surgical facilities. These were not available at the place at which this case presented. Moreover, even with these facilities, an unskilled operator may be unable to achieve satisfactory haemostasis. In 1986, Dan et al.[6] reported bad outcomes in 12% of 25 cases directly admitted to neurosurgical units, against 35% in 101 patients first admitted to hospitals without neurosurgical services: while there were many reasons for this, delay or inadequate operations were among the causes of bad outcome. In metropolitan centres, it is possible to direct admission of head injuries to hospitals with neurosurgical services, but in thinly populated parts of the world, it is inevitable that cases of extradural haemorrhage will present far from a hospital with modern facilities.

To meet the needs of such patients, three strategies of management by country medical practitioners have been devised:

- The country medical practitioner may diagnose the condition, secure the airway, and arrange urgent transfer to a neurosurgical unit for emergency treatment.
- The country medical practitioner may carry out the whole emergency management of the extradural haematoma by whatever operative method he or she can undertake.
- The country medical practitioner may diagnose and initiate emergency treatment, including evacuation of the haematoma, while a neurosurgical team is dispatched to the country hospital to complete the operation and to secure haemostasis.

The first strategy may be successful, especially if an infusion of mannitol has been given to gain temporary control of intracranial pressure. However, if there is active extradural bleeding, cerebral compression will continue, and irreversible brain damage may result. Simpson et al. argued that this strategy should not be used if the transfer time exceeded two hours,[7] but this was an arbitrary time limit, and a longer delay might be acceptable in some circumstances.

The second strategy requires the country surgeon to be trained and equipped to do the whole operation, and to organize subsequent postoperative treatment. This strategy is appropriate when it is impossible to transfer the patient safely and with sufficient speed. Nordstrom et al. advocated this system in Sweden, where flying conditions may prevent air retrieval.[8] In Australia, flying conditions are usually good; however, in very remote parts of the country, distances may make this strategy appropriate.

The third strategy requires that the country practitioner can diagnose and locate the extradural haematoma, and evacuate the clot sufficiently to relieve the compression of the brain; while this is being accomplished, the neurosurgeon flies to the country centre and assists in securing haemostasis and in planning after care.[7,9]

These strategies are all sometimes appropriate; each has its place in Australian practice. The choice of management is best made in a dialogue between the country practitioner, the neurosurgeon and the retrieval specialist, who will best know the flight problems and probable weather conditions. The need for immediate informed discussion between these management partners has been stressed by many writers; it has been presented in a brochure prepared by the Neurosurgical Society of Australasia and the Royal Australasian College of Surgeons, entitled 'The management of acute neurotrauma in rural and remote locations'.[10] The case reported here shows how complex are the decisions imposed when a very acute extradural haemorrhage presents in a very remote country town, with no facilities for emergency operation.

McKissock in 1960 wrote that 'the earliest possible diagnosis plan and the most urgent possible surgical treatment are the only measures that will effectively reduce the excessively high mortality'.[11] This statement still applies even in a time of much improved communications and means of transport.

ACKNOWLEDGEMENTS

We thank Mr Kevin Handley of the Australian Camel Racing Association for the expert advice on the problems of this report and also Professor A.J. McLean of the Road Accident Research Unit, University of Adelaide, for his comments on the helmet.

