Cord Compression by Extramedullary Hematopoiesis in Polycythemia Vera

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A 73-year-old male with polycythemia vera and a history of prostate cancer presents to an outside hospital complaining of back pain of two months duration. He denied fevers, chills, night sweats, weight loss, lower extremity weakness and decreased sensation. Other than chronic constipation and urinary hesitancy, his review of systems was unremarkable. A spinal x-ray revealed a T12 vertebral fracture and the patient was transferred to Thomas Jefferson University Hospital for further management.

His polycythemia vera was last treated with phlebotomy 1 year ago. The patient had been treated with hydroxyurea in the past, but it was discontinued secondary to thrombocytopenia. A splenectomy had been performed four months prior to admission for persistent thrombocytopenia. Bone marrow examination prior to admission revealed a hypercellular bone marrow with myeloid and megakaryocytic hyperplasia, and moderate increase in reticulin fibers. BCR/ABL translocation was negative by reverse transcriptase PCR.

Clinical examination revealed no spinal or paraspinal tenderness. Strength was intact except for mild decreased strength and sensation in the left lower extremity with absent deep tendon reflexes. Sphincter tone was preserved.

An MRI revealed an extensive epidural mass spanning the length of the thoracic epidural space and the paraspinal areas with spinal cord compression from T6-T8 (Fig. 1A). A biopsy of this mass revealed megakaryocytes and maturing myeloid and erythroid precursors compatible with extramedullary hematopoiesis (Fig. 2). The patient underwent radiation therapy with a total dose of 1500 cGy. His symptoms rapidly improved, with complete resolution of his symptoms by the end of his treatment. A repeat MRI two months later showed marked improvement in the epidural mass (Fig. 1B).
Discussion
Extramedullary hematopoiesis (EMH) is a common finding in many chronic hematologic disorders, such as in hemoglobinopathies, lymphoma, leukemia and myeloproliferative disorders. The most common sites are the spleen and liver. The adrenal glands, kidneys, pericardium and epidural space are more unusual sites. The following table is a list of documented sites of extramedullary hematopoiesis in order of frequency.

Table 1. Sites of Documented Extramedullary Hematopoiesis

<table>
<thead>
<tr>
<th>Spleen</th>
<th>Liver</th>
<th>Kidney</th>
<th>Adrenal glands</th>
<th>Heart</th>
<th>Lymph node</th>
<th>Thymus</th>
<th>Lung and pleura</th>
<th>Retroperitoneal adipose tissue</th>
<th>Gastrointestinal lymphatics</th>
<th>Dura mater</th>
<th>Broad ligament</th>
<th>Breast</th>
<th>Sweat glands of hands and feet</th>
<th>Prostate and epididymis</th>
<th>Dura mater (spinal)</th>
<th>Thoracic duct</th>
</tr>
</thead>
</table>

The location of the spinal cord compression in all except one case was in the mid-lower thoracic region. The lesions in the epidural space causing cord compression are most common in the mid-lower thoracic region. It is thought that this is because the spinal canal is narrower in this area.

The pathophysiology of extramedullary hematopoiesis in the epidural space has not been fully elucidated; however, there are several theories. One suggests direct extension of bone marrow into the epidural space from the vertebral column or ribs through bone erosion or fracture. Alternatively, bone marrow elements may develop from primitive tissues resting along the spinal axis. Other theories include the escape of progenitor cells from the marrow with emboli to other organs, and new colony development from multipotent cells in the epidural space.

Diagnosis of spinal cord compression due to EMH has been reported using conventional and CT myelography, CT and MRI. Because many of the cases in the literature were reported in the 1970s, eight of the seventeen cases were diagnosed by myelogram, three by CT and five by MRI. On CT, EMH appears as a homogenous, well-circumscribed soft-tissue mass in the epidural area. CT is able to accurately show the location and size of the mass as well as its relationship to other neighboring structures such as the spinal cord and vertebrae. Myelography can demonstrate constriction of the subarachnoid space and compression of the spinal cord. However, it is invasive and requires contrast administration. MRI, now the recommended test of choice, is able to visualize cord compression and paraspinal masses without contrast administration. On T1 or T2 weighted spin echo, extramedullary hematopoiesis appears as a higher signal intensity compared to adjacent marrow of the vertebral bodies. MRI is also useful in differentiating EMH from other diagnoses, such as epidural abscess, neoplastic invasion and vertebral fracture from trauma.

