The Medicine Forum

Volume 4 *Winter 2003* Article 9

2003

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Recommended Citation

Reale, Lisa; Zrada, Steve; and Martinez, Jose (2003) "Cord Compression by Extramedullary Hematopoiesis in Polycythemia Vera," *The Medicine Forum*: Vol. 4, Article 9.
DOI: https://doi.org/10.29046/TMF.004.1.010
Available at: https://jdc.jefferson.edu/tmf/vol4/iss1/9

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).

Figure 1. (A) Extensive tissue abnormality seen throughout the thoracic spine, involving the spinal canal, with mixed signal characteristics on this T2-weighted image. (B) Marked improvement of epidural mass two months later.

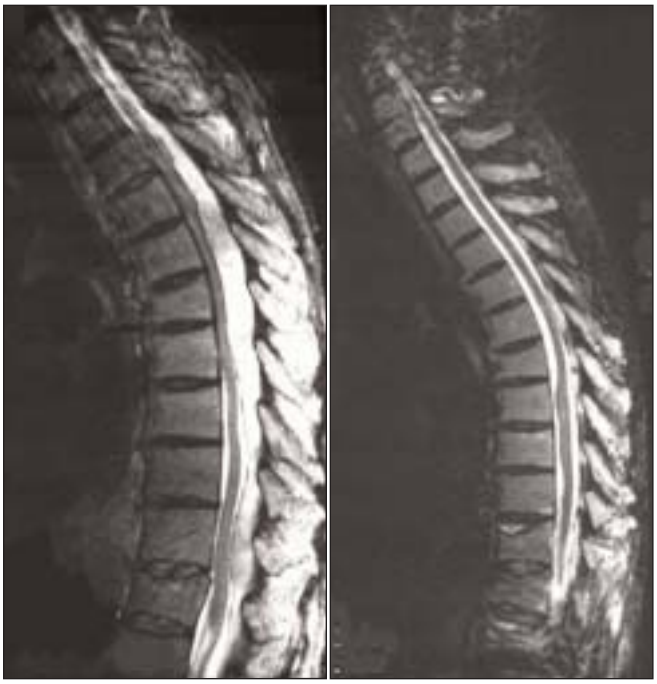

Figure 2. High power view of epidural mass biopsy, revealing megakaryocytes and maturing myeloid and erythroid precursors.

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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[1]. The adrenal glands, kidneys, pericardium[2] and epidural space1 are more unusual sites. The following table is a list of documented sites of extramedullary hematopoiesis in order of frequency[1,3]. Table 2 is a compilation of case reports of extramedullary hematopoiesis causing cord compression in myeloproliferative disorders, in particular myelofibrosis and polycythemia vera. The time from diagnosis of a myeloproliferative disorder ranged from newly diagnosed to twenty years. Of the seventeen cases found in the literature including this case report, only four of the eighteen cases presented with back pain[4,5,6]. In all of the cases that reported symptoms, the patients complained of neurologic deficits. The duration of symptoms ranged from two weeks to 1 year. The white count ranged from 1,600 – 100,200/mL, hemoglobin ranged from 5.6 – 20.1 g/dL and platelets ranged from 8,000 – 935,000/mL. There was no correlation between blood counts and the severity of their symptoms nor the number of years from the diagnosis. The proliferative phase of polycythemia vera may portend a poorer prognosis[8,9], however, there was no correlation between blood counts and severity of symptoms nor the number of years from diagnosis.

Table 1. Sites of Documented Extramedullary Hematopoiesis

Spleen
Liver
Kidney
Adrenal glands
Heart
Lymph node
Thymus
Lungs and pleura
Retroperitoneal adipose tissue
Gastrointestinal lymphatics
Dura mater
Broad ligament
Breast
Sweat glands of hands and feet
Prostate and epididymis
Dura mater (spinal)
Thoracic duct

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[10].

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[10].

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[8,9]. 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[11]. Myelography can demonstrate constriction of the subarachnoid space and compression of the spinal cord[9]. However, it is invasive and requires contrast administration. MRI, now the recommended test of choice[12], 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[13]. MRI is also useful in differentiating EMH from other diagnoses, such as epidural abscess, neoplastic invasion and vertebral fracture from trauma[14].

EMH is highly sensitive to ionizing radiation, requiring a dose of only 10-30 Gy[15,16]. Radiation therapy is now the current recommended treatment[5]. In the past, surgical excision followed by radiation had been recommended[8,17,18]. 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

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https://jdc.jefferson.edu/tmf/vol4/iss1/9
DOI: https://doi.org/10.29046/TMF.004.1.010

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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].