REFERENCES

1. Gilligan JE, Griggs WM, Jelly MT et al. Mobile intensive care services in rural South Australia. MJA 1999; 171: 617–620.
2. Bulliet RW. The camel and the wheel. Cambridge: Harvard University Press, 1975: 36.
3. Gibbs RM. A history of South Australia. Adelaide: Balara, 1969: 58.
4. Stephanov S. Postoperative mortality in acute extradural haematoma. Br J Surg 1993; 7: 461–463.
5. Mendelow AD, Karml MZ, Paus KJ, Fuller GA, Gillingham FJ. Extradural haematoma. Effect of delayed treatment. BMJ 1979; 1: 1240–1242.
6. Dan NG, Berry G, Kwok B et al. Experience with extradural haematomas in New South Wales. Aust NZ J Surg 1986; 56: 353–541.
7. Simpson DA, Heyworth JS, Mclean AJ. Extradural haemorrhage: Strategies for management in remote places. Injury 1988; 19: 309–312.
8. Nordstom CH, Messeter K, Sundburg G, Wahlander S. Severe traumatic brain lesions in Sweden. Part I: Aspects of management in non neurosurgical clinics. Brain Inj 1989; 3: 253–264.
9. Jones NR, Molloy CY, Kloeden CN, North JB, Simpson DA. Extradural haematoma: Trends in outcome over 35 years. Brit J Neurosurg 1993; 7: 469–471.
10. Neurosurgical Society of Australasia. The management of acute neurotrauma in rural and remote locations. A set of guidelines for the care of head and spinal injuries. 2nd ed. Royal Australasian College of Surgeons, 2000.
11. McKissock W, Taylor JC, Bloom WH. Extradural haematoma observation on 125 cases. Lancet 1960; 2: 167–172.

Extramedullary haemopoiesis in thalassemia intermedia presenting as paraplegia

Tze-Ching Tan[1] FRCS, Joanne Tsao[2] FRCR, Fung-Ching Cheung[1] FRCS

Departments of [1]Neurosurgery and [2]Diagnostic Radiology, Queen Elizabeth Hospital, Kowloon, Hong Kong SAR, China

Summary Extramedullary haemopoiesis causing spinal cord compression is a rare manifestation of thalassemia. We describe a 17 year old male with thalassemia intermedia who presented with progressive paraplegia and sphincter disturbance. Magnetic resonance imaging revealed an epidural lesion extending from T5 to T8 compressing the spinal cord. The patient recovered completely

after surgical decompression with postoperative radiation therapy. Histological examination of the lesion confirmed the diagnosis of extramedullary haemopoiesis. Clinical awareness of this phenomenon with early treatment is essential for optimizing the neurological outcome. © 2002 Published by Elsevier Science Ltd.

Journal of Clinical Neuroscience (2002) **9**(6), 721–725

DOI: 10.1054/jocn.2001.1038, available online at http://www.idealibrary.com on IDEAL®

Keywords: cord compression, extramedullary haemopoiesis, thalassemia

Received 21 September 2001
Accepted 14 February 2002

Correspondence to: Akira Nakamizo MD, Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. Tel.: +81-92-642-5524; Fax: +81-92-642-5526; E-mail: nakamizo@ns.med.kyushu-u.ac.jp (A. Nakamizo).

INTRODUCTION

Extramedullary haemopoiesis (EMH) occurs as a compensatory phenomenon in chronic anaemias such as thalassemia, myelofibrosis and sickle cell anaemia.[1–3] The liver, spleen and lymph nodes are frequently affected organs.[4] Involvement of the spine causing spinal cord compression is rarely reported.[1–22] A thalassemic patient with spinal EMH presenting with cord compression and paraplegia is presented.

CASE REPORT

A 17 year old Chinese male with a known history of thalassemia intermedia presented with progressive lower limb weakness over a period of three weeks, and difficulty in micturition for two days. Physical examination revealed pallor and jaundice. The spleen was enlarged 11 cm below the left costal margin. On neurological examination, bilateral lower limb weakness was elicited with power of grade 3/5. The knee and ankle reflexes were brisk. Plantar responses were upgoing. There was sensory loss to pin-prick starting from the T7 dermatome downwards. Proprioception was absent in both lower limbs. The anal tone was preserved. Examination of the upper limbs and cranial nerves was normal.

Complete blood picture yielded a haemoglobin of 8.8 gm/dl, and a haematocrit of 26.9%, with hypochromic, microcytic anaemia. Haemoglobin electrophoresis showed 49.7% HbF and 8% HbA_2. Skull and chest X-rays demonstrated trabecular configuration of the bone with thickening of the calvaria and the costochondral junctions. A paraspinal mass was projected over the right lower zone of the chest roentgenogram (Fig. 1).

