

Spinal epidural extramedullary hematopoiesis during the complicated course of polycythemia vera

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ABSTRACT

Extramedullary hematopoiesis (EMH) may uncommonly develop during the course of polycythemia vera (PV). We herein present a 57-year-old patient with spinal epidural EMH that developed during the complicated course of PV and his outcome under different treatment modalities including hydroxyurea, ³²P, radiotherapy and surgery.

Key Words: Epidural space, hematopoiesis, extramedullary, myeloid metaplasia, polycythemia vera, spinal cord

ÖZET

Polisitemi veranın karmaşık seyri sırasında spinal epidural ekstrapedüller hematopoiez

Ekstrapedüller hematopoiez (EMH), polisitemi vera (PV)'nin seyrinde nadir olarak gelişebilir. Bu vaka raporu PV'nin karmaşık seyri sırasında spinal epidural EMH gelişen 57 yaşında bir hastanın hidroksiüre, ³²P, radyoterapi ve cerrahi dahil değişik tedaviler sonunda durumu tartışıldı.

Anahtar Sözcükler: Epidural mesafe, ekstrapedüller hematopoiez, miyeloid metaplazi, polisitemi vera, spinal kanal

INTRODUCTION

Extramedullary hematopoiesis (EMH), developing as a response to deficiency in bone marrow production, might rarely complicate the enigmatic course of polycythemia vera (PV)^[1-10]. EMH can more commonly invade the spleen and liver^[1-4]. EMH in the spinal epidural space, leading to severe neurological disability, seldom takes place^[1-8].

CASE REPORT

A 57-year-old male with a history of PV referred to our hospital for renal failure in November 2004. On the admission, he had paraplegia with strength of 1/5 and reduced sensibility, loss of proprioception bilaterally. Hydroxyurea and phlebotomies were discontinued about 10 months before the admission due to development of bicytopenia. Massive hepatosplenomegaly was present on physical examination. Bicytopenia was detected with a hemoglobin level of 10 g/dL and platelets of 90000/mm³. His leukocyte count was 14000/mm³. His creatinine and blood urea nitrogen (BUN) levels were 2.5 mg/dL and 58 mg/dL, respectively. Bone marrow examination yielded extensive fibrosis. All of these clinicopathologic data suggested that postpolycythemic myeloid metaplasia developed in the patient.

He had been diagnosed as PV after a gastric bleeding in 1981. Five mCi of ³²P were given initially. Thereafter, intermittent phlebotomies had been performed with an average of three times per month and allopurinol to control hyperuricemia additionally. He was feeling well for seven years until back pain complaints began. He experienced anemia occasionally as a consequence of extensive phlebotomies during that seven-years period. Radiological examination was performed for his complaints and a spinal mass lesion which was consistent with EMH between T3-L1 vertebrae was detected. Hydroxyurea 1000 mg/day was added to phlebotomies to slow the progression of EMH.

In August 1998, he suffered from progressive gait instability, urinary retention and back pain. Cranial and spinal magnetic reso-

nance imaging (MRI) showed a lobulated posterior epidural nodular mass lesion with paravertebral expansion, which was considered as EMH before. The mass lesion was fusiform in shape and spinal cord compression was most evident between T4 and T9 levels (Figure 1). A total of 175 Gy external radiotherapy was given fractionally in seven days. Complete neurological recovery was achieved after radiotherapy.



Figure 1. Sagittal MRI images of epidural mass extending between T3 to L1 (T1-weighted image).

In April 2003, back pain and walking difficulty had started again. Mass lesion detected by MRI had been progressed. Same dose and fashion of external radiotherapy was instituted once more, additionally 5mCi of ^{32}P , but no neurological improvement had been noted and he underwent surgery. The mass lesion between T2 and T10 vertebrae was extirpated. Pathological examination yielded EMH. His neurological deficit persisted after the surgery. Control MRI showed no bleeding or residual mass. The patient developed complete paraplegia and urinary retention during his follow-up.

DISCUSSION

Although most often develops in thalassemias, EMH had also been described in other hematologic disorders like PV, myelofibrosis, myelodysplastic syndromes, and sickle cell anemia^[1-8]. Most frequent sites of EMH are the spleen, liver and lymph nodes, which are involved in fetal hematopoiesis. However, EMH can involve any other organ, such as kidney, pericardium, lungs, thoracic cavity, adrenals, thyroid, thymus, prostate gland and breast^[1-4]. Formation mechanism of EMH still remains mystery in such tissues. Current hypotheses are immigration of pluripotent stem cells from bone marrow by undetermined stimuli, extrusion through thinned out expanded bones, arising from primitive blood-forming precursor cells^[1,2]. Cranium and spinal epidural spaces are very rare sites of EMH^[1-4]. When spinal epidural space is involved, EMH arises from mid-lower thoracic region^[1,2,6-8]. MRI is a useful imaging tool not only for diagnosis of EMH but also for guidance of therapy and follow-up. Characteristic MRI features of EMH were defined before^[1-3,6,7].

EMH is believed to develop as a compensatory mechanism to anemia in patients with some hematological disorders characterized by chronic overproduction of red blood cells^[1-7]. The mechanisms for the formation of EMH during the course of PV are not exactly known. EMH occurs mostly during the spent phase of PV, which may be attributed to development of anemia. Reports on the regression of extrame-

dullary hematopoietic tissue in thalassemias by transfusion of red blood cells support the theory of "anemia is a stimulus for formation of EMH"^[1,2,6]. Based on this theory of PV, EMH might be considered as a complication of anemia associated with the disease course. Phlebotomy-based treatment approach may result in the increased incidence of myelofibrosis with myeloid metaplasia^[9,10]; however, there is no correlation between the extent of EMH and bone marrow hematopoietic activity in PV in the absence of chemotherapy or radiotherapy^[9]. Moreover, extramedullary tissue regression by red blood cell (RBC) transfusions has never been reported in anemic PV patients. Due to the autonomous nature of PV, it seems impossible to improve EMH by RBC transfusions.

Treatment options for EMH in general, are radiotherapy, surgery or combinations of these modalities^[1-4]. Hydroxyurea and blood transfusions are suggested to slow progression of EMH in thalassemia patients. Radiation is recommended as an initial therapy since hematopoietic tissues are extremely radiosensitive^[1-6]. It can be used as adjunctive therapy to surgery as well. Ideal radiation dose for controlling EMH is not been established definitively, but reported dosages in literature are between 600 and 3500 rads^[1-6]. In our patient, a total dose of 175 rads was sufficient to control EMH initially. Radiotherapy has recurrence rates as high as 19%; however, can be used repeatedly. Pancytopenia is another pitfall of radiation^[1]. Surgery is recommended for patients refractory to radiotherapy because diffuse nature of disease makes it not feasible to total excision and there is high recurrence rate after surgery^[1,4,6]. EMH tissue is extremely vascular and serious bleeding may complicate surgery^[2]. In our case, radiotherapy was successful initially but failed as well as surgery. Hydroxyurea might have slowed progression of EMH in our patient. However, in such cases, early radiotherapy should be considered for controlling EMH to save neurological functions.

Anemia may be a causative or at least a facilitating factor for development of EMH in PV as in thalassemias. Radiotherapy is probably the best treatment choice comparing with the other modalities for management of paraspinal EMH, and it should be used earlier especially for those patients whose lesions have potential of severe disability.

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