

## Essential Primary Thrombocytosis in a Diabetic Patient

### Abstract

Essential thrombocytosis also referred to as essential thrombocythemia, idiopathic thrombocytosis, primary thrombocytosis and hemorrhagic thrombocythemia is an uncommon myeloproliferative disorder of unknown cause in which marked proliferation of the megakaryocytes in the bone marrow leads to elevation of the platelet count.

We report here a case of type 2 diabetic patient with essential thrombocytosis.

### Introduction

Essential thrombocytosis is a

#### Address for correspondence:

Prof. V Mohan,  
Chairman and Chief,  
Dept. of Diabetology,  
Dr. Mohan's M. V. Diabetes Specialities  
Centre & Madras Diabetes Research  
Foundation, 6, Conran Smith Road,  
Gopalapuram, Chennai - 600 086, India.  
E-mail: mvdsc@vsnl.com  
Website: www.mvdsc.org

clonal disorder of unknown etiology involving multipotent hematopoietic progenitor cell and is manifested clinically by the overproduction of platelet in the absence of a definable cause<sup>1</sup>. It has to be distinguished from the more common, non-clonal reactive form of thrombocytosis. There is an unexplained female predominance in contrast to reactive thrombocytosis where no gender bias exists and it is extremely rare in childhood<sup>2</sup>. Because thrombocytosis is often a predominant feature of other chronic myeloproliferative disorders the treatment and prognosis of which differ from essential thrombocytosis and because no clonal marker is available for this disorder, clinical criteria have been proposed to distinguish it from other chronic myeloproliferative disorders like chronic myelogenous leukemia, polycythemia vera or

In this report, a case of essential thrombocytosis occurring as a routine finding in a diabetic patient attending a tertiary diabetic center is presented.

This case is reported for its rarity and also to demonstrate the value of doing a routine hemogram in diabetic centers where quite often, routine investigations like this tend to be missed.

myelodysplasia<sup>3</sup> as shown below

### The polycythemia study group diagnostic criteria for essential thrombocytosis<sup>4</sup>

1. Platelet count >6,00,000/ml.
2. Hemoglobin <13 g/dl.
3. Normal red cell mass.
4. Absence of known cause o

reactive thrombocytosis.

5. Absence of Philadelphia chromosome and bcr-abl gene rearrangement.
6. Presence of marrow iron.
7. Absence of myelofibrosis.
8. Absence of myelodysplasia clinically and by cytogenetic analysis.
9. Absence of splenomegaly.

We report below on a type 2 diabetic patient with essential thrombocytosis who satisfied the above criteria.

### Case report

A 66-year-old female type 2 diabetic patient presented to our center for routine assessment and control of her diabetic status.

Patient was a known diabetic of 16 years duration and had a positive family history of diabetes. She was treated with oral hypoglycemic agents all along. She was a known hypertensive and was on treatment for ischemic heart disease. She underwent hysterectomy at the age of 50 years for dysfunctional uterine bleeding

On physical examination, her height was 148 cm and weight 58.2 kg. There was no pallor, icterus, clubbing, edema or lymphadenopathy. Pulse rate was 78/min and BP 120/80 mmHg. The respiratory rate was 20/min. Temperature was normal (98.4°F) and there was no bony tenderness anywhere.

On systemic examination, neurological examination revealed absence of ankle jerks in both lower limbs and all peripheral

pulses were normal. Other systems were found to be clinically normal. Fundus (retinal) examination was normal. Ear, nose, throat and dental examinations were also normal.

Investigations revealed fasting blood sugar of 152 mg/dl, post-prandial blood sugar of 299 mg/dl and HbA<sub>1c</sub> of 10.2%. The lipid profile was normal. Urine examination was normal. Blood urea was 31 mg/dl, creatinine 0.9 mg/dl and 24 hours protein excretion <100 mg/dl. Microalbuminuria was negative. Hemogram revealed white blood cells count of 7,540 cells/cumm, polymorphs 64.1%, lymphocytes 24.9%, monocytes 4.2%, eosinophils 1.3%, red blood cells 4.93 millions/cumm, hemoglobin 12.1 g/dl and hematocrit 39.3%. The platelet count was found to be 11,18,000/μl. The platelet distribution width was normal. Peripheral smear revealed marked thrombocytosis including giant platelets. ESR, bleeding time, clotting time, prothrombin time (coagulation profile normal), serum iron studies, serum uric acid, liver function test, serum electrolytes, serum protein C, protein S and C-reactive protein were all normal. Chest X-ray was normal. ECG showed non-specific "T" wave changes in all leads. Carotid and peripheral doppler studies were normal.

Biothesiometry showed evidence of large fiber sensory neuropathy in both lower limbs. Ultrasound abdomen revealed bilateral small kidneys but all other organs were found to be normal.

As her platelet count was very

high, a hematology opinion was sought. Bone marrow study was done. Bone marrow cytology by pearl stain revealed normal appearing megakaryocytes in adequate number with mild eosinophilia. Trepphine BM biopsy revealed hypercellular marrow with mild increase in megakaryocytes and increase in eosinophils. Leucocyte alkaline phosphatase score was mildly increased.