Magnetic resonance imaging (MRI) of the thoracic spine was performed using a 1.0 T system. A lobulated posterior epidural mass within the spinal canal extending from T5 to T8 was shown on sagittal MR images (Fig. 2). Axial views of the epidural mass revealed an oedematous, compressed spinal cord (Fig. 3). Bilateral lobulated paraspinal masses between T8 and T10 were visible on axial images of the thorax (Fig. 4). The paraspinal and epidural masses were hypointense on T1, hyperintense on T2 and exhibited slight gadolinium enhancement. The clinical diagnosis was spinal cord compression secondary to extramedullary haemopoiesis.

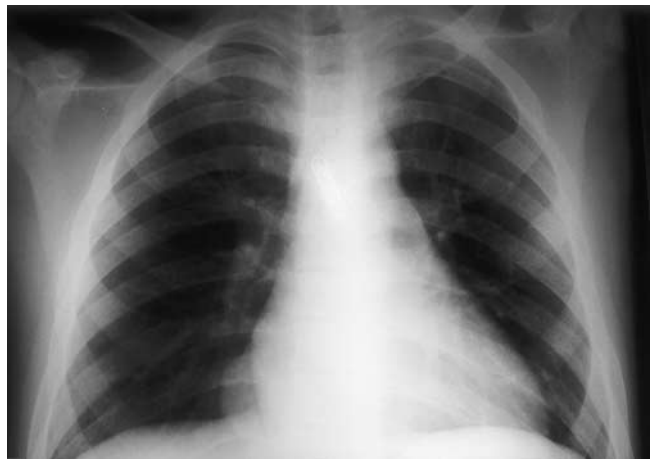

Fig. 1 Chest roentgenograph demonstrating expanded anterior rib ends consistent with medullary hyperplasia. A paraspinal mass is seen in the right lower zone.

OPERATION AND POSTOPERATIVE COURSE

The patient received 1000 ml of blood transfusion. His condition failed to improve and an emergency laminectomy from T6 to T7 was performed the next day. Intraoperatively, a posterior epidural vascular mass was discovered indenting the cord between T5 and T8. The lesion was easily stripped off the dura and completely excised. The diagnosis of extramedullary haemopoiesis was confirmed by histological examination of the mass.

The muscle power of the patient improved to grade 4/5 on the first postoperative day. He was ambulant with a stick after two weeks. After a month, the patient had made a full neurological recovery, and was walking independently. He was given 2000 rads of local spinal irradiation administered in ten fractions when the wound had healed. The patient received repeated blood transfusions, maintaining the haemoglobin level at 9 g/dl to suppress the extramedullary haemopoiesis. MRI of the spine performed six months after surgery showed complete resolution of cord compression, with no evidence of intraspinal EMH tissue.

DISCUSSION

The most common sites of EMH are the liver and spleen, followed by the adrenals, kidneys, lymph nodes, mediastinum, pericardium and lungs.[3–7] Spinal EMH causing cord compression in thalassemia, first described by Gatto et al. in 1954,[13] is extremely rare.[1–15,17–21] A study of 138 thalassemic patients showed the notable absence of this phenomenon,[23] while a recent report revealed an incidence of only 0.8%.[9]

A number of mechanisms have been postulated to account for the predilection for involvement of the thoracic region in spinal EMH. These include extension of EMH tissue through the thinned trabeculae at the proximal rib ends,[24] direct expansion from adjacent vertebral bone marrow,[25] and development of EMH tissue from branches of the intercostal veins.[26] The narrow central canal,[11,14] and limited mobility[4] of the thoracic spine predisposes itself to spinal cord compression.

