Multiple Sclerosis and Related Disorders 4 (2015) 590–593

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Case report

Primary spinal oligoastrocytoma mimicking longitudinally extensive transverse myelitis

T.R. Yeo [a,*], C.F. Wong [b], J.J.X. Lee [c], V.Z.Y. Ng [a], K. Tan [a]

[a] Department of Neurology, National Neuroscience Institute, 11 Jalan Tan Tock Seng, 308433 Singapore, Singapore
[b] Department of Pathology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, 308433 Singapore, Singapore
[c] Department of Medical Oncology, National Cancer Centre Singapore, 11 Hospital Drive, 169610 Singapore, Singapore

ARTICLE INFO

Article history:
Received 16 July 2015
Received in revised form
16 August 2015
Accepted 20 September 2015

Keywords:
Spinal oligoastrocytoma
Spinal cord tumor
Histopathology
Biopsy
Longitudinally extensive transverse myelitis
Longitudinally extensive spinal cord lesion

ABSTRACT

Longitudinally extensive transverse myelitis (LETM) is most commonly associated with neuromyelitis optica spectrum disorders (NMOSD). However, a wide range of etiologies may produce longitudinally extensive spinal cord lesions (LESCLs) on imaging. We highlight the case of a patient with a spinal cord tumor whose imaging showed LESCL and was diagnosed with LETM. He did not respond to immunosuppression and subsequently developed a progressive and protracted clinical course. Thoracic cord biopsy performed 6 years after symptom onset showed primary spinal oligoastrocytoma. We discuss the features that should raise suspicion of a neoplasm in the context of LESCL and serve a reminder that not all LESCLs are inflammatory.

1. Introduction

Longitudinally extensive transverse myelitis (LETM) is defined as an intramedullary lesion extending over 3 or more vertebral segments in the context of suspected inflammatory spinal cord syndrome (Kitley et al., 2012). It is most commonly associated with neuromyelitis optica spectrum disorders (NMOSD) and is an important feature of the 2015 international consensus diagnostic criteria for neuromyelitis optica spectrum disorders (Wingerchuk et al., 2015). However, longitudinally extensive spinal cord lesions (LESCLs) can not only be seen in immune mediated inflammatory-demyelinating conditions, but also in a diversity of pathologies that include infectious, vascular, neoplastic, paraneoplastic and metabolic causes (Kitley et al., 2012). These etiologies need to be carefully considered in a patient presenting with LESCL.

2. Case report

A 51-year-old Chinese male presented to another hospital in July 2008 with gradual onset bilateral thigh numbness and weakness over a few months. Magnetic resonance imaging (MRI) of the thoracic spine showed a non-enhancing T2-hyperintense lesion from T8 to T12 with cord expansion (Fig. 1A). Syphilis serologies, anti-double stranded DNA antibody, complement levels, anti-Ro antibody, anti-La antibody, anti-Smith antibody, anti-ribonucleoprotein antibody, anti-topoisomerase 1 antibody and erythrocyte sedimentation rate were normal. Lumbar puncture was not performed and he was not treated with immunosuppression.

He presented to our hospital in August 2009 with progressive lower limb weakness, erectile dysfunction and urinary retention. Examination revealed spastic paraparesis and sensory level at T12. MRI spine showed a T2-hyperintense lesion from T6 to T12 with patchy contrast enhancement and cord expansion (Fig. 1B–E). Axial imaging showed it occupying nearly the entire cross-section of the cord at T8 with subtle contrast enhancement (Fig. 1F and G). MRI brain was normal. Cerebrospinal fluid (CSF) analysis showed 6 cells/μL, protein level of 41 mg/dL and oligoclonal bands negative. Serum aquaporin-4 (AQP4) antibody, human immunodeficiency virus serology, anti-nuclear antibody, anti-cardiolipin immunoglobulins and anti-neutrophil cytoplasmic antibody were negative. He was diagnosed with LETM and treated with pulsed intravenous (IV) methylprednisolone 1 g daily for 5 days followed by oral prednisolone taper, with symptomatic and objective improvement. He was able to ambulate independently, but this improvement plateaued after one month.

