

SHORT REPORT

The role of radiation therapy in the management of spinal cord compression due to extramedullary haematopoiesis in thalassaemia

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Abstract

Extramedullary haematopoiesis associated with thalassaemia leading to spinal cord compression is an extremely rare event in the course of the disease. The efficacy of radiation therapy is advocated in the management of such a complication. Two patients with thalassaemia, who had presented with spinal cord compression, were successfully treated by a modest dose of local radiotherapy. In one of the patients, however, radiotherapy was resorted to after an initial decompressive laminectomy and partial removal of the intraspinal haematopoietic mass proved unsuccessful. The other patient was managed solely by radiation therapy.

Extramedullary haematopoiesis (EMH) is a common manifestation of severe thalassaemia and it may involve various organs of the body such as liver, spleen, and lymph nodes.¹⁻⁶ The clinical features secondary to EMH are variable and depend on the site of formation of the haematopoietic tissue. The onset of unexpected clinical signs may be the first indication that haematopoiesis is spreading to an atypical area. Spinal cord compression (SCC) as a consequence of EMH in the intraspinal epidural space is an extremely rare complication. We report two cases of thalassaemia that had presented with SCC. A review of the literature is discussed highlighting the role of radiation therapy in the management of such patients.

Case 1

This was a 21 year old male who presented to us in April 1985 complaining of a progressive weakness and paraesthesia of both legs during the previous three weeks. He also noticed an inability to walk without support and difficulty in passing urine for the previous two weeks. The patient was a known case of thalassaemia and splenectomy had been performed four years previously. On examination, the patient was of average build with a mild pallor. Neurological examination disclosed muscle weakness of both the lower limbs (Power-grade 3/5). The deep tendon reflexes at the knee and ankle were exaggerated and the bilateral plantar response was extensor. Vibratory and positional sensations were impaired

and there was a complete loss of touch and pinprick sensation below the level of T7.

The radiograph of the skull and spine demonstrated a diffuse osteoporosis but no well defined paravertebral mass was evident. Myelogram, however, revealed a complete extradural block at the level of T9. The CSF examination proved noncontributory. His haemoglobin (Hb) was 8.7 g/dl, haematocrit 28% and white blood cell count (WBC) $7.4 \times 10^9/L$. The differential count revealed a slight shift to the left (metamyelocyte 2%, myelocyte 2%). Platelets were adequate. The peripheral smear showed anisopoikilocytosis with microcytosis and hypochromia. A few target cells were also noticed. There were three normoblasts/100 WBC. The corrected reticulocyte count was 2%. A haemoglobin electrophoresis showed 21% Hb F and 2.6% Hb A₂.

At laminectomy a brownish, soft, vascular extradural mass was seen extending from T5-T9. Only a partial excision of the mass could be accomplished. The histopathological examination of the excised mass confirmed it to be haematopoietic tissue. The postoperative course was uneventful. However, in view of the incomplete excision of the mass and a negligible neurological recovery, radiotherapy was started two weeks after surgery. A total dose of 30 Gy was delivered by a telecobalt unit, over a period of three weeks in 15 sessions. There was a marked neurological improvement at the end of radiation treatment and the patient continued to improve. No complication was observed during or after radiotherapy. The patient has been doing well for a period of five years.

Case 2

A 33 year old male presented to us in August 1989 complaining of increased tiredness in both his legs on walking which he had experienced for six months. This was more prominent while climbing stairs and associated with altered tactile sensation. He also had hesitancy of micturition. The symptoms remained static during that period although there had been some progression over the previous two weeks. The patient had been diagnosed as suffering from thalassaemia major since the age of five years. Both his father and mother also had thalassaemia minor (HbF 13.7% and 1%, Hb A₂ 2.4% and 5.4% respectively) although none

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Received 8 April 1991.
Accepted 3 June 1991

of the siblings were affected. Neurological examination showed muscle wasting of both the lower extremities with reduced power (grade 4/5). The deep tendon reflexes were exaggerated and the plantar response was extensor. There was impairment of tactile sensation below the level T6.