The diagnosis of spinal EMH is made on clinical and radiographic findings. Clinical suspicions may be raised by a history of thalassemia, and auxiliary evidence of EMH such as hepatosplenomegaly or lymphadenopathy. Plain radiographs often reveal well demarcated paraspinal masses,[6,15] and bony

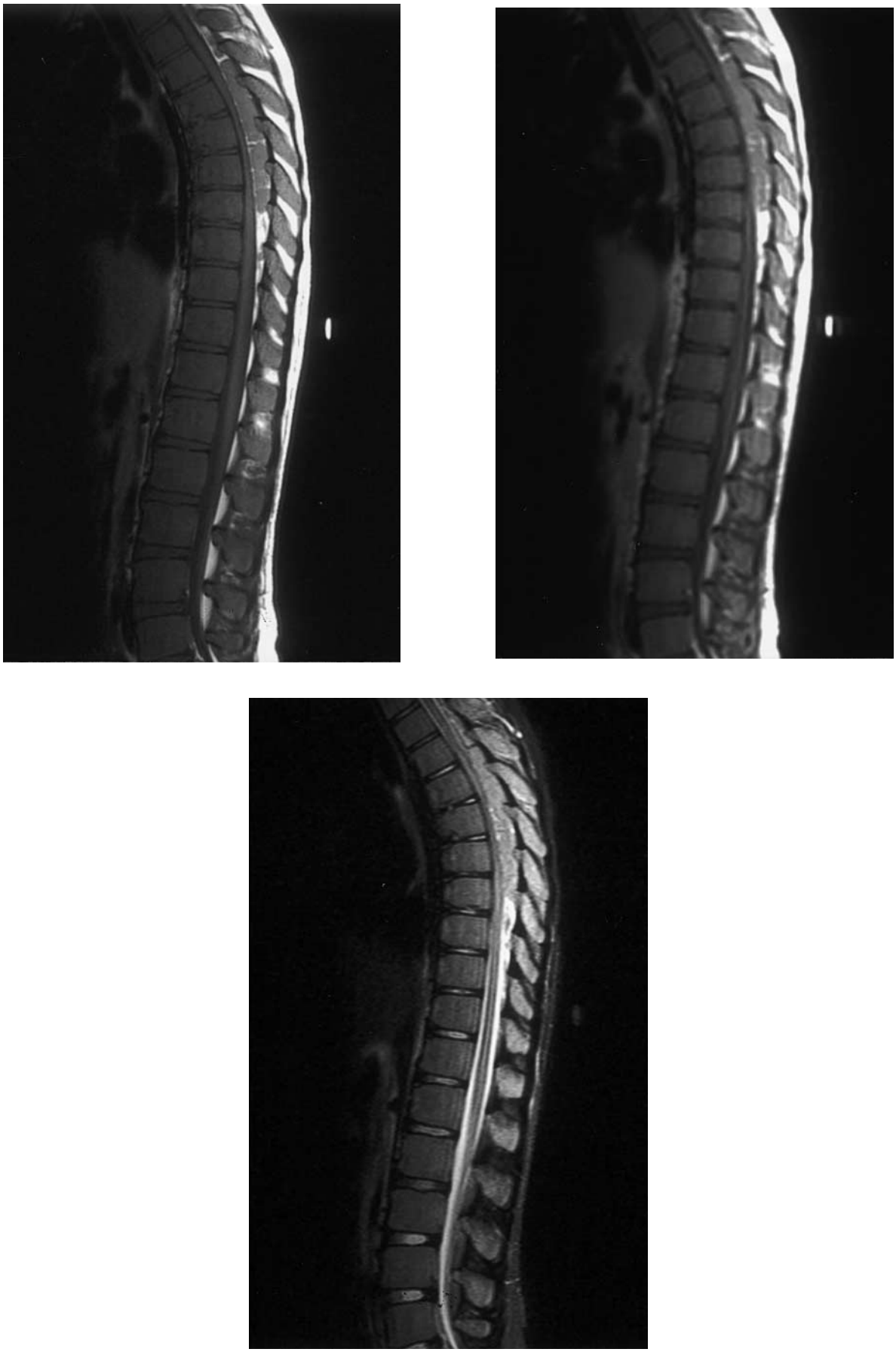

Fig. 2 Preoperative sagittal MR images of the posterior epidural mass extending between T5 to T8. A marker has been placed at T11. Left: T1-weighted hypointense image without enhancement. Centre: T2-weighted hyperintense image. Right: Post-gadolinium: slight enhancement of the mass is seen. Note the cord compression from T5 to T8 levels.

