ASYMPTOMATIC MULTIPLE MYELOMA PRESENTING AS EPISTAXIS- RARE PRESENTATION - A CASE REPORT

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ABSTRACT
Multiple myeloma (MM) is a plasma cell dyscrasia that accounts for almost 10% of all hematologic malignancies. Anemia, bone pains, renal failure are the most common symptoms at presentation. We report a case of a 53 female came to ENT OPD with history of recurrent epistaxis was finally diagnosed as Multiple myeloma (MM). Initially routine investigations Hemogram show anemia 6.8g/dl, Total leucocyte count 8700/cumm, platelets 238000/cumm and peripheral smear show significant rouleaux formation. ESR is 120mm at the end of one hour. Liver function test reveals high serum total proteins 14.8g/dl with globulin 11.3 & albumin 3.5(A:G reversal). Further bone marrow aspiration analysis and serum protein electrophoresis and skeletal X rays supported MM diagnosis. This case is interesting as uncommon presentation of epistaxis & laboratory approach including routine peripheral smear examination, serum proteins levels gives early clue to diagnosed a case of asymptomatic MM. This case may promote the possible involvement of plasma cell myeloma in the differential diagnosis of patients with unexplained epistaxis. In this case study we also present a thorough review of the literature with regard to the association between MM and tendency of hemorrhage.

KEYWORDS: Epistaxis; Plasma cell dyscrasia; lab diagnosis.

INTRODUCTION
Epistaxis, or bleeding from the nose, is a common complaint in a patient visiting ENT OPD. Most nose bleeds are benign, self-limiting, and spontaneous, but some can be recurrent. Many uncommon causes are also noted. More than 90% of bleeds occur anteriorly and arise from Little’s area, where the Kiesselbach plexus forms on the septum.1

According to the available medical literature, the commonest cause of adulthood epistaxis is idiopathic, which accounts for 70 to 80% of the cases. The true prevalence of epistaxis is not known, because most episodes are self-limiting and thus are not reported.2

Multiple myeloma (MM), also known as plasma cell myeloma, is a malignant hematological neoplasm, characterized by clonal proliferation of plasma cells in the bone marrow and associated with the overproduction of structurally homogeneous immunoglobulins. New diagnostic criteria of MM require the presence of at least 10% plasma cells on examination of the bone marrow (or biopsy of tissue with monoclonal plasma cells), monoclonal protein in the serum or urine, and evidence of end-organ damage.3

In this report we describe a case which was finally diagnosed as MM, but was initially manifested as nasal bleed alone. Epistaxis with normal platelet count in the course of MM is extremely rare.

CASE REPORT
A 53-year-old female came to ENT OPD Yashoda hospitals, malakpet, hyderabad with history of periodic nasal bleed (epistaxis) of 3 to 4 weeks duration. The bleeding was spontaneous without antecedent trauma. The episodes of epistaxis usually lasted for about five minutes. Pressure to the nares would stop the bleeding. She denied easy bruising, petechiae, spontaneous hemarthrosis, or rashes. She denied new bone or joint pain. On general examination, patient was pallor. ENT examination including indirect laryngoscopy and diagnostic nasal endoscopy were normal. There is no deviation of nasal septum.

At the initial examination, laboratory results were as follows: red blood cells 2.30millions/cumm (4–5.5millions/cumm); hemoglobin 6.8g/dl (12–15 g/dl); white blood cells 8700/cumm (4000–11000/cumm); platelets, 2.38 laks/cumm (1.5–4.5laks/cumm); Peripheral blood leishman stained smear show bluish discoloration.
macrophoscopically & microscopic findings reveal normocytic normochromic RBCs with significant rouleaux formation (FigA) and erythrocyte sedimentation rate (ESR)120mm/h (10–20 mm/h). Coagulation study were normal. Biochemical examination revealed Total serum protein 14.8g/dl(6.3-8.5gms/dl); albumin 3.5(3.5-5.1gms/dl); globulin 11.3 (2.3-3.5gms/dl); Total bilirubin 0.9 (0.2-1.3mg/dl), alkaline phosphatase 76(38-126U/L), SGOT 22(14-60U/L) & SGPT18(9-69U/L) were normal. Electrolytes, KFT and plasma sugar were in normal limits.Urine examination show mild proteinuria. Bence-jones protein was negative.

