

MULTIPLE MYELOMA PRESENTING WITH BLEEDING DIATHESIS

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Haemostatic defect due to platelet dysfunction rarely occurs in multiple myeloma. This report describes a 71-year old patient with multiple myeloma presented with severe bone pain and bleeding gums. Bone marrow biopsy revealed 65% plasma cells with atypical features. Coagulation profile showed normal prothrombin time and activated partial thromboplastin time whereas bleeding time performed by Ivy method was prolonged to 12 minutes (normal 2 – 7 minutes)

HISTORY AND INVESTIGATIONS

A 71 year old female presented in the department of Medicine, Ghurki Trust Teaching Hospital, Lahore with severe pain anterior thoracic and lumbosacral region of 02 years duration. The pain was non-radiating, aggravating on body movements and on respiration. The patient also developed progressive generalised body weakness, accompanied by low grade fever for the last 07 months. There was history of loss of weight for the last 06 months. Productive cough with expectoration of yellowish coloured sputum was also an intermittent accompaniment of the above mentioned features for the last 05 months.

Since 01 month, there was a complaint of bleeding from the gums, mostly triggered during chewing of food. Bleeding used to recede spontaneously but recur on deglutition.

On physical examination, pallor was present. Lymph nodes were not palpable. There was no sign of bleeding diathesis. Gums were normal with almost edentulous features most probably related to the age of the patient.

LAB INVESTIGATIONS

Haemoglobin 6.8 g/dl, total WBC count: $3.8 \times 10^9/L$ with normal differential count except for a few lymphocytes with plasmacytoid features (lymphoplasmacytic cells), Platelets: $180 \times 10^9/L$ ESR: 160 mm at the end of first hour by Westergren method. Morphology revealed marked rouleaux formation with macrocytosis, N.R.B.C: 2/100 WBC (leucoerythroblastic picture). Coagulation profile showed prolonged bleeding time 12.0 min by Ivy method. (Normal 3-7 minutes), normal prothrombin time (PT) and activated partial thromboplastin time (APTT).

Serum calcium level was at the upper limit of normal (9.8 mg/dL) with normal alkaline phosphatase level. Urea and creatinine levels were 80.0 mg/dL and 1.2 mg/dL respectively. Serum β_2 microglobulin level was 2.0 ug/dL. Patient's serum was positive for monoclonal dense band in gamma globulin region (M. band). Screening test for Bence Jones proteins in the urine was also positive. X-Ray of the skeleton showed multiple osteolytic lesions in the lumbar and lower thoracic regions with a collapse of vertebral bodies at the level of T11, T12 and L2, L3. The vault of skull and pelvis also showed multiple osteolytic lesions.

Bone marrow aspiration revealed egg shell consistency of cortex of bone, with appreciation of multiple cavitative areas at the site of posterior iliac spine. Microscopic examination showed 65% plasma cells mostly with atypical features (large size, binucleate or trinucleate forms). Megakaryocytes were present in adequate number in bone marrow aspirated material.

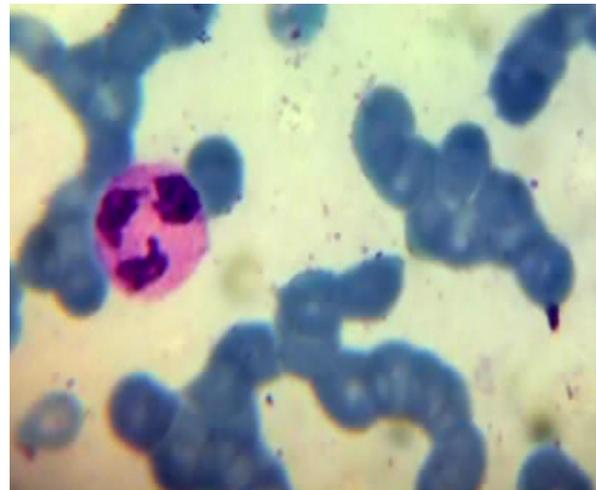


Fig. 1: Peripheral blood film showing marked rouleaux formation.