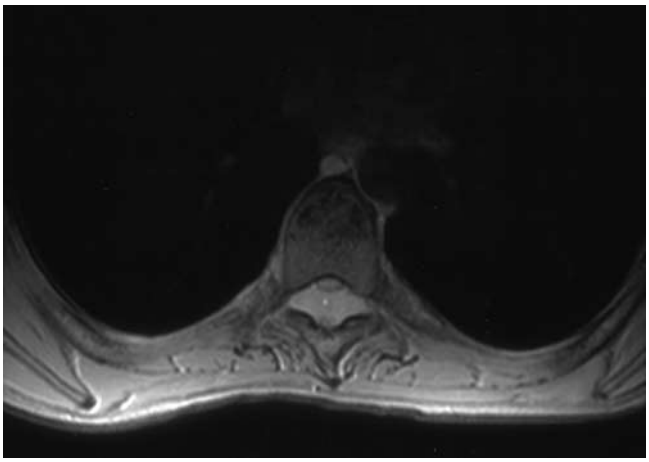

Fig. 3 Axial T2-weighted MR image shows the mass causing anterior compression of the spinal cord. Increased signal within the spinal cord is suggestive of oedema.

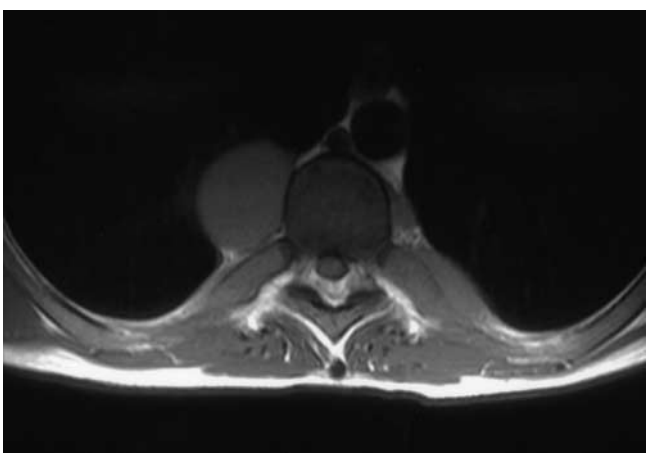

Fig. 4 Axial T1 MR images show bilateral paraspinal masses of extramedullary haematopoietic tissue. Note the widened posterior ribs representing red marrow expansion.

changes associated with chronic anaemia such as trabeculation, widened ribs or thickened calvaria.[6] Bony destruction or pathological fractures are absent.

MRI is currently the gold standard for demonstrating spinal EMH.[8,16,17] The advantages of MRI are myriad: it allows multiplanar imaging and produces superior soft tissue delineation with high sensitivity. On MRI, EMH tissue possesses signal intensity similar to that of the adjacent red marrow in the vertebral bodies. Gadolinium enhancement is minimal or absent,[8,17] differentiating it from other epidural lesions such as abscesses or metastases. Being non-invasive, MRI is the ideal imaging modality for follow up assessment.