Age/Sex	Diagnosis	Symptoms	Symptom Duration	Lab Values	Radiologic Findings	Treatment	Response
36 yo male[4]	Myelofibrosis (7 yrs)	Back pain, B/L leg weakness and Numbness	2 weeks	WBC normal Hgb 5.6 Plt 8,000	Paravertebral mass @ T2-11, comp @ T5-8 (CT)	1600cGy over 14 days with IV dexamethasone	Complete clinical recovery
61 yo male[11]	Myelofibrosis (10 yrs)	Progressive parapesis	2 months	WBC 5.6 Hgb 5.9	Paravertebral mass @T8, comp @mid-thoracic level (MRI)	300 Gy over 10 fractions with IV dexamethasone	Complete recovery over 2 wks
67 yo male[9]	Myelofibrosis (1.5 yrs)	Progressive B/L lower limb heaviness	9 months	Plt 20,000	Extradural mass, comp @ T6-7 (MRI)	Partial laminectomy /2500 cGY in 5 daily doses over 1 week	Steady improvement
46 yo male[8]	Proliferative phase of PV (newly dx)	Paraplegia	6 months	WBC 9.3 Hgb 20 Plt 240,000	Extradural mass from T4-6 (CT)	Laminectomy/ phlebotomy 3x/week	Died 5 month later
70 yo male[17]	PV (15 yrs) Myelofibrosis (2 yrs)	Paraplegia	4 months	WBC 64 Hgb 12 Plt 150,000	Complete block @ T3-4 (myelogram)	Surgical excision/ Laminectomy	Progressed to AML, died
37 yo male[21]	Myelofibrosis	—	—	—	Paravertebral mass in thoracic region, comp from T3-5, L1-2 (myelogram)	2000 rads	Complete recovery
36 yo male[22]	Myelofibrosis (6 yrs)	Lower extremity weakness	—	—	Comp in upper thorac /lumbar (myelogram)	Radiation with IV dexamethasone	Rapid clinical improvement
52 yo male[9]	Proliferative phase of PV (newly dx)	Quadriplegia	5 months	WBC 17.5 Hgb 20.1 Plt 185,000	Extradural mass with complete block@C5 (CT)	Single fraction of 1500 Gy	Died of respiratory failure
74 yo female[5]	Myelofibrosis (3 yrs)	Low back pain, leg numbness, weakness	6 months	WBC 4 Hgb 9.1 Plt 106,000	Paravertebral mass, complete block @T4 (myelogram)	Laminectomy/3000 rads in 200 rad fractions over 3 week	Complete relief of back pain
68 yo male[23]	Myelofibrosis (20 yrs)	Leg stiffness, weakness	6 months	WBC 21.3 Hgb 19.5 Plt 450,000	Extradural mass from T4-8 (myelogram)	Laminectomy/900 rads for 3 days/steroids	No change @ 6 months
50 yo male[24]	Myelofibrosis (20 yrs)	Decreased sensation in feet b/l	1 year	Hgb 16.4	Extradural mass from T3-12, block @T3 (myelogram)	Laminectomy/1000 rads in 5 doses over seven days	Symptoms free @ 6 weeks
31 yo male[6]	Myelofibrosis (6 yrs)	Back pain, B/L leg weakness	1 year	—	T6 comp	Laminectomy/XRT	Clinical improvement
58 yo female[25]	Myelofibrosis (newly dx)	B/L leg stiffness, numbness	3 months	WBC 15.3 Hgb 17.2 Plt 221,000	Compression@ T12 (myelogram)	Laminectomy/1000 rads	Clinical Improvement
43 yo female[26]	PV (15 yrs)	B/L lower ext numbness, weakness	—	WBC 52 Hgb 39 Plt 935,000	Epidural mass comp @ T2-L3 (MRI)	XRT/steroids	Died
75 yo male[3]	Myelofibrosis (newly dx)	Difficulty walking	2 months	WBC 8.1 Hgb 10.9 Plt 458,000	Not done	No treatment	Died
60 yo male[1]	Myelofibrosis (8 months)	Sudden onset of weakness/sphincter dysfunction	—	WBC 9.8 Hgb 4.5 Plt fl	Extradural mass block @ T8 (myelogram)	Laminectomy/XRT	Died soon after
68 yo male[27]	PV (40 yrs) Myelofibrosis (2 yrs)	B/L leg weakness	4 weeks	Plt 9,000	Epidural mass, comp @ T8-9 (MRI)	22 Gy in 4 fractions, Dexamethasone 4 mg QID	Rapid Improvement
56 yo male[28]	Myelofibrosis (8 months)	Back pain, weakness	8 months	—	Block from T4-11 (myelogram)	Laminectomy/2000 rads	Unchanged
54 yo male[29]	Myelofibrosis (3 yrs)	LE weakness	3 years	—	Block @L3 (myelogram)	No treatment	Died 6 months later
73 yo male	PV	Back pain	2 months	WBC 100.2 Hgb 11.6 Plt 68,000	Epidural mass, compression @T6-8 (MRI)	XRT	Rapid clinical improvement

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DOI: https://doi.org/10.29046/TMF.004.1.010