He remained stable till February 2010 when he noted worsening lower limb weakness. Further pulsed IV methylprednisolone did not provide improvement and he required ambulatory

* Corresponding author. Fax: +65 63577137
E-mail addresses: yeo.tianrong@singhealth.com.sg (T.R. Yeo), chin_fong_wong@ttsh.com.sg (C.F. Wong), joycelyn.lee.j.x@nccs.com.sg (J.J.X. Lee), valerie.ng@mohh.com.sg (V.Z.Y. Ng), kevin_tan@nni.com.sg (K. Tan).

http://dx.doi.org/10.1016/j.msard.2015.09.003
2211-0348/

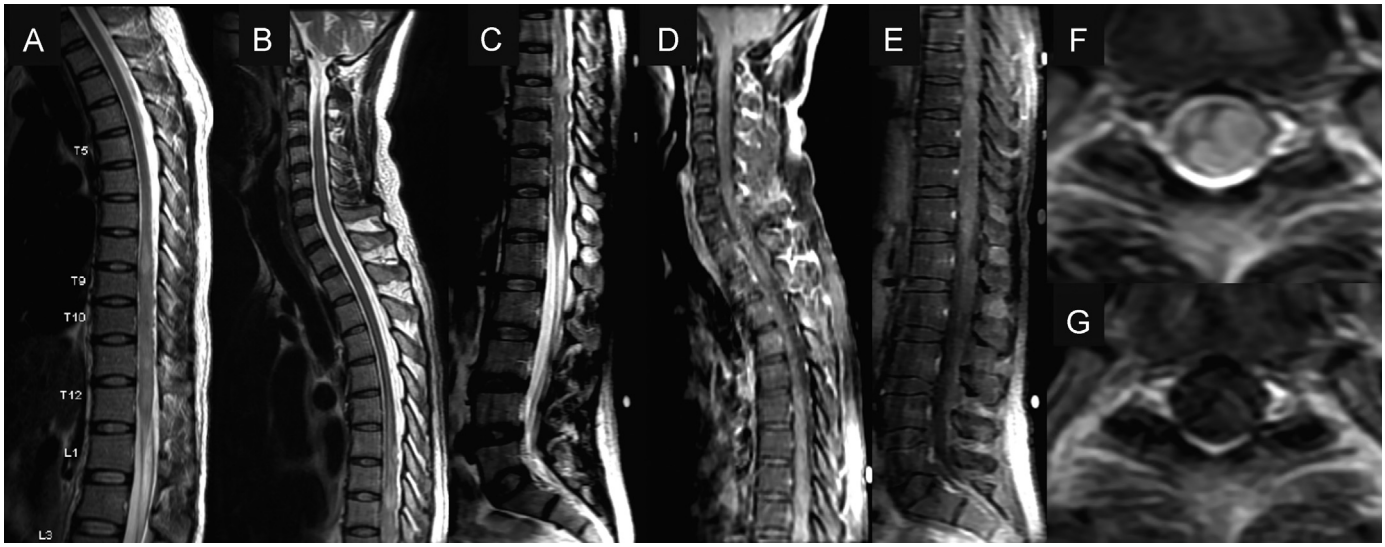

Fig. 1. Serial MRI spine from 2008 to 2009. (A) MRI spine showing T2-hyperintense lesion from T8 to T12 with cord expansion in 2008. (B, C) Rostral extension of T2-hyperintense lesion to T6 with cord expansion and (D, E) subtle patchy contrast enhancement in 2009. (F) Axial imaging showing the lesion occupying nearly the entire cross-section of the cord at T8 with (G) subtle contrast enhancement in 2009.