Computed tomography (CT) is a valuable investigation for patients in whom MRI is contraindicated or unavailable. CT guided needle biopsy of paraspinal masses is possible for tissue diagnosis,[22] but the procedure carries the risk of catastrophic haemorrhage and is therefore not usually advocated.[2,26] ^{99m}Tc bone scan has been used to diagnose paraspinal EMH,[27] but the diagnosis within the epidural space may be difficult due to the proximity to bone marrow.[8] Myelography is declining in popularity due to its invasiveness, the need for cisternal puncture in cases of complete block preventing passage of radiographic contrast,[2,21] and reports of neurological deterioration following the procedure.[5,7]

Considerable controversy exists regarding the ideal treatment of spinal cord compression due to EMH. Management options include surgery, transfusion therapy, radiotherapy or any combination of these modalities. More recently, the use of drugs such as hydroxyurea which act by enhancing haemoglobin levels has been reported.[28,29]

Laminectomy is indicated in cases of acute presentation which do not respond to adequate transfusion or radiotherapy,[2,8,11,21] as illustrated by the present patient. Surgery confers the benefits of immediate relief of cord compression and histological diagnosis. Disadvantages include the risks of operating on anaemic individuals who are predisposed to shock, incomplete excision in cases of diffuse involvement,[5,7,12] instability[7] and kyphosis associated with multilevel laminectomy.

Blood transfusions relieve chronic anaemia and suppress extramedullary haemopoiesis. It has been used as the principal treatment modality in cases of spinal EMH where surgical decompression or radiotherapy were contraindicated e.g. pregnancy[10,18] or severe anaemia.[19] Coskun et al. reported a patient who required laminectomy when neurological deterioration developed despite adequate transfusion.[17] While blood transfusion may prevent further progression of EMH, it is unable to reverse preexisting cord compression. Its role in the management of patients with symptoms of acute onset is therefore limited.[1,19] However it is a useful adjuvant treatment after surgical decompression.[5,8]

Radiation therapy (RT) alone has been reported to yield excellent results with neurological improvement observed as soon as 3–7 days after initiation of treatment.[11,15] Haemopoietic tissue is extremely radiosensitive and undergoes shrinkage after RT, with a decrease in volume by as much as 16.4%.[32] Dosages reported in the literature range from 900–3500 rads.[3,11,20,21] A high risk of recurrence,[3] up to 19%, is the main drawback of RT.[21] Fortunately, these recurrences are often amenable to further RT. Tissue oedema associated with radiation can sometimes result in neurological deterioration during the initial phase of treatment,[5,22] which is minimized by concomitant high dose steroid therapy. In addition to primary treatment, radiotherapy is commonly employed as a post-operative adjunct following laminectomy to reduce the likelihood of recurrence.[8,9,11] The immunosuppressive effect of RT should be monitored with frequent peripheral blood counts as the resultant pancytopenia may further aggravate the condition.[3,18,22]

New advances in the treatment of thalassemia include the use of drugs such as hydroxyurea, sodium butyrate and erythropoietin which boost haemoglobin levels.[28–33] Patients with spinal EMH have been successfully treated with hydroxyurea alone[28,29] or in conjunction with transfusion therapy.[31] Hydroxyurea works by enhancing foetal haemoglobin production, hence reducing transfusion requirements.[33] It is particularly applicable to thalassemic patients who are unable to receive blood transfusions due to alloimmunization.[30] However, the benefits of hydroxyurea in spinal EMH remain to be proven.

The diagnosis of spinal EMH is suggested by a history of chronic haemolytic anaemia, evidence of EMH elsewhere, symptoms of cord compression and radiographic evidence of an intraspinal epidural lesion. A high index of suspicion with early treatment is essential to avoid irreversible neurological sequelae. The role of magnetic resonance imaging in diagnosis and follow up cannot be overemphasized. In the event of acute

neurological deterioration, surgical decompression with post-operative radiotherapy and blood transfusion is recommended.

ACKNOWLEDGEMENT

The authors acknowledge Hung Lau, FRACS, for editing the manuscript, and Emily Tin for tracing the patient records.

