Neurología. 2019;34(4):270—282

SOCIEDAD ESPAÑOLA DE NEUROLOGIA

NEUROLOGÍA

www.elsevier.es/neurologia

LETTERS TO THE EDITOR

Reversible paraparesis secondary to spinal cord compression in a patient with ß-thalassaemia☆

Compresión medular con paraparesia reversible en paciente con ß-talasemia

Dear Editor:

ß-Thalassaemia is a group of autosomal recessive forms of anaemia caused by decreased or absent synthesis of the β chains of haemoglobin. The condition is endemic to the Mediterranean region. Thalassaemia major manifests with symptoms of haemolytic anaemia and extramedullary haematopoiesis. Spinal cord compression is an extremely rare complication of extramedullary haematopoiesis, observed in fewer than 1% of patients. We present the case of a patient with progressive paraparesis secondary to thoracolumbar spinal cord compression by epidural masses resulting from extramedullary haematopoiesis; the patient was treated with haemotherapy, hydroxycarbamide, and radiotherapy.

The patient was a 28-year-old woman who was diagnosed with ß-thalassaemia major at the age of 5; she underwent splenectomy and received periodic blood transfusions. Due to the transfusions received, the patient has Child—Pugh class A liver disease secondary to hepatitis C virus infection. She was lost to follow-up some years previously. She visited the emergency department due to urinary retention and spastic paraparesis. She reported a 2-month history of ataxia and progressive sensory impairment in the lower limbs. The physical examination showed malar prominence, depressed nasal bridge, pale skin, and mild jaundice. The patient showed loss of strength in the lower limbs (4/5), associated with hyperreflexia, ankle clonus, bilateral Babinski sign, and sensory level at T10. Results from a complete blood count were normal except for a haemoglobin level of 6 g/dL and mild leukocytosis. A chest and abdomen MRI scan revealed spinal cord compression by paravertebral and epidural masses located at T5-T9, associated with signs of myelopathy at T9; the paravertebral mass measured 6.8 cm × 5.1 cm on the axial plane. The lumbar spine also displayed multiple nodules deforming and compressing the thecal sac, compatible with extramedullary haematopoiesis (Fig. 1).

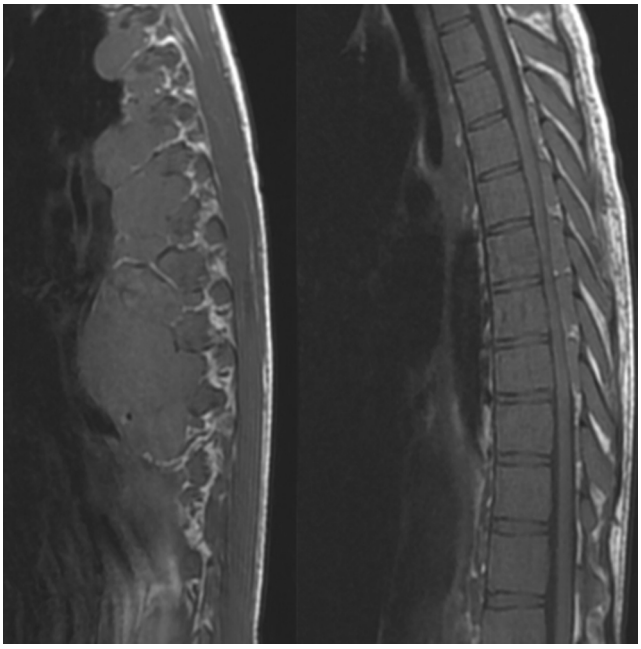

Figure 1 A thoracolumbar MRI scan revealed spinal cord compression due to paravertebral and epidural masses at the level of T5-T9, associated with signs of myelopathy at T9; the paravertebral mass measured 6.8 cm × 5.1 cm on the axial plane. The lumbar spinal cord displayed multiple nodules compressing the thecal sac, compatible with extramedullary haematopoiesis.