EMH is highly sensitive to ionizing radiation, requiring a dose of only 10-30 Gy. Radiation therapy is now the current recommended treatment. In the past, surgical excision followed by radiation had been recommended. Surgery has the advantage of a definitive histologic diagnosis as well as immediate decompression. However, an invasive approach may be an unacceptable risk for the patient. Two of the published cases were treated with surgical excision and...
laminectomy without radiation. Neither patient improved with this modality. Seven patients were treated with combination surgery and XRT. Five of the seven having steady improvement. One of the two patients who did not respond, was pancytopenic at the time of diagnosis and the other had markedly elevated counts in all three cell lines compared to those who did respond. Eight patients were treated with radiation alone, with six having rapid clinical improvement. One of the two patients who did not respond was only given one dose of 1500 Gy and the other had a markedly elevated platelet count compared to those who did respond. The dosage of radiation ranged from 10 to 300 Gy with no difference in improvement with higher dosages. Blood transfusions have also been used in the treatment of EMH, primarily with the hemoglobinopathies. The goal is to keep the hemoglobin level greater than 10 g/dL to decrease the stimulus for further EMH.19,20

### Case Presentations

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Symptom Duration</th>
<th>Lab Values</th>
<th>Radiologic Findings</th>
<th>Treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 yo male</td>
<td>Myelofibrosis (7 yrs)</td>
<td>Back pain, B/L leg weakness and Numbness</td>
<td>2 weeks</td>
<td>WBC normal</td>
<td>Paravertebral mass @ T2-11, comp @ T5-8 (CT)</td>
<td>1600 cGy over 14 days with IV dexamethasone</td>
<td>Complete clinical recovery</td>
</tr>
<tr>
<td>61 yo male</td>
<td>Myelofibrosis (10 yrs)</td>
<td>Progressive paraparesis</td>
<td>2 months</td>
<td>WBC 5.6</td>
<td>Paravertebral mass @ T8, comp @ mid-thoracic level (MRI)</td>
<td>500 Gy over 10 fractions with IV dexamethasone</td>
<td>Complete recovery over 2 wks</td>
</tr>
<tr>
<td>67 yo male</td>
<td>Myelofibrosis (1.5 yrs)</td>
<td>Progressive B/L lower limb heaviness</td>
<td>9 months</td>
<td>Plt 20,000</td>
<td>Extramedullary mass, comp @ T6-7 (MRI)</td>
<td>Partial laminectomy, phlebotomy 3x/week</td>
<td>Died 5 month later</td>
</tr>
<tr>
<td>46 yo male</td>
<td>Proliferative phase of PV (newly dx)</td>
<td>Paraplegia</td>
<td>6 months</td>
<td>WBC 9.3, Hgb 20, Plt 240,000</td>
<td>Extramedullary mass from T4-6 (CT)</td>
<td>Laminectomy/ phlebotomy 5x/week</td>
<td>Died of respiratory failure</td>
</tr>
<tr>
<td>70 yo male</td>
<td>PV (15 yrs) Myelofibrosis (2 yrs)</td>
<td>Paraplegia</td>
<td>4 months</td>
<td>WBC 6.4, Hgb 12, Plt 150,000</td>
<td>Complete block @ T3-4 (myelogram)</td>
<td>Surgical excision/ Laminectomy</td>
<td>Progressed to AML, died</td>
</tr>
<tr>
<td>37 yo male</td>
<td>Myelofibrosis</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2000 rads</td>
</tr>
<tr>
<td>36 yo male</td>
<td>Myelofibrosis (6 yrs)</td>
<td>Lower extremity weakness</td>
<td>—</td>
<td>—</td>
<td>Comp in upper thorac/lumbar (myelogram)</td>
<td>Radiation with IV dexamethasone</td>