A radiograph of the spine showed rarefaction of the vertebral bodies and revealed a paraspinal mass along the thoracic vertebrae. A CT scan of the spine confirmed the presence of a mass which was more prominent on the left and extending from T2–T8. It was found to be encroaching into the spinal canal through the intervertebral foramina. No myelography was carried out. His Hb was 8.7 g/dl, haematocrit 21% and MCV 64 fl. The total and differential leucocyte count was normal. Platelets were adequate. The peripheral smear showed a marked anisopoikilo-cytosis with microcytosis and hypochromia as well as the presence of few target cells. There were 6 normoblasts/100 WBC. A haemoglobin electrophoresis showed a considerably elevated concentration of Hb F (81%) and Hb A₂ (3.3%).

Following the diagnosis of spinal cord compression due to EMH in the paraspinal space associated with thalassaemia, local radiation therapy to the EMH mass was started. A dose of 30 Gy was delivered in 20 fractions over a period of four weeks on a telecobalt unit encompassing the apparent extension of the paraspinal haematopoietic mass. There was a significant neurological recovery at the end of treatment. The patient is still doing well.

Discussion

EMH generally occurs in a variety of haematological disorders where the normal functioning of the blood forming organs is disturbed. It is a common manifestation in thalassaemia where it occurs as a compensatory phenomenon in order to combat long standing anaemia. Any of the fetal blood forming centres may thus be activated but the organs most commonly involved are liver, spleen and the lymph nodes.^{1–6}

It occurs rarely in the kidney, breast, heart, adrenals, pleura, retroperitoneal fat, paravertebral gutter and ribs.^{2,3,5} EMH in the spinal epidural space is uncommon and the development of SCC as a consequence of intraspinal EMH is an extremely rare complication in thalassaemic patients. Though this complication has been reported relatively more commonly in thalassaemia compared with various other haematological disorders, its occurrence is still rare.^{5,7} Logothetis *et al*⁸ in a survey of 138 cases of thalassaemia major were unable to find a single case with SCC. Prabhakar *et al*⁹ found only one case presenting with SCC in a survey of 120 thalassaemic patients. The first case of SCC due to EMH associated with thalassaemia was described by Gatto *et al*¹⁰ and since then thirty seven additional cases have been reported (table).^{1–21}

The management of such patients remains controversial and as most of the cases have been reported sporadically no definite guidelines have yet been formulated. Although a few authors have observed a dramatic response

Table Reported cases of extramedullary haematopoiesis compressing the spinal cord in thalassaemia

Author, year	Age/Sex/Race	Extent of lesion	Myelogram	Treatment	Result
1 Gatto <i>et al</i> , ¹⁰ 1954	26/M/Italian	T5–T10	Incomplete cord lesion	SX + RT	PR
2 Marinozzi, ²¹ 1958	4/F/Italian	T8–T12	—	None	Died autopsy carried out
3 Sorsdahl <i>et al</i> , ¹ 1964	40/M/Negro American	T5–T8	—	SX	CR
4 Hongladarom and Hongsaprabhas, ¹¹ 1965	26/M/Thai	T7–T9	Complete block at T7	SX	NR
5 Cauthen <i>et al</i> , ² 1968	22/M/Thai	T6–T8	Complete block at T8	SX	NR
6 Heffner and Koehl, ³ 1970	47/M/Negro American	T4–T8	Complete block at T7	SX + RT	CR
7 Luyendijk <i>et al</i> , ¹² 1975	21/M/Italian	T8–L3	—	None	Died autopsy carried out
8 Bate and Humphries, ¹⁹ 1975	42/M/Negro Surinam	T5–T7	Incomplete block T5–T8	SX + RT	CR
9 Cross <i>et al</i> , ⁴ 1977	22/M/Greek	—	—	Ht	CR
10 Mihindikulasuriya <i>et al</i> , ⁵ 1977	44/M/Negro Jamaican	T4–T9	Complete block at T8	SX + RT	CR
11 Prabhakar <i>et al</i> , ⁹ 1980	25/F/Negro Jamaican	T6	Complete block at T6	SX + RT	CR
12 Wilson <i>et al</i> , ¹⁶ 1980	24/F/Ceylonese	T4–T9	Complete block at T9	SX	CR
13 Issaragrisil <i>et al</i> , ⁷ 1981	21/M/Indian	T7–T10	Complete block at T9	SX + RT	CR
14 Francesconi <i>et al</i> , ¹² 1981	28/M/Italian	—	—	RT + HT	CR
15 Luitzes <i>et al</i> , ⁶ 1982	17–40/Thai	T4–T12	ND–5 partial block–4 complete–2	SX + RT–2	CR
16 Abbassioum and Jamshidi, ¹⁴ 1982	M–10, F–2 (12 pts)	—	Partial block T8–T9	RT alone–9	CR
17 David and Bala Subramaniam, ¹⁵ 1983	24/F/French	T4–T9	—	HT–1	CR
18 Mann <i>et al</i> , ¹³ 1987	55/M/Dutch	T4–T8	Complete block at T5	RT alone	CR
19 Papavasiliou and Sandilos, ¹³ 1987	—	—	—	SX + RT	CR
20 Jackson <i>et al</i> , ¹⁸ 1988	28/F/Malaysian	T4–T12	Partial block T5–T12	SX + RT	CR
	21/F/Chinese	T3–T8	Complete block T4–T7	SX + HT	CR
	14–50/M–4, F–1 (5 pts.)	—	—	RT alone	CR (All pts)
	24/M/Negro	T4–T10	Complete block T4–T10	RT alone	CR

