of cases were due to acute infections. There were 11 patients with thrombocytosis secondary to pulmonary tuberculosis. Four patients, two with septic arthritis and two with acute osteomyelitis, had counts of $> 999 \times 10^9 l^{-1}$.

Rebound thrombocytosis occurred in 151 patients. This followed bleeding in 70 (46.4%) cases, iron deficiency anaemia in 32 (21.1%) cases, cancer chemotherapy in 14 (9.3%) cases and steroid therapy for immune thrombocytopenia in one patient. Thrombocytosis was observed towards term pregnancy or immediately after labour in 34 (22.5%) patients.

Thrombocytosis secondary to tissue damage occurred following major surgery in 117 cases, multiple fractures in 18 cases, myocardial infarction in 3 cases, burns in 3 cases and pancreatitis in 2 cases. Thrombocytosis following cardiopulmonary bypass was seen in 12 cases.

Of 28 (3.6%) patients with thrombocytosis secondary to haemolytic anaemia, 26 cases were due to sickle cell disease or thalassaemia, and two had autoimmune haemolytic anaemia.

Among chronic inflammatory disorders causing thrombocytosis, rheumatoid arthritis (35.3%), seronegative arthritis (14.7%) and inflammatory bowel disease (6.9%) were the most common.

Among renal disorders giving rise to thrombocytosis in 36 patients, chronic renal failure was the cause in 20 cases, acute renal failure in 10 cases and nephrotic syndrome in 5 cases.

There were 46 (6%) patients with thrombocytosis at the initial presentation of malignancy. The malignancy most commonly associated with thrombocytosis was lymphoma (Hodgkin's disease in 10 cases, Non-Hodgkin's lymphoma in 5 cases). Two patients (primary hepatocellular carcinoma, Non-Hodgkin's lymphoma) had counts of $> 999 \times 10^9 l^{-1}$.

Myeloproliferative disorders accounted for 26 (3.3%) cases. There were 11 patients with essential thrombocythaemia, ten with polycythaemia rubra vera, four with chronic granulocytic leukaemia and one with myelofibrosis. One patient with polycythaemia rubra vera and persistent thrombocytosis developed bilateral iliac vein thrombosis and pulmonary embolism during the study period.

Multiple causes occurred in 47 (6%) cases. Infection, surgery, malignancy, splenectomy and chronic inflammatory disorders were the most common contributing factors for thrombocytosis in these patients. The latter tended to have higher platelet counts [mean = $814 \times 10^9 l^{-1}$ (SD 263)].

The miscellaneous group consisted of patients with bronchial asthma, allergic reactions, lithium administration and gout.

Discussion

Thrombocytosis occurs in a variety of clinical conditions, ranging from infections to malignancy. Primary disorders of thrombopoiesis, namely myeloproliferative disorders, accounted for only a small fraction of patients with thrombocytosis in this study. The finding of a platelet count in the range 500–$750 \times 10^9 l^{-1}$ was found to be of little discriminatory value, as this occurred in a variety of conditions. Platelet counts of $\geq 1000 \times 10^9 l^{-1}$ were often due to a combination of factors or myeloproliferative disorders, or occurred following splenectomy. Thrombocytosis associated with malignancy occurred in fewer patients than has been reported previously [4]. The association of thrombocytosis with chronic inflammatory disorders such as rheumatoid arthritis, other collagen vascular disorders and inflammatory bowel disease was similar to that reported in an earlier study [3].

The mechanisms underlying thrombocytosis, which occurs in a wide range of conditions, have not been fully elucidated. The regulation of platelet production is thought to be mediated by thrombopoietin, a humoral factor that is produced in the kidney parenchyma. Other potential regulatory

mechanisms may also exist [5]. In myeloproliferative disorders there is an autonomous increase in the production of platelets. Thrombocytosis seen in infections and certain inflammatory states may be an acute phase reaction similar to the occurrence of a raised sedimentation rate [6, 7]. It is not clear why certain chronic infections such as tuberculosis are particularly associated with thrombocytosis [8]. It has been suggested that this may represent part of a haematological stress syndrome [9]. The spleen is believed to have a major role in the regulation of platelet kinetics, and this may explain the thrombocytosis associated with splenectomy and conditions that cause hyposplenism [10]. Persistent thrombocytosis following splenectomy has been shown to correlate with the continuing anaemia [11]. Whether a similar correlation exists in patients with other conditions that give rise to hyposplenism is not clear. Thrombocytosis following surgery has been related to bleeding and/or thrombocytopenia at the time of surgery [12]. Thrombocytosis following therapy with cytotoxic drugs is believed to be a rebound phenomenon secondary to transient marrow suppression. Drugs such as vincristine cause the development of thrombocytosis via a different mechanism.

The finding of a high platelet count on routine blood examination has both diagnostic and therapeutic implications. In the majority of cases this is an acute phase phenomenon in response to infection, tissue damage, blood loss or anaemia. The platelet counts in such instances seldom exceed 999×10^9 l^{-1}. In the absence of these conditions chronic inflammatory disorders, malignancy or myeloproliferative disorders must be considered. In many instances multiple aetiological factors may be responsible for thrombocytosis.

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