<td>Rapid clinical improvement</td>
</tr>
<tr>
<td>52 yo male</td>
<td>Proliferative phase of PV (newly dx)</td>
<td>Quadriplegia</td>
<td>5 months</td>
<td>WBC 17.5, Hgb 20.1, Plt 185,000</td>
<td>Extramedullary mass with complete block@CS (CT)</td>
<td>Single fraction of 1500 Gy</td>
<td>Died of respiratory failure</td>
</tr>
<tr>
<td>74 yo female</td>
<td>Myelofibrosis (3 yrs)</td>
<td>Low back pain, leg numbness, weakness</td>
<td>6 months</td>
<td>WBC 4, Hgb 9.1, Plt 106,000</td>
<td>Paravertebral mass, complete block @ T4 (myelogram)</td>
<td>Laminectomy/9000 rads in 200 rad fractions over 3 week</td>
<td>Complete relief of back pain</td>
</tr>
<tr>
<td>68 yo female</td>
<td>Myelofibrosis (20 yrs)</td>
<td>Leg stiffness, weakness</td>
<td>6 months</td>
<td>WBC 21.3, Hgb 19.5, Plt 450,000</td>
<td>Extramedullary mass from T4-8 (myelogram)</td>
<td>Laminectomy/9000 rads for 5 days/steroids</td>
<td>No change @ 6 months</td>
</tr>
<tr>
<td>50 yo male</td>
<td>Myelofibrosis (20 yrs)</td>
<td>Decreased sensation in feet b/l</td>
<td>1 year</td>
<td>Hgb 16.4</td>
<td>Extramedullary mass from T3-12, block @ T3 (myelogram)</td>
<td>Laminectomy/1000 rads in 5 doses over seven days</td>
<td>Symptoms free @ 6 months</td>
</tr>
<tr>
<td>31 yo male</td>
<td>Myelofibrosis (6 yrs)</td>
<td>Back pain, B/L leg weakness</td>
<td>1 year</td>
<td>—</td>
<td>T6 comp</td>
<td>Laminectomy/XRT</td>
<td>Clinical improvement</td>
</tr>
<tr>
<td>58 yo female</td>
<td>Myelofibrosis (newly dx)</td>
<td>B/L leg stiffness, numbness</td>
<td>3 months</td>
<td>WBC 15.3, Hgb 17.2, Plt 221,000</td>
<td>Compression@ T12 (myelogram)</td>
<td>Laminectomy/1000 rads</td>
<td>Clinical Improvement</td>
</tr>
<tr>
<td>43 yo female</td>
<td>PV (15 yrs) Myelofibrosis (newly dx)</td>
<td>B/L lower ext numbness, weakness</td>
<td>—</td>
<td>WBC 52, Hgb 39, Plt 995,000</td>
<td>Epidural mass comp @ T2-L3 (MRI)</td>
<td>XRT/steroids</td>
<td>Died</td>
</tr>
<tr>
<td>75 yo male</td>
<td>Myelofibrosis (newly dx)</td>
<td>Difficulty walking</td>
<td>2 months</td>
<td>WBC 8.1, Hgb 10.9, Plt 450,000</td>
<td>Not done</td>
<td>No treatment</td>
<td>Died</td>
</tr>
<tr>
<td>60 yo male</td>
<td>Myelofibrosis (8 months)</td>
<td>Sudden onset of weakness/sphincter dysfunction</td>
<td>—</td>
<td>WBC 9.8, Hgb 4.5, Plt 11</td>
<td>Extramedullary mass block @ T8 (myelogram)</td>
<td>Laminectomy/XRT</td>
<td>Died soon after</td>
</tr>
<tr>
<td>68 yo male</td>
<td>PV (40 yrs) Myelofibrosis (2 yrs)</td>
<td>B/L leg weakness</td>
<td>4 weeks</td>
<td>Plt 9,000</td>
<td>Epidural mass, comp @ T8 (MRI)</td>
<td>22 Gy in 4 fractions, Dexamethasone 4 mg QID</td>
<td>Rapid Improvement</td>
</tr>
<tr>
<td>56 yo male</td>
<td>Myelofibrosis (8 months)</td>
<td>Back pain, weakness</td>
<td>8 months</td>
<td>—</td>
<td>Block from T4-11 (myelogram)</td>
<td>Laminectomy/2000 rads</td>
<td>Unchanged</td>
</tr>
<tr>
<td>54 yo male</td>
<td>Myelofibrosis (3 yrs)</td>
<td>LE weakness</td>
<td>3 years</td>
<td>—</td>
<td>Block @ L3 (myelogram)</td>
<td>No treatment</td>
<td>Died 6 months later</td>
</tr>
<tr>
<td>73 yo male</td>
<td>PV</td>
<td>Back pain</td>
<td>2 months</td>
<td>WBC 100.2, Hgb 11.6, Plt 68,000</td>
<td>Epidural mass, compression @ T6-8 (MRI)</td>
<td>XRT</td>
<td>Rapid clinical improvement</td>
</tr>
</tbody>
</table>
References