REFERENCES

1. Parsa K, Oreizy A. Nonsurgical approach to paraparesis due to extramedullary hematopoiesis. Report of two cases. J Neurosurg 1995; 82: 657–660.
2. Oustwani MB, Kurtides ES, Christ M, Ciric I. Spinal cord compression with paraplegia in myelofibrosis. Arch Neurol 1980; 37: 389–390.
3. Papavasiliou C, Sandilos P. Effect of radiotherapy in symptoms due to heterotopic marrow in beta-thalassemia. Lancet 1987; 1: 13–14.
4. Abbassioun K, Amir-Jamshidi A. Curable parpalegia due to extradural hematopoietic tissue in thalassemia. Neurosurgery 1982; 11: 804–807.
5. Mann KS, Yue CP, Chan KH, Ma LT, Ngan H. Paraplegia due to extramedullary hematopoiesis in thalassemia. Case report. J Neurosurg 1987; 66: 938–940.
6. David CV, Balasubramaniam P. Paraplegia with thalassemia. Aust NZ J Surg 1983; 53: 283–284.
7. Amirjamshidi A, Abbassioun K, Ketabchi SE. Spinal extradural hematopoiesis in adolescents with thalassemia. Report of two cases and a review of the literature. Childs Nerv Syst 1991; 7: 223–225.
8. Lau SK, Chan CK, Chow YY. Cord compression due to extramedullary hemopoiesis in a patient with thalassemia. Spine 1994; 19: 2467–2470.
9. Prabhakar S, Chopra JS, Khosla VK, Dash S, Banerjee AK. Spinal cord compression in homozygous beta thalassemia. Surg Neurol 1980; 13: 351–354.
10. Singounas EG, Sakas DE, Hadley DM et al. Paraplegia in a pregnant thalassemic woman due to extramedullary hematopoiesis: successful management with transfusions. Surg Neurol 1991; 36: 210–215.
11. Singhal S, Sharma S, Dixit D et al. The role of radiation therapy in the management of spinal cord compression due to extramedullary hematopoiesis in thalassemia. J Neurol Neurosurg Psychiatry 1992; 55: 310–312.
12. Luitjes WF, Braakman R, Abels J. Spinal cord compression in a new homozygous variant of beta-thalassemia. Case report. J Neurosurg 1982; 57: 846–848.
13. Gatto I, Terrana V, Biondi L. Compressione sul midollo spinale da proliferazione di midollo osseo spazio epidurale in sogetto affetto da malattia di Cooley splenectomizato. Haematologica 1954, 38: 61–76.
14. Luyendjik W, Went L, Schaad HD. Spinal cord compression due to extramedullary hematopoiesis in homozygous thalassemia: case report. J Neurosurg 1975; 42: 212–216.
15. Kaufmann T, Coleman M, Giardina P, Nisce LZ. The role of radiation therapy in the management of hematopoietic neurologic complications in thalassemia. Acta Haematol 1991; 85: 156–159.
16. Guermazi A, Miaux Y, Chiras J. Imaging of spinal cord compression due to thoracic extramedullary haematopoiesis in myelofibrosis. Neuroradiology 1997; 39: 733–736.
17. Coskun E, Keskin A, Suzer T, Sermez Y, Kildaci T, Tahta K. Spinal cord compression secondary to extramedullary hematopoiesis in thalassemia intermedia. Eur Spine J 1998; 7: 501–504.
18. Phupong V, Uerpairojkij B, Limpongsanurak S. Spinal cord compression: a rareness in pregnant thalassemic woman. J Obstet Gynaecol Res 2000, 26: 117–120.
19. Mancuso P, Zingale A, Basile L, Chiaramonte I, Tropea R. Cauda equina compression syndrome in a patient affected by thalassemia intermedia: complete regression with blood transfusion therapy. Childs Nerv Syst 1993; 9: 440–441.
20. Hassoun H, Lawn-Tsao L, Langevin ER, Lathi ES, Palek J. Spinal cord compression secondary to extramedullary hematopoiesis: a noninvasive management based on MRI. Am J Hematol 1991; 37: 201–203.
