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TRANSFUSION THERAPY AS A SOLE TREATMENT OPTION IN A THALASSEMIA PATIENT WITH ACUTE PARAPLEGIA - A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Spinal haematopoiesis is an extremely rare phenomenon in patients with Thalassemia intermedia. Various modes of therapy are available. Our patient with Thalassemia intermedia who developed paraplegia due to spinal haematopoiesis was successfully treated with blood transfusion alone.

Key Words: Extra medullary haematopoiesis, Thalassemia intermedia, Paraplegia

INTRODUCTION

Thalassemia intermedia is so far recognized as a transfusion independent form of B Thalassemia¹. Paraplegia in these patients, a very rare phenomenon, is secondary to spinal haematopoiesis^{2, 3, 4} and its occurrence in females is even rarer⁵. Because of the paucity of such cases, no evidence-based guidelines are available. Treatment options include blood transfusion, surgical decompression, radiotherapy, hydroxyurea administration and steroid therapy, either alone or in combination. Choice of a therapeutic modality is based on patient's clinical condition and past treatment history.

We present the case of a young girl with thalassemia intermedia who developed paraplegia due to spinal haematopoiesis and was successfully treated with blood transfusion alone.

CASE REPORT

A 17 years old female, known to have thalassemia intermedia since the age of 7 years, also glucose 6-phosphate dehydrogenase (G6PD) deficient for last 3 years, functional class 1, presented in ER with 15 days history of diarrheal illness, followed by fever and difficulty in walking for one week and urinary retention for one day. She spiked fever to a maximum of 102 degree F without chills or rigors. Her gait difficulty had a very progressive course and she became bed bound within a week of onset. Weakness and numbness was present equally in both lower extremities. A day prior to presentation, she developed urinary retention. There was no history of trauma, backache, sore throat, rash,

blurring of vision, diplopia, facial weakness, shortness of breath, difficulty in swallowing, abdominal pain, nausea, vomiting, jaundice or seizures and. There was no history of recent administration of any vaccine.

On examination, she was alert and oriented. Higher mental function and speech were normal. Gait could not be assessed due to lower limb weakness. All cranial nerves were intact. She had decreased tone in both lower limbs with a power of 1/5 (MRC Scale) in both lower limbs. Deep tendon reflexes were brisk bilaterally and ankle clonus was present with plantars being bilaterally extensor. A sensory level was found to be at D7.

Her blood workup showed: haemoglobin of 7 gram/dL and the peripheral blood film was consistent with thalassemia intermedia. There was mild elevation in indirect bilirubin which was attributed to on-going intravascular haemolysis secondary to her blood disorder. Urine detailed report showed mild infection. Rest of the laboratory workup including electrolytes were normal.

MRI of her dorsal spine with contrast revealed intraspinal lobulated masses, compressing the spinal cord and exiting nerve roots.

Diffuse altered marrow signals from all the visualized bones which are hypointense on both T1 and T2 weighted images. In addition there are also expansion of the clivus, diploic spaces of skull, sternum and ribs. There are multiple paravertebral masses in the visualized dorsal spine at multiple levels from T3-T8. Multiple lobulated masses are seen in spinal canal at multiple

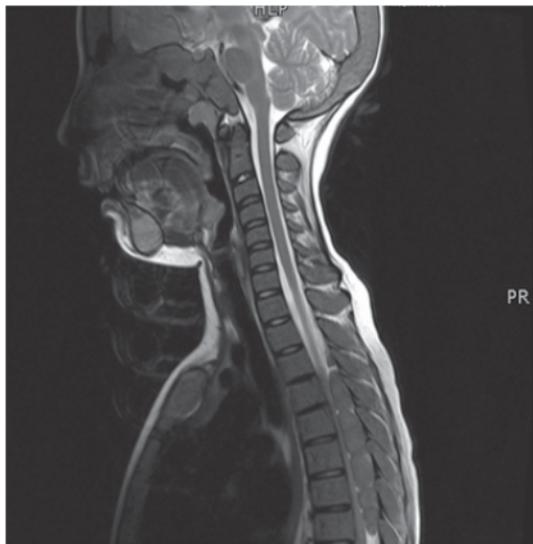


Fig 1.T2 weighted MRI Image of cervical and upper dorsal spine mid-sagittal slice