A diagnosis of essential thrombocytosis was made and patient was started with hydroxyurea 500 mg thrice weekly and oral anticoagulants. The patient showed drop in platelet count to 380,000/μl and has done well on follow-up for over a year. For the diabetes, we started her on twice daily insulin along with oral hypoglycemic agents and the diabetes was stabilized well.

### Discussion

Diabetic subjects are prone to thrombosis through a complex interplay of hyperlipidemia, platelets, fibrinolysis, thrombosis and endothelial injury. Diabetic subjects also have increased levels of plasminogen activator inhibitor, von Willebrand factor, factors VIII and VII, fibrinogen and thrombin-antithrombin complexes. All these prolong the survival of clots on injured endothelium. Additional factors like decreased levels of antithrombin III, protein C and protein S increase the predisposition to thrombosis<sup>5,6</sup>. Platelet adhesion and aggregation are also enhanced in diabetic patients, further contributing to the

procoagulant milieu<sup>7</sup>. The release of thromboglobulin and factor 4 from platelets is increased in diabetic individuals<sup>5,7</sup>. In the diabetic state, there is increased platelet derived nitric oxide destruction, contributing to increased platelet aggregation and adhesion to endothelial cells.

Other platelet abnormalities in diabetic include decreased platelet survival, increased platelet generation of vasoconstrictor prostanoids, reduced platelet generation of prostacyclin and increased glycosylation of platelet proteins<sup>7</sup>. One of the mechanisms by which diabetes inhibits the cardioprotective effects of estradiol in diabetic women may relate to abnormal function of the platelet. The major clinical manifestations are thrombosis and hemorrhage, probably reflecting both qualitative and quantitative abnormalities in platelets.

In this report, we present a case of essential thrombocytosis occurring as a routine finding in a diabetic patient attending a tertiary diabetic center. Our patient was asymptomatic at the time of diagnosis. The blood investigations and bone marrow reports are suggestive of essential thrombocytosis and all common causes of reactive thrombocytosis were ruled out by appropriate investigations<sup>8</sup>. It is suggested that a cytogenetic evaluation is necessary to determine if the thrombocytosis is due to chronic myelogenous leukemia or a

myelodysplastic disorder such as the 5q-syndrome. Also because the bcr-abl translocation can be present in the absence of Philadelphia chromosome, it has been suggested that gene re-arrangement studies should be performed in all patients with thrombocytosis in whom a cytogenetic study is normal<sup>9</sup>. Essential thrombocytosis allows long-term survival and the average survival after diagnosis is >15 years. However, there is a 5% risk of transformation to acute leukemia over a 20-year period.

Although we were unable to carry out cytogenetic investigations, we conclude that this diabetic patient has essential thrombocytosis as it satisfies the Polycythemia Study Group Diagnostic Criteria for Essential Thrombocytosis. The risk of thrombosis can be reduced by reduced platelet count to <500,000/ $\mu$ l<sup>10</sup>.

This case is reported for its rarity and also to demonstrate the value of doing a routine hemogram in diabetic centers where quite often, routine investigations like this tend to be missed.

### References

1. Adamson JW, Fialkow PJ, Murphy S, Prchal JF and Steinmann L. Polycythemia vera: Stemcell and probable clonal origin of the disease. *N. Engl. J. Med.* 1976;295:913-916.
2. Dame C and Sutor AH. Primary and secondary thrombocytosis in childhood. *Br. J. Haematol.* 2005;129:165-177.
3. Cotran RS, Vinaykumar MD and Collins T. Hemodynamic disorders thrombosis and shock. In: *Tucker Collins-Robin's Textbook of Pathology* 16th Edition, Mitchell RN and Cotran RS (Eds.), Harcourt Publishing International Company, Singapore 1999:118-138.
4. Spivak JL. Polycythemia vera and other myeloproliferative diseases. In: *Harrison's Principles of Internal Medicine* 14th Edition, Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL and Longo DL (Eds.), McGraw Hill Co. Inc., USA. 1998:679-684.
5. Sowers JR. Diabetes mellitus and cardiovascular disease in women. *Arch. Intern. Med.* 1998;158:617-621.
6. Davi G, Catalano I, Aversa I, et al. Thromboxane biosynthesis and platelet function in type 2 diabetes mellitus. *New Engl. J. Med.* 1990;322:1769.
7. Clarkson P, Celemajer DS, Yue DK, et al. Essential thrombocytosis in insulin dependant diabetes mellitus related to the duration of disease and LDL cholesterol level. *Circulation* 1995;92: 1101-1107.
8. McMullin MF, Bareford D and Campbell P. Guidelines for the diagnosis investigation and management of polycythemia erythrocytosis. *Br. J. Haematol.* 2005;130:174-195.
9. Johnson B, Mertens F, Fioretos T, et al. Remarkably long survival of a patient with Ph1 -positive CML and 5 bcr rearrangement. *Leukemia* 1990;6:448-449.
10. Dwson AA and Ogston D. The influence of the platelet count on the incidence of thrombotic and haemorrhagic complication in polycythemia vera. *Postgrad. Med. J.* 1970;46:76-78.