Based upon prolonged bleeding time with normal platelet count, platelet aggregation / function study was performed using platelet agonists (ADP, adrenaline, thrombin, collagen and ristocetin).

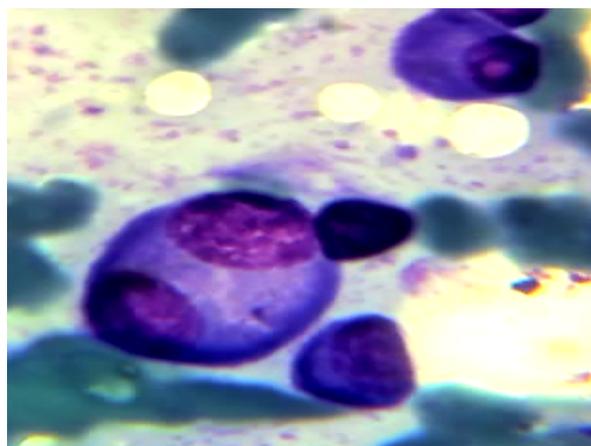


Fig. 2: Bone marrow aspirate shows malignant plasma cells (Myeloma cells).

PLATELET AGGREGATION – PRINCIPLE

Blood is centrifuged gently to obtain platelet rich plasma which is stirred in a cuvette at 37°C between a light source and photo cell. When an agonist is added, the platelets aggregate absorb less light so that transmission increases and is detected by movement of a pen on the chart recorder. The addition of different agonists, at a range of concentrations, allow the detection of certain aggregation defects. The reagents (thrombin, adrenalin, ADP, collagen, ristocetin) bind to specific platelet membrane receptors, activating platelets through the platelet membrane phospholipid, and leading ultimately to a series of reactions which culminate in shape change, granule release and aggregation. These responses depend on the normal function of platelets, the level of inhibitory substances such as paraproteins and the concentration of the agonist used.

The **result** showed generalised decreased aggregation with the available platelet agonists (ADP, thrombin, ristocetin, adrenalin). Thus a close relationship was seen between the functional activity of platelets and the level of disease activity/paraproteinaemia.

DISCUSSION

Multiple Myeloma (M.M) accounts for approximately 1% of all malignancies and 10% of haematological tumours. Myeloma is a disease of neoplastic plasma cells that synthesize abnormal amount of immunoglobulin or immunoglobulin fragments.¹ Clinical manifestations are heterogeneous and include the formation of tumour, monoclonal immunoglobulin production, decreased immunoglobulin secretion by normal plasma cells, impaired haematopoiesis, defect in haemastasis with

normal platelet count and coagulation factors,³ osteolytic bone lesions, hypercalcaemia and renal dysfunction.

Coagulopathy in M.M is well documented but is rarely a clinical problem.⁴ In addition to the risk of thrombosis in M.M patients, which is linked to hypercoagulable state by acquired deficiency of protein C or as part of paraproteinaemia,⁶ bleeding manifestation can be due to perivascular amyloidosis,⁵ acquired inhibitor to factor VIII, X or platelet quantitative or qualitative functional impairment.² This may result in chronic recurrent bleeding of the gums, respiratory and gastrointestinal tract. The bleeding time is usually prolonged and in vitro platelet function is abnormal.⁷

Pathogenesis of haemostatic defect in Multiple Myeloma due to qualitative platelet defect occurs in 2 ways: coating of platelets by the abnormal myeloma protein leading to false negative aggregation response of platelets to agonists especially ristocetin. The other is inhibition of fibrin aggregation due to binding of antibody portion of myeloma protein to fibrin during clotting. This probably represents the most common coagulopathy in patients with myeloma. This form of coagulopathy also manifests in the form of decreased platelet aggregation in response to agonists such as ADP, thrombin, adrenaline, collagen and ristocetin. It may also be mentioned that haemostatic defect due to thrombocytopenia is a less frequent phenomenon due to overproduction of IL – 6 by bone marrow stromal cells, tumour cells and other normal accessory cells which possess thrombopoietic activity.

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