

CASE REPORT

MANAGEMENT OF EXTRAMEDULLARY HAEMATOPOISES IN THALASSAEMIA WITH RADIOTHERAPY: A CASE REPORT AND REVIEW OF LITERATURE

B Thejaswini¹, J Bindhu¹, R Nanda¹, K Aradhana¹

Author's Affiliations: ¹Associate prof, Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore.

Correspondence: Dr. Thejaswini.B, Email: thejaswini.mesh@gmail.com

ABSTRACT

Extramedullary haematopoiesis (EMH) is a very rare cause for spinal cord compression but is a well described entity with relation to chronic haemolytic anemias like thalassemia. Radiation therapy has a documented role in the management of this condition. We would like to report a case of a 28 year old man with underlying thalassemia major presenting with paraparesis and sensory loss, successfully treated with radiotherapy.

Key words: Thalassemia, Extramedullary haematopoiesis, Spinal cord compression, , Radiotherapy

INTRODUCTION

Extramedullary haematopoiesis (EMH) is an uncommon manifestation in severe thalassemia. Spinal cord compression is a consequence of EMH in the intraspinal epidural space. Intrathoracic EMH tissue most commonly occurs in the posterior mediastinum and in the lower thoracic paraspinal area. There is also a postulate that EMH is due to direct extension from bone marrow by the development of extramedullary haematopoietic tissue from branches of the intercostal veins⁽³⁾. The cases most commonly present with paraparesis and sensory deficit rather than paraplegia. We present one such patient coming with the same pattern successfully managed with radiotherapy.

CASE REPORT

This was a 28 year old teacher referred to us for consideration of radiotherapy in February 2009. He had initially presented with progressive weakness, stiffness and parasthesia of both lower limbs of 3 months duration. During the last 2 weeks he had developed low back pain and ataxia. There were no bladder and bowel dysfunction. There was no history of fever or previous injury to the back. He was a known case of thalassemia major, diagnosed in 1996 but on irregular treatment. On examination the patient was of average built with severe pallor and jaundice. Neurological examination revealed spastic paraparesis (Nurick's grade 3) of grade 4- to 4+ /5 power and graded sensory loss below the level of T-3. The bilateral plantar

were extensor and deep tendon reflexes were exaggerated in both lower limbs.

The MRI of the spine showed a soft tissue mass lesion in the epidural space from D3 to D9. Evidence of Expansile costovertebral junctions with perifocal thickened soft tissue were seen involving D3-D10 (Figure 1 & 2)

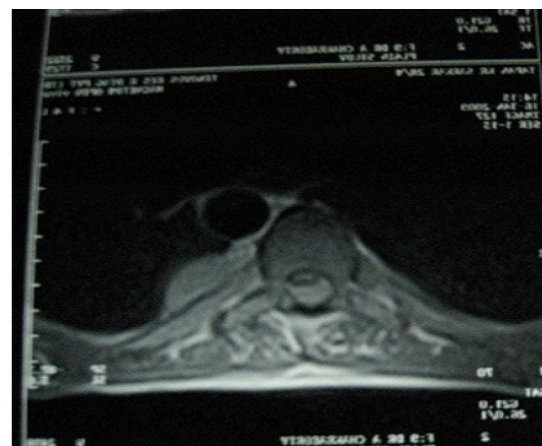


Figure 1: Axial T2W image showing soft tissue intensity in the epidural and paravertebral space

Spinal cord edema was present from D2-D10. The visualized sternum showed medullary expansion in the manubrium and body of sternum. The CSF examination was non contributory.

His haemoglobin was 8 g/dl, haematocrit 26.6% and white blood cell count $3.4 \times 10^9/L$. The differential count was in normal range. Platelets were

adequate. Peripheral smear showed anisopoikilocytosis with microcytosis and hypochromia (Fig 3).