SX = Surgery, RT = Radiotherapy, HT = Hypertransfusion therapy, CR = Complete response, NR = No Response, PR = Partial Response, ND = Not done.

following decompressive surgery¹⁻⁵ there is generally no positive outcome.⁹⁻¹³ Total surgical excision of the EMH mass is not always possible probably due to the diffuse nature of the process.¹³ In some authors' experience radiation therapy proved beneficial when an initial surgical excision had failed. Until recently, surgical excision followed by radiation therapy remained the recommended treatment.^{2,6,9,10,12,14,15} However, radiotherapy alone is now gradually emerging as the treatment of choice. Of the 38 reported cases of SCC, radiotherapy alone was employed in the management of 17 patients,^{7,13,16-18} with all the patients showing a dramatic response. In a series of 12 new cases, Issaragrisil *et al*⁷ treated nine patients by radiotherapy alone and achieved a complete neurological recovery in all. In two patients, however, SCC symptoms subsequently recurred but, at different levels and also responded to radiotherapy. No complication was observed during or after radiotherapy.

Papavasiliou and Sandilos¹³ observed a similar dramatic response to radiotherapy in five patients with thalassaemia who had developed SCC. In one of their patients symptoms recurred months after initial treatment but were again successfully alleviated after a second course of radiation therapy. These series form the major bulk of the patients reported to date and their authors recommend radiotherapy alone as a standard treatment for this complication. The mass lesion consisting of haematopoietic tissue appears to be particularly sensitive to the ionizing radiation and a modest radiation dose of 10-30 Gy seems adequate for achieving a rapid and lasting response.^{7,13,17,18} Usually the improvement is clinically evident after an average of three treatments and a near complete recovery is generally observed by the end of the treatment.

Another potential treatment is blood transfusion. It suppresses the erythropoiesis which results in a regression of EMH mass, thereby relieving the pressure symptoms to some extent. However, improvement is usually incomplete and the symptoms recur shortly after. Some authors, however, have reported hypertransfusion therapy to be useful in achieving a long term control of the pressure symptoms.^{19,20}

The site of SCC due to EMH masses has been found to be in the mid and lower thoracic region of the spine in almost all the patients. The reasons for such a predilection are obscure, although it could be related to the smaller diameter of the spinal canal in this area.⁶

In our two cases, radiation treatment proved beneficial and resulted in immediate neurological improvement. Case 1 had earlier had

surgical excision of the mass but no improvement was observed in the following two weeks. He recovered completely after radiotherapy and to date is free of any recurrence. Case 2 has shown significant immediate neurological improvement after treatment with radiation alone although follow up time is short.

Based on our current limited experience, and a review of the literature, a prompt recognition of the syndrome and early treatment with radiotherapy is recommended in the management of SCC due to EMH in thalassaemic patients to prevent irreversible damage to the spinal cord. Surgery may be considered in the event of progressive neurological deficit despite radiotherapy.

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