Figure A: Leishman stain blood film show significant rouleaux formation(black arrow).

Bone marrow aspiration cytology smears show increased in plasma cells(50%) (Fig B). Plasma cells consisting mature plasma cells having round eccentric nuclei, clumped chromatin and perinuclear hof and immature forms having abundant cytoplasm and fine chromatin. Few binucleate forms seen.

Figure B: Bone marrow aspirate smears with many plasma cells (black arrow).

A skeletal survey X ray skull AP & Lateral view showed osteolytic lesion involving skull (Fig C) vault suggestive of myeloma. X ray paranasal sinuses show haziness in right maxillary sinus suggestive of sinusitis.

Figure C: X ray skull show osteolytic lesion(black arrow mark).

Serum protein electrophoresis which showed presence of M band in gamma region.

Immunofixation study show increased in IgG, kappa light chain and serum Beta 2 microglobulin(Table 1). Finally based on early clue of significant rouleaux formation, high serum protein with A:G reversal, increased plasma cells in bone marrow, M band and increased IgG and kappa light chain diagnosed as IgG Kappa multiple myeloma stageIII.
TABLE 1.

<table>
<thead>
<tr>
<th>Test Report Status</th>
<th>Results</th>
<th>Biological Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYELOMA BAND</td>
<td>DETECTED</td>
<td>NOT DETECTED</td>
</tr>
<tr>
<td>IGG BAND</td>
<td>POSITIVE</td>
<td>NOT DETECTED</td>
</tr>
<tr>
<td>IGM BAND</td>
<td>NOT DETECTED</td>
<td>NOT DETECTED</td>
</tr>
<tr>
<td>IGA BAND</td>
<td>NOT DETECTED</td>
<td>NOT DETECTED</td>
</tr>
<tr>
<td>KAPPA BAND</td>
<td>POSITIVE</td>
<td>NOT DETECTED</td>
</tr>
<tr>
<td>LAMBDA BAND</td>
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<td>NOT DETECTED</td>
</tr>
<tr>
<td>TOTAL IGA</td>
<td>&lt;0.24 Low</td>
<td>0.52 - 4.68 g/L</td>
</tr>
<tr>
<td>TOTAL IGG</td>
<td>96.70 High</td>
<td>6.5 - 16.4 g/L</td>
</tr>
<tr>
<td>TOTAL IGM</td>
<td>0.29 Low</td>
<td>0.39 - 3.38 g/L</td>
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<tr>
<td>SERUM LIGHT CHAINS</td>
<td></td>
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<tr>
<td>(KAPPA &amp; LAMBDA)</td>
<td></td>
<td></td>
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<tr>
<td>KAPPA LIGHT CHAIN</td>
<td>639.00 High</td>
<td>.30 - 19.40 mg/L</td>
</tr>
<tr>
<td>LAMBDA LIGHT CHAIN</td>
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<td>5.71 - 26.30 mg/L</td>
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<tr>
<td>KAPPA LAMBDA RATIO</td>
<td>639 High</td>
<td>0.26 - 1.65</td>
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<tr>
<td>B2-MICROGLOBULIN</td>
<td>6037.0 High</td>
<td>609.0 - 2366.0 ng/mL</td>
</tr>
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</table>

The patient received bortizomib based chemotherapy (Bortizomib, Dexamethasone Lenalidomide and liposomal doxorubicin) every 21 days. After two cycles of this regimen; the total protein levels comes down.