The patient was diagnosed with spinal cord compression secondary to extramedullary haematopoiesis. Treatment was started with 16 mg intravenous dexamethasone and

☆ Please cite this article as: Duque SG, Jureschke FR, Leal RG. Compresión medular con paraparesia reversible en paciente con ß-talasemia. Neurología. 2019;34:270—272.

blood transfusions; haemoglobin level reached 12.5 g/dL at 72 hours after admission. She also received radiotherapy in the area affected by extramedullary haematopoiesis (2 Gy in 10 fractions of 200 cGy), and was administered hydroxycarbamide 500 mg/day. The patient improved progressively, recovering urinary function, strength, and sensitivity almost completely by 14 days after admission. At 18 months, the patient has no neurological symptoms and has haemoglobin levels above 10 g/dL; she receives blood transfusions on a monthly basis and hydroxycarbamide at 500 mg/day.

Extramedullary haematopoiesis is a common compensatory mechanism in cases of poorly controlled haemolytic anaemia. Its incidence in patients with β-thalassaemia major who are receiving multiple blood transfusions is below 1%; location is paraspinal in 11% to 15% of cases.[1] Spinal cord compression is most frequent at the thoracic level, given the restricted mobility and the smaller diameter of the spinal canal in this area; up to 80% of cases are asymptomatic, however.[2] Neurological symptoms range from low back pain to paraplegia. MRI typically reveals paraspinal masses. These are isointense on T1- and T2-weighted sequences when they are recent and hypervascular, whereas older or regressing masses are either hyperintense, if they are predominantly fatty, or hypointense if they contain iron deposits.[1] Unlike metastases, these masses do not show gadolinium uptake.[3] Biopsy is not recommended for diagnosis due to the high risk of massive bleeding[2]; this technique is only used for elderly patients in cases of high suspicion of malignancies, or in those displaying non-specific symptoms and imaging findings. Differential diagnosis should include metastasis, epidural abscess, multiple myeloma, and lymphoma; however, extramedullary haematopoiesis is usually simple to diagnose unless the patient displays a single, unilateral, active lesion.[2]

Several other cases of extramedullary haematopoiesis have been published since Gatto et al.[5] reported the first case in 1954; management continues to be controversial, however. At present, treatment aims to raise haemoglobin levels above 10 g/dL[6] with blood transfusions. Given that extramedullary haematopoiesis is a compensatory mechanism for anaemia, transfusions reduce the need for this mechanism, quickly reducing the size of haematopoietic masses. The first transfusions are usually combined with administration of hydroxycarbamide[7]; this ribonucleotide reductase inhibitor stimulates the synthesis of fetal haemoglobin, decreasing the need for extramedullary haematopoiesis. Despite the usefulness of combination therapy with hydroxycarbamide plus haemotherapy, the drug's profile for long-term use is not fully established.[8,9]

Combination therapy usually results in slow, incomplete recovery.[10] Therefore, patients with acute, severe neurological involvement also require low-dose radiotherapy (900-3500 cGy), which is associated with positive outcomes within 3-7 days in over 50% of cases, given that haematopoietic tissue is highly radiosensitive.[1,10] Patients with mild neurological involvement only receive radiotherapy if haemotherapy fails or in the event of recurrence; radiotherapy is the best option to prevent recurrences.[5]

Decompressive laminectomy is indicated for refractory cases or when other treatments are contraindicated.[3,4] This surgical technique achieves immediate decompression and enables histological diagnosis, but is associated with a high risk of bleeding. In the long term, the condition may cause kyphosis and instability; surgical correction of kyphosis should be performed when possible. Sudden excision of haematopoietic elements in these patients may lead to decompensation of the underlying disease. Patients usually display diffuse involvement of several vertebral bodies, which makes surgery suitable only in cases of acute, severe, progressive neurological involvement.

ß-Thalassaemia may cause reversible paraplegia; the condition should therefore be included in the differential diagnosis of compressive lesions in patients with chronic anaemia. Unlike in such other causes of spinal cord compression as tumours or trauma, medical treatment alone (haemotherapy, hydroxycarbamide, and low-dose radiotherapy) can lead to early recovery in patients with extramedullary haematopoiesis; surgery should be limited to cases with poor clinical progression. Personalised treatment may therefore achieve complete, stable recovery of neurological symptoms.