Figure 2: Paramedian T1W Post contrast image showing soft tissue intensity in the paravertebral space

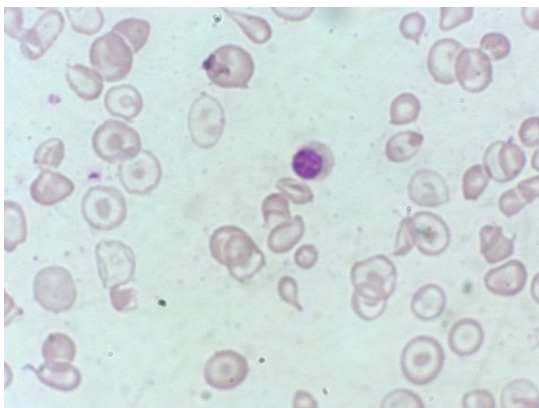


Figure 3: Microscopic Pictograph showing severe anisopoikilocytosis with microcytic hypochromic erythrocytes. Many target cells, dacryocytes and a nucleated erythrocyte seen

A haemoglobin electrophoresis showed an HbF of 43.15g/dl and an A band was seen in the E/C region (56.86%) suggestive of Hb E β Thalassaemia major. Chest radiography showed reticular pattern of bones; feature of haemopoetic disorder. Ultrasonography showed gross splenomegaly, the spleen measuring 20 cm and mild hepatomegaly. In view of the above investigational findings suggesting of a severe haemolytic disorder and the typical MRI findings, a diagnosis of extramedullary haematopoiesis with cord compression (D3- D9) secondary to Thalassaemia major was made.

Radiotherapy: He received an equivalent dose of 20 Gy over a period of two weeks on telecobalt machine with conventional fractionation. He tolerated treatment well and had a remarkable response within 1 week of treatment.

After 14 Gy of treatment he had subjective improvement of around 50% in motor weakness, around 80% reduction in pain and sensory deficit. At the time of discharge, he had complete relief from pain. He had normal power in lower limbs with residual spasticity and parasthesia. He was independent and ambulatory without support. For management of his haemolytic anemia patient had been advised conservative management with blood transfusion and hydroxyurea. During the course of his treatment there was reduction of Jaundice, total bilirubin level reduced from 10.8mg/ dL to 1.5 mg/ dL at the time of discharge and haemoglobin levels improved to 8.5 mg/ dL.

At 9 months follow up, he was doing well and resumed his work. He had mild residual hypertonia of both lower limbs and had completely recovered in terms of neurological deficits (Nurick's grade 1). After 5 years of treatment with radiotherapy patient reported to us performing his normal routine and has no neurological deficits.

DISCUSSION

Paravertebral pseudotumors form a rare complication in a variety of haematological disorders. The disorders where extramedullary haematopoiesis are commonly seen are thalassaemia, polycythemia rubra vera, myelofibrosis and other hemoglobinopathies.^{1,2} The common sites of EMH are the liver, spleen and lymphnodes. It is more rarely seen in kidneys, breast, adrenal gland, dura matter, pleura, retroperitoneal fat, paravertebral gutters, ribs and skin.³⁻⁸

The source of masses formed by EMH is controversial. One hypothesis suggests that blood forming elements are extruded through weakened trabecular bone into the surrounding tissue where they proliferate, this is supported by the radiological continuity of the epidural mass and intramedullary marrow.⁹

The thoracic spine predisposes to spinal cord compression due to narrow central canal and limited mobility of the thoracic spine. Spinal cord compression due to epidural haematopoietic tissue has been documented in 75 cases in literature until 2005. EMH associated with thalassaemia was first described by Gatto et al.¹⁰

Table 1: Results of Radiation (single modality) in EMH management

Author	N	RT dose	Response	Recurrence rate
Papavassliov ¹³	5	8.5 to 24 Gy	CR (5)	(NA) less than 1 year follow up
Issaragrisil ¹⁴	9	15-35	CR (8)	(3/9) 33%

Key : CR – Complete clinical response, NA = No applicable, RR – Relapse rate

The optimal management of EMH with spinal cord compression remains controversial. The treatment modalities available ranges from transfusions to down regulate erythropoietin to medical management with hydroxyurea and to a more aggressive approach with local radiotherapy or surgery and/or a combination of these therapies.^{5,9} In this case, radiotherapy was considered the treatment of choice and surgical intervention was not favored in view of risk of severe haemorrhage, long segment of disease and possibility of incomplete resection.