DISCUSSION

MM is the second most prevalent hematological malignancy, representing 2% of all cancer mortalities. The annual incidence of multiple myeloma is 4.3 per 100,000 people, but the incidence ranges from 1 per 100,000 for people who are 40 to 49 yr of age to 49 per 100,000 population for those who are 80 yr of age. The median age of diagnosis for multiple myeloma is between 66 and 70 years. Myeloma is more common in African Americans compared with white persons and less common in Asians. Men are more commonly affected then women.\(^4\)

Anemia, renal failure, skeletal destruction, recurrent infections and hypercalcemia are the most common features of the disease. Cases of MM with Epistaxis alone is uncommon. MM require the presence of at least 10% plasma cells on examination of the bone marrow (or biopsy of tissue with monoclonal plasma cells), monoclonal protein in the serum or urine and evidence of end-organ damage. Although usually restricted to the bone marrow, extramedullary involvement of this disease can occur in up to 20% of cases. The most common extramedullary site is the upper respiratory tract, including the oropharynx, nasopharynx, nasal cavities, sinuses and larynx.\(^4,5\)

Elevated protein concentration may expand the plasma volume and displace some of the RBCs, thereby reducing the hemoglobin concentration disproportionately to the total RBC mass and exaggerating the anemia. It also render a bluish background to a stained peripheral blood smear as in this case. Rouleaux formation, the linear alignment of at least 4 RBCs in a thin area of a blood smear resembling a stack of coins, is caused by changes in the surface charge of the erythrocyte membrane when this membrane is coated with excessive amounts of protein such as globulins and fibrinogen. The most common cause of Rouleaux formation, however, is paraproteinemia due to a monoclonal gammopathy. Rouleaux formation often increases the erythrocyte sedimentation rate as well.\(^6\)

Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS), Waldenstrom's Macroglobulinemia (WM), Amyloidosis (AAL) or Multiple Myeloma (MM) may present both thrombotic and bleeding complications. Bleeding is commonly associated with treatment or disease related thrombocytopenia while thrombosis may be related to paraneoplastic phenomena.\(^7\)

Tharough reviewing the limited literatures associated with hemorrhage in MM patients, Acquired von Willebrand disease has been described occasionally in MM and AAL but rarely induce clinically relevant bleeding. Some pathophysiological mechanisms include the interference of circulating monoclonal proteins with platelet function and coagulation factors or acquired von Willebrand disease. The possibility of a monoclonal protein interference with the polymerization of fibrin monomers, resulting in an acquired dysfibrinogenemia. The markedly elevated serum total protein concentration
was caused by unregulated synthesis of a monoclonal immunoglobulin as occurs typically in patients with a plasma cell dyscrasia such as multiple myeloma or Waldenström’s macroglobulinemia.[8,9] The diagnosis of multiple myeloma requires the correlation of morphologic, radiologic and laboratory findings. Instead of complex scheme of major and minor criteria, the current minimal criteria for myeloma include bone marrow plasmacytosis (10%) or plasmacytoma, increased serum proteins of at least 3g/dl if IgG or 2g/dl if IgA, lytic bone lesions and monoclonal light chain in urine, at least 1g per 24 hr. In our case patient does not have symptoms related to myeloma except anemia and presence of plasmacytosis in bone marrow (50%) and increased serum proteins.

Treatment recommendations based on individual patient and disease characteristics. Combinations of bortezomib/dexamethasone or provide durable responses and are indicated for most patients. Other rituximab with cyclophosphamide/dexamethasone/bendamustine. Our patient responded very well with Combinations of bortezomib/dexamethasone.[10]

CONCLUSION
MM is a systemic disease which may be rarely presented with epistaxis alone. It should be kept in mind epistaxis in elderly patient usually idiopathic, correlation of simple basic investigations like peripheral smear findings together with high serum proteins, A:G reversal helps as early clue for diagnosis of asymptomatic myeloma, also to retain organ damage in course of myeloma.

REFERENCES