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Review article

Paraneoplastic neuromyelitis optica spectrum disorder: A case report and review of the literature

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ABSTRACT

Neuromyelitis optica spectrum disorders (NMOSD) are demyelinating, autoimmune diseases affecting the central nervous system. Typically, recurrent optic neuritis and longitudinal extensive transverse myelitis dominates the clinical picture. In most cases NMOSD are associated with autoantibodies targeting the water channel aquaporin-4 (AQP-4). NMOSD usually present in young adults. Clinical findings suggestive of NMOSD in elderly patients should raise the suspicion of a paraneoplastic etiology. To our knowledge, we report the first case of a 66 year-old female patient with paraneoplastic NMOSD that is associated with squamous cell lung carcinoma. Anti-AQP-4 was present in both the serum and cerebrospinal fluid of the patient. However, immunhistological staining of the malignant tissue did not show presence of AQP-4 on the surface of tumour cells.

1. Introduction

Neuromyelitis optica spectrum disorders (NMOSD) are demyelinating, autoimmune diseases affecting the central nervous system (CNS). Typically, recurrent optic neuritis and longitudinal extensive transverse myelitis dominates the clinical picture. In most cases NMOSD are associated with autoantibodies (IgG) targeting the water channel aquaporin-4 (AQP-4) [1]. AQP-4 is a transmembrane protein found on the surface of astrocyte projections constituting to the blood-brain barrier (BBB) and is concerned with regulating water movement between the cerebrospinal fluid (CSF), blood and brain [2]. NMOSD usually present in young adults. Clinical findings suggestive of NMOSD in elderly patients should raise the suspicion of paraneoplastic aetiology.

To our knowledge, we report the first case of paraneoplastic NMOSD secondary to squamous cell lung carcinoma. We also aimed to summarize previously reported cases of paraneoplastic NMOSD.

2. Case report

A 66 year-old female patient presented to the Emergency Department with complaints of sudden onset left lower extremity weakness, numbness and reduced sensation that started 3 days prior to presentation. She was unable to walk on the second day of her illness. She also complained of sudden onset urinary incontinence.

She had a history of myelodysplastic syndrome (MDS) with refractory anaemia for which she received regular blood transfusions every 3–4 weeks. She smoked a pack of cigarette a day. She denied regular alcohol consumption or illicit drug use.

On admittance she had severe monoparesis (2/5) of the left leg with diminished reflexes and sensory loss. She had urinary incontinence. Contrast enhanced MRI of the lower thoracic and lumbar spine showed a long T2 hyperintense lesion extending from 4th to 10th thoracic vertebrae (Fig. 1). As an additional finding, a neoplasm (approximately 20 mm in diameter) in the 6th segment of the left lung was suspected. A CT guided biopsy of the lesion was not successful. After consultation with a haematologist, despite of a possible lung tumour, to treat a suspected funicular myelosis, parenteral vitamin B12 supplementation was initiated. Over the next few days, the patient's condition did not improve. Paresis and sensory disturbance of the right leg also developed. In the

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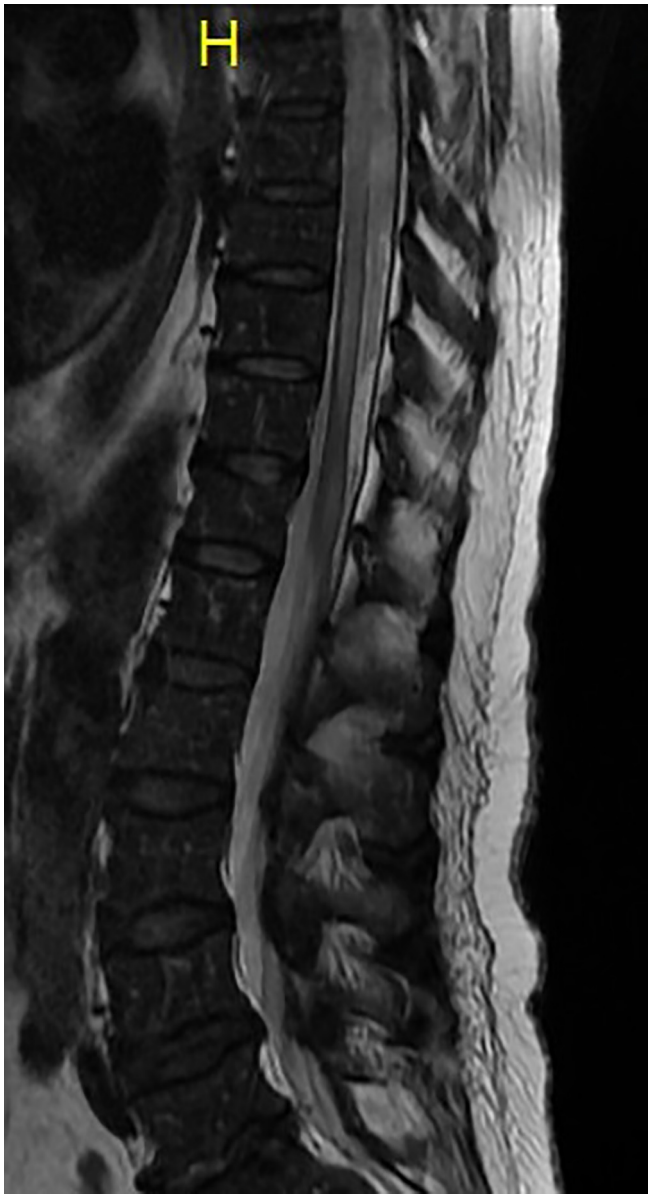

Fig. 1. MRI of the lower thoracic and lumbar spine showing a long T2 hyperintense lesion in the thoracic segment of the spinal cord.