21. Jackson DV Jr, Randall ME, Richards F 2nd. Spinal cord compression due to extramedullary hematopoiesis in thalassemia: long-term follow-up after radiotherapy. Surg Neurol 1988; 29: 388–392.
22. De Klippel N, Dehou MF, Bourgain C, Schots R, De Keyser J, Ebinger G. Progressive paraparesis due to thoracic extramedullary hematopoiesis in myelofibrosis. Case report. J Neurosurg 1993; 79: 125–127.
23. Logothetis J, Constantoulakis M, Economidou J et al. Thalassemia major (homozygous beta-thalassemia). A survey of 138 cases with emphasis on neurologic and muscular aspects. Neurology 1972; 22: 294–304.
24. Da Costa JL, Loh YS, Hanam E. Extramedullary hematopoiesis with multiple tumour-simulating mediastinal masses in hemoglobin E-thalassemia disease. Chest 1974; 65: 210–212.
25. Lyall A. Massive extramedullary bone marrow formation in a case of pernicious anaemia. J Pathol Bacteriol 1935; 41: 469–472.
26. Cone SM. Bone marrow occurring in intercostal veins. JAMA 1925; 84: 1732–1733.
27. Bronn LJ, Paquelet JR, Tetalman MR. Intrathoracic extramedullary hematopoiesis: appearance on 99mTc sulfur colloid marrow scan. AJR Am J Roentgenol.1980; 134: 1254–1255.
28. Cianciulli P, di Torritto TC, Sorrentino F, Sergiacomi L, Massa A, Amardori S. Hydroxyurea therapy in paraparesis and cauda equina syndrome due to extramedullary haematopoiesis in thalassemia: improvement in clinical and haematological parameters. Eur J Haematol 2000; 64: 426–429.
29. Saxon BR, Rees D, Olivieri NF. Regression of extramedullary haemopoiesis and augmentation of fetal haemoglobin concentration during hydroxyurea therapy in beta thalassemia. Br J Haematol 1998; 101: 416–419.
30. Olivieri NF, Rees DC, Ginder GD et al. Treatment of thalassemia major with phenylbutyrate and hydroxyurea. Lancet 1997; 350: 491–492.
31. Konstantopoulos K, Vagiopoulos G, Kantouni R et al. A case of spinal cord compression by extramedullary haemopoiesis in a thalassemic patient: a putative role for hydroxyurea? Haematologica 1992; 77: 352–354.
32. Cianciulli P, Sorrentino F, Morino L et al. Radiotherapy combined with erythropoietin for the treatment of extramedullary hematopoiesis in an alloimmunized patient with thalassemia intermedia. Ann Hematol 1996; 72: 379–381.
33. Arruda VR, Lima CS, Saad ST, Costa FF. Successful use of hydroxyurea in beta-thalassemia major. N Engl J Med 1997; 336: 964.

Spinal leptomeningeal metastases following glioblastoma multiforme treated with radiotherapy

Andrew Lindsay MBBS, **David Holthouse** MBBS HON, **Peter Robbins** MBBS HON FRCPA, **Neville Knuckey** MD FRACS

Department of Neurosurgery, Sir Charles Gairdner Hospital, Nedlands, WA and The Western Australian Centre for Pathology and Medical Research, QE II Medical Centre, Nedlands, Western Australia

Summary A case of glioblastoma with leptomeningeal spread after control of the primary lesion by radiation therapy. A discussion is made regarding leptomeningeal metastatic disease with reference to the literature. © 2002 Elsevier Science Ltd. All rights reserved.

Journal of Clinical Neuroscience (2002) **9**(6), 725–728

DOI: 10.1054/jocn.2002.1079, available online at http://www.idealibrary.com on IDEAL®

Keywords: glioblastoma, leptomeningeal metastasis, radiotherapy

Received 15 November 2001
Accepted 23 January 2002

Correspondence to: Mr N. Knuckey Department of Neurosurgery, Nedlands, Western Australia. Tel.: 0893462865; Fax: 0893463824; E-mail: nknuckey@health.gov.wa.au