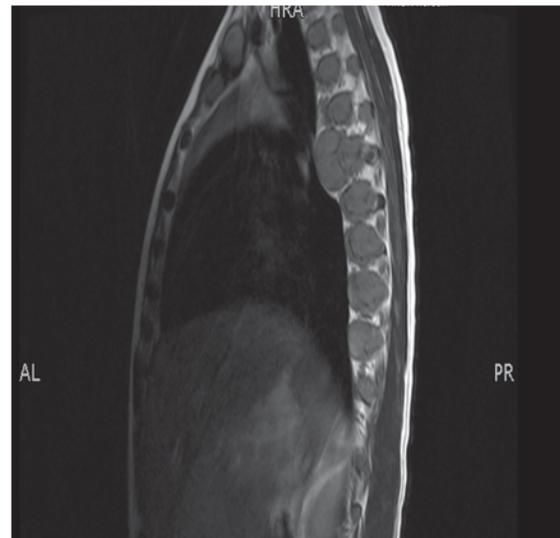


Fig 2.T2 weighted MRI Image of dorsal spine



Fig 3.T2 weighted MRI Image of dorsal spine

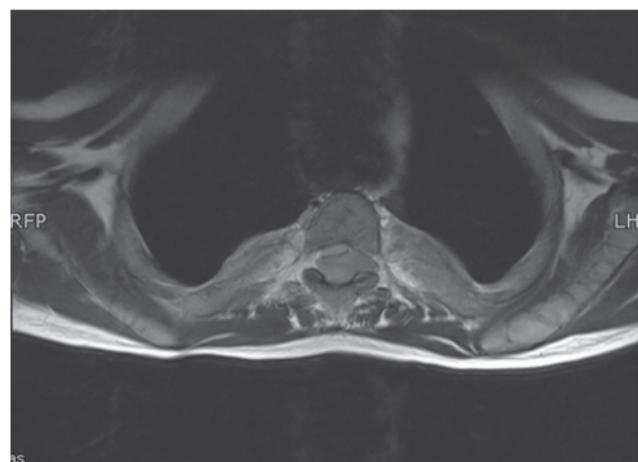


Fig 3.T1 weighted MRI Image

levels starting from T3-T8. These are iso- to hypointense on both T1 and T2 and show diffuse restriction. These masses are causing significant compression of the dorsal spinal cord and pushing it anteriorly and also extending to the neural foramina at all these levels causing significant compression of exiting nerve roots. All the above described findings are in keeping with thalassemia leading to extramedullary haematopoiesis with multiple paravertebral and intraspinal lobulated masses which are compressing the spinal cord and exiting nerve roots from T3 down to T8 level.

Discussion

Thalassemia, a hereditary haemoglobinopathy has many

subtypes. Patient under discussion was suffering from ? thalassemia intermedia .This form lies mid-way between ? thalassemia major and minor and is usually referred to as transfusion independent thalassemia¹. Autosomal recessive in inheritance, it is diagnosed on the basis of haemoglobin (Hb) electrophoresis that shows large amounts of Hb A? (????)and foetal Hb(??β?). There is scarcity of normal adult haemoglobin Hb A(??β?).

Inability to meet tissue demand, inadequacy of circulation and ineffective erythropoiesis form the basis of extramedullary haematopoiesis(EMH) in such patients⁶. Usual sites are liver, spleen and lymph nodes^{7,8}. However depending on the severity almost any tissue of the body

can be involved e.g., adrenal glands, thymus, hilum, prostate, kidneys, breasts, dura matter, adipose tissue, skin, broad ligaments, heart, pleura, retroperitoneal tissue, even cranial and peripheral nerves and spinal canal⁹⁻¹⁶. About 11-15% patients of Thalassemia intermedia develop Intrathoracic EMH^{2,3}. Neurological symptoms due to these intraspinal pseudotumours are even rarer¹⁷.

The first case of spinal cord compression secondary to EMH was reported by Gatto et al in 1954¹⁸. In spine, lower dorsal region is usually involved where restricted mobility and narrow spinal canal predisposes to cord compression^{19,20}, resulting in neurological symptoms, varying from mild back pain and paraesthesias to profound motor weakness and sphincter disturbance. Manifestations of neurological symptoms depend on the chronicity of the disease and are most commonly encountered in third and fourth decades⁵ but a few cases have also been seen in first ten years of age^{8,21}. More cases have been reported in males as compared to females reaching a ratio of 5:1⁵. Complete paraplegia has been reported very rarely in thalassemia and occurs more frequently with other blood disorders such as polycythaemia rubra vera and sickle cell anaemia⁵.