Radiotherapy has been shown to be effective in the majority of patients with symptomatic EMH.^{11,12} The mass lesion consisting of haematopoietic tissue appears to be particularly sensitive to ionizing radiation and a radiation dose of 10-30 Gy seems adequate. Hydroxyurea (HU) is a well known chemotherapeutic agent acts by enhancing the HbF production and erythropoiesis. In doses of 10-20mg/Kg/ day in an intermittent on continuous schedule has been shown to have sustained haematological efficacy with minimal toxicity. However leucopenia and thrombocytopenia have been documented which is usually reversible after a few days of discontinuation.⁵

Surgical decompression provides immediate relief of the spinal cord compression and also allows a histological confirmation.⁸ However when the evidence of EMH is clinically confirmed, histological proof may not be mandatory.

So we conclude that radiotherapy is an effective safe and recommended modality of treatment for spinal cord compression due to EMH. Moderate dose radiotherapy of 20 to 30 Gy has minimal toxicity, negligible risks and provide rapid and long term neurological stability. Radiation should be considered as the preferred treatment modality with subsequent support by other treatments as intensive blood transfusion and hydroxyurea treatment as deemed necessary in EMH with spinal cord compression.

Acknowledgements: We thank Dr. Yeshwant Pawar, Dept of Radiotherapy and Dr. Manish, Neurosurgeon for their technical assistance and material support.

REFERENCE

1. Kaustav Talapatra, Bhushan Nemade, Manish Saiddha et al. Extramedullary Haematopoiesis causing spinal cord compression: A rare case presentation with excellent outcome. *Ann Indian Acad Neurol* 2207;10:115-117.
2. Munn RK, Kramer CA, Arnold SM. Spinal cord compression due to extramedullary haematopoiesis in beta thalassaemia intermedia. *Int J Radiat Oncol Biol Phys* 1998;42:607-9.
3. Tan TC, Tsao J, Cheong FC. Extramedullary Haematopoiesis in thalassaemia intermedia presenting as paraplegia. *J Clin Neurosci* 2002;9:721-5.
4. Ohta V, Schichmate H, Nagashimak. Spinal Cord compression due to extramedullary haematopoiesis associated with polycythemia Vera: Case report (*Neural Med chin* 2002;42:40-3.
5. Caric H, Wegener M, Debadin KM, Kokne E. Treatment with hydroxyurea in thalassaemia intermedia with paravertebral pseudotumors of extramedullary haematopoiesis. *Ann Hematol* 2002;81: 478-82.
6. Saghafi M, Shirdel A, Lori S M. Extramedullary haematopoiesis with spinal cord compression in thalassaemia intermedia. *Eur J Intern Med* 2005;6:596-7.
7. Sardanl OS, Tayler PE, Nuges WA. Extramedullary haematopoiesis, mediastinal masses and spinal cord compression. *JAMA* 1964;5:343-7.
8. Luijes WF, Brookman R, Abets J. Spinal cord compression in a new homozygous variant of Thalassaemia. Case report. *J Neurosurg* 1952;57: 846-8.
9. Rado G, Loona L, Laorentio B et al. Thoracic Spinal cord compression secondary to Extramedullary haematopoiesis in thalassaemia intermedia, successfully treated with local radiotherapy and hydroxyurea: A case report and review of literature. *Haema* 2005;8(4):661-664.
10. Gatto T, Terrana V, Biondi L. Compressions substeletto spinale da proliferazioni di middula osseonello spazio epidurale in sugetts affeto da malattia di, cofley splenectomizzato, *Haematologica* 1954;38:61-70.
11. Russo D, Pileri S, Barbieri et al. Spinal Cord compression by Extramedullary haematopoietic tissue in thalassaemic patient. Prompt effect of radiotherapy. *Haematologica* 1989;74:495-0498.
12. Singhal S, Sharma S, Dixit S et al. The role of radiation in the management of soinal cord compression due to Extramedullary haematopoiesis in thalassaemia. *J Neural Neurosurg Psychiatry* 1992;55:310-312.
13. P Parasilou C, Gouliamos A, Deligiorgi E et al. Masses of myeloidipose tissue radiological and clinical consideration. *Int J Radiat Oncol Biol Phys* 1990;19:985-993.
14. Issaragrisil S, Pian Kijagum, Wasi D. Spinal cord compression in thalassaemia. Report of 12 cases and recommendations for treatment. *Arch Intern Med* 1981;141: 1033-1036.