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S.G. Duque[a,*], F.R. Jureschke[b], R.G. Leal[b]
[a] *Servicio de Neurocirugía, HM Hospitales, Hospital Universitario HM Sanchinarro, Madrid, Spain*
[b] *Servicio de Neurocirugía, Hospital General Universitario Gregorio Marañón, Madrid, Spain*

* Corresponding author.
E-mail address: Saragduque83@hotmail.com (S.G. Duque).
2173-5808/

Diagnosis of POEMS syndrome in a patient with long-standing neuropathy☆

Diagnóstico de síndrome de POEMS tras neuropatía de larga evolución

Dear Editor:

Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome is a rare multisystemic disease of paraneoplastic origin, which represents a true clinical challenge. It is caused by a plasma cell disease and its symptoms are numerous and varied. The acronym refers to the combination of the most frequently manifesting signs and symptoms: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes.[1] However, some of these symptoms are absent in some cases, and are not necessary for establishing diagnosis. It has been suggested that overproduction of vascular endothelial growth factor (VEGF), secreted by neoplastic plasma cells, may be responsible for most symptoms.[2] The diagnostic criteria are:

- Major criteria (both mandatory): polyneuropathy (mainly demyelinating) and monoclonal proliferation of plasma cells.
- Major criteria (at least one must be present): Castleman disease, sclerotic bone lesions, and increased VEGF levels.
- Minor criteria (at least one must be present): organomegaly (splenomegaly, hepatomegaly, adenopathies); extravascular volume overload (oedemas, pleural oedema, ascites); endocrinopathies (adrenal, thyroid, pituitary, pancreatic); skin changes (hyperpigmentation, hypertrichosis, acrocyanosis, white nails); papilloedema; and thrombocytosis/polycythaemia.

We present a case of POEMS syndrome in a 71-year-old woman who was transferred to the haematology department for a polycythaemia study after a stroke. Her personal history included arterial hypertension, untreated C virus—related chronic liver disease, and Paget disease of bone; she was under follow-up by the neurology department due to a 3-year history of mixed progressive polyneuropathy, with no response to several lines of treatment. Blood analysis showed a haemoglobin level of 18.6 g/dL and a haematocrit level of 58%. The rest of the examination yielded normal results. Erythropoietin levels were normal and the patient was negative for the v617f mutation of the *JAK2* gene. A screening test for acquired and inherited thrombophilia obtained negative results.

Further testing revealed low levels of monoclonal IgA-lambda protein, which was not detectable in the urine. During follow-up, the patient attended the emergency department due to dyspnoea with mild exertion, and a bilateral pleural effusion with transudate features (cardiac and infectious causes were ruled out) (Fig. 1A). A high-resolution thoracic CT scan revealed sclerotic bone lesions in the right fifth rib and the L1 vertebra (Fig. 1B). A magnetic resonance imaging scan and full CT scan showed multiple osteosclerotic lesions, hepatosplenomegaly, and bilateral pleural effusion with minimal free abdominal fluid (Fig. 1C). As POEMS syndrome was suspected, we requested a VEGF determination (>1000 pg/mL; normal values, <128 pg/mL) and biopsy of the rib lesion (not conclusive). Bone marrow biopsy revealed no pathological infiltration. The patient met 2 mandatory criteria, 2 major criteria, and several minor criteria; therefore, diagnosis of POEMS syndrome was established.

Considering the patient's age and comorbidities, an autologous stem cell transplantation was ruled out[2] and treatment with melphalan + dexamethasone was started. The patient's condition improved slightly, with decreased pleural effusion and reduced oedema of the lower limbs; repeated hospitalisation was not required. As polyneuropathy did not improve after 4 cycles of treatment, treatment was started with bortezomib. After 2 cycles, the paraprotein became undetectable and pleural effusion and oedema in the lower limbs disappeared. Haemoglobin and VEGF levels normalised and no new sclerotic lesions were detected on the follow-up magnetic resonance imaging scan. Eight months after finishing treatment, the patient remained stable and neuropathy slightly improved; he was able to start treatment for hepatitis C virus (Table 1).

POEMS syndrome is an infrequent entity which falls within the group of plasma cell dyscrasias. Given the rareness, variability, and complexity of forms of onset, diagnosis of POEMS syndrome may be delayed by a median of 13-18 months.[3] Therefore, initial clinical suspicion, based on a good history taking and physical examination, is essential to identify which laboratory tests and radiological studies may ultimately enable us to establish a definitive diagnosis.

☆ Please cite this article as: Plaza C, Arquero T, García-Raso A, Llamas P. Diagnóstico de síndrome de POEMS tras neuropatía de larga evolución. Neurología. 2019;34:272—274.