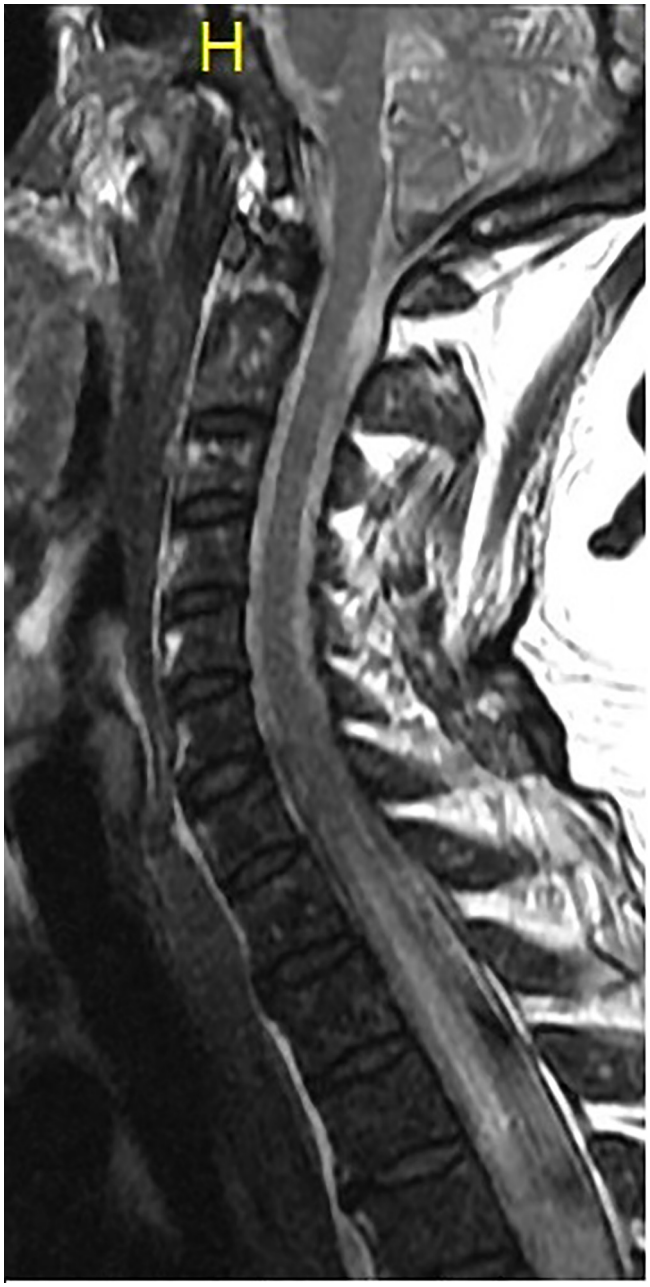

Fig. 2. MRI of the cervical and upper thoracic spine showing T2 hyperintense lesion in the spinal cord below the 7th cervical segment.

CSF mildly increased protein level (0.57 g/l; normal range: 0.2–0.4 g/l) and white cell count (8 white cells, mostly lymphocytes) were found. Furthermore, matching oligoclonal bands (OCB) in both the serum and CSF of the patient were detected. Tests for mycobacteria, CMV, HSV and EBV were negative. The patient's autoimmune panel (including ANA, anti-dsDNA, anti-SS-A and SS-B, anti-Scl-70, anti-Jo-1, anti-RNP-70, anti-RNP/Sm, anti-centromere B) was normal. The tumour marker, carcinoembryonic antigen (CEA) was elevated (8.17 ng/ml, normal range <4.70 ng/ml). Bone marrow-biopsy did not show signs of transformation of MDS to acute myeloid leukaemia.

A further worsening of the patient's condition was detected, paresis and sensory loss presented on the upper extremities and trunk. A contrast enhanced MRI of the cervical and upper thoracic spine found T2 hyperintense lesion in the spinal cord between the 7th cervical and the 10th thoracic segment (Fig. 2).

Later on, the patient complained of blurry vision on both eyes, more severely affecting the left eye. MRI of the brain showed T2 hyperintense lesions in both optic nerves, affecting the left nerve more profoundly. A repeated lumbar puncture found a protein level of 0.85 g/l and 15 white cells (dominantly lymphocytes) in the CSF. Furthermore, Lactobacillus crispatus cultured from the sample that was thought to be contamination, but antibiotic treatment, ceftriaxone was initiated.

Despite our efforts, the patient's condition deteriorated further. In the meantime we repeated the lung biopsy (only a small tissue sample was obtained), which confirmed a squamous cell carcinoma. AQP-4 autoantibodies were detected in the serum and in the CSF. No other autoantibodies (amphiphysin, CV2-CRMP5 [collapsin response mediator-protein-5], Ma2 [Ta], RI [ANNA2], Yo [PCA1], Hu [ANNA1]) were detected in the serum of the patient. Based on the patient's progressing neurological state, MRI findings (optic neuritis of both optic nerves and long extensive transverse

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