Diagnosis is based on neuroimaging. Magnetic resonance imaging (MRI) remains the gold standard which delineates spinal extramedullary haematopoiesis as iso-intense mass with a high spinal intensity rim on T₁-weighted images and a hyperintense mass on T₂-weighted images²². Gadolinium enhancement is minimal or absent differentiating it from other epidural lesions such as abscesses or metastases^{23,24}. Older inactive lesions show high signal intensity in both T₁ and T₂ weighted MR images due to fatty infiltration or low signal intensity in both T₁ and T₂ weighted MR images due to iron deposition²⁵⁻²⁸. Histopathological diagnosis by biopsy is not always recommended and usually reserved for either elderly patients or in whom diagnosis is doubtful⁸.

Treatment is usually governed by patient's clinical status i.e. mode of onset and severity of the symptoms, size of the masses and past treatment history. Because of the paucity of such cases no evidence-based guidelines are available to be followed. Therapeutic modalities include surgical decompression, radiotherapy, blood transfusion, steroid therapy, hydroxyurea administration. Usually a combination of aforementioned options has been reported to give relapse free results.

Transfusion therapy helps in alleviating the symptoms by correcting anaemia which in turn reduces the tissue demand, down-regulates erythropoietin and lessens the need for EMH. Use of blood transfusion as a sole treatment option is controversial. Some schools of thought believe that it gives partial recovery and temporary relief from the symptoms²⁴. Therefore, at present it is reserved for patient with minor neurological deficits^{8,29} or in special situations like pregnancy where surgery or radiotherapy may be harmful³⁰. However, cases have been reported where transfusion therapy was used exclusively as the first choice^{17,19,29,32,33}. Apart from being cost effective, an added advantage of transfusion therapy from the rest of treatment options is that it can be used as a non-invasive diagnostic tool where a prompt response to blood transfusion supports the notion that extramedullary haematopoiesis was the cause of symptoms³¹.

Surgery has usually been reserved for patients who present with acute paraplegia. Surgical decompression by far has been mostly used⁵ giving promising results in thalassemia major patients³⁴. Major threat in surgical decompression is increased chances of bleeding and predisposition to shock due to increased vascularity of the tissue³⁵.

Irradiation causes radiosensitive extramedullary hematopoietic tissue to shrink resulting in clinical improvement. Almost half of the patients start benefiting within a week^{36,41,42,43}. There are case reports where paraplegia has been successfully treated with radiotherapy^{43,44}. Radiation induces pancytopenia leading to immunosuppression, local side effects of radiotherapy and cumbersome calculation of irradiation dose makes it a less popular choice. It carries a high risk of recurrence up to^{19-37%3,36}.

Hydroxyurea stimulates synthesis of foetal haemoglobin and therefore decreases the need for EMH^{45,46}. Patients with spinal EMH have been successfully treated with hydroxyurea alone⁴⁶, especially those who due to alloimmunisation are unable to receive blood transfusion⁴⁷. It is also given in combination with transfusion^{45,48} and radiotherapy^{45,49}.

Steroids by their property of reducing inflammation and oedema have also been used as adjunct therapy either postoperatively or along with blood transfusion¹. A case report suggests that Dexamethasone in bolus dose of 10 mg followed by 4 mg every 6 hours for 3 days with transfusion gives promising response⁵⁰.

Conclusion

As paraplegia resulting from cord compression due to extramedullary haematopoiesis is extremely rare, it surfaces as both a diagnostic as well as a therapeutic challenge. Opting for single or a combination of therapies depends on patients past medical history and current severity of symptoms. Blood transfusion is a cost effective treatment of choice giving reasonable recovery once optimum levels of Hb have been achieved. Target Hb should be above 10 gm.%.⁵¹. It also serves as a non diagnostic invasive tool. Follow up MRI every 6 months for two years, followed by once in a year, helps in keeping a close surveillance of Thalassemia patients with spinal haematopoiesis³⁴.

Conflict of interest statement: The authors have no conflicts of interest to disclose. This study did not receive external funding.

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