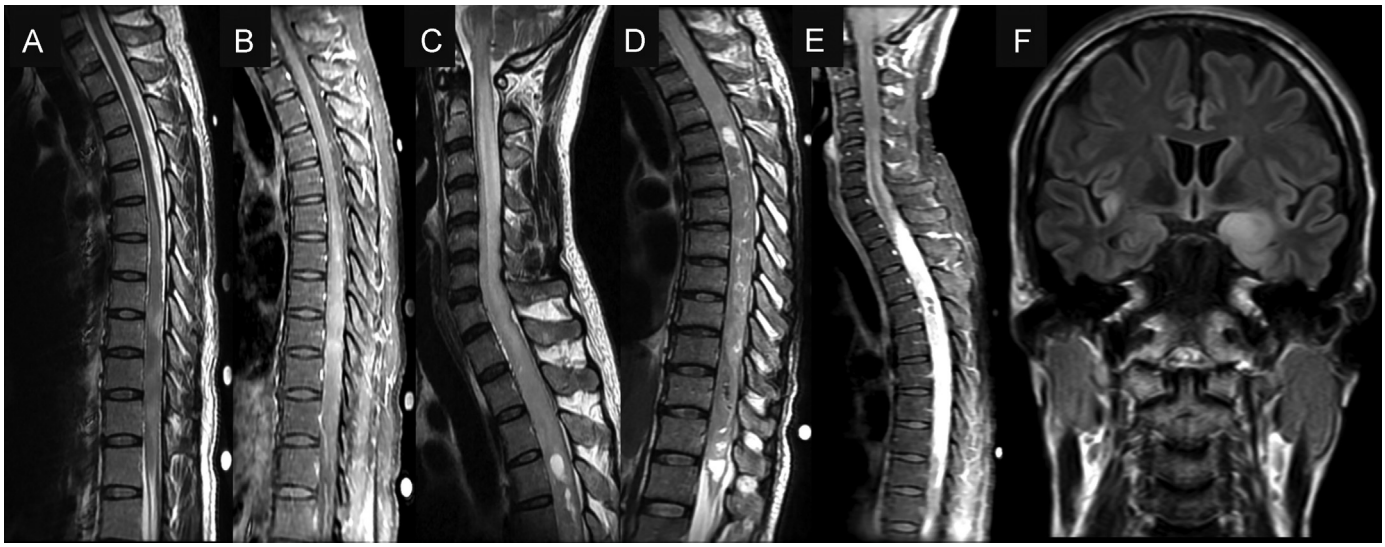

Fig. 2. Serial MRI spine and brain from 2010 to 2014. (A) Slight rostral extension of T2-hyperintense lesion to T5/6 junction with increased cord expansion and (B) increased heterogeneous contrast enhancement in 2010. (C, D) Extensive T2-hyperintense lesion from cervico-medullary junction to conus with marked cord expansion, cystic changes and (E) avid contrast enhancement in 2014. (F) MRI brain showing FLAIR abnormalities in the left medial temporal lobe, left caudate nucleus and right insular region in 2014.

assistance by September 2010. Radiological progression was noted with increased cord swelling and contrast enhancement (Fig. 2A and B). There was no response to additional pulsed steroids and 5 doses of monthly IV cyclophosphamide (15 mg/kg). He declined plasma exchange. In January 2011, his sensory level had progressed up to T8 and he required intermittent urinary catheterization. Repeat MRI spine showed stable findings. He declined further treatment with Rituximab as well as surveillance imaging. In 2012, he had become wheelchair-bound and subsequently developed recurrent urinary tract infections and pressure sores.

In February 2014, he developed gradual onset bilateral upper limb weakness. Examination revealed weakness of C7, C8 and T1 segments with complete paralysis of his lower limbs. MRI spine showed a T2-hyperintense, enhancing, cervico-medullary junction to conus lesion with marked cord expansion and cystic changes (Fig. 2C–E). In view of the clinical progression and neuroimaging findings, neoplasm was considered. Histology of cord biopsy performed at T10 confirmed World Health Organization (WHO) grade III oligoastrocytoma (Fig. 3). Fluorescent in-situ hybridization analysis of 1p19q chromosomal co-deletion was negative. MRI brain showed intracranial involvement with multiple areas of fluid attenuated inversion recovery (FLAIR) abnormalities (Fig. 2F). Palliative chemotherapy with temozolomide was commenced without clinical or radiological improvement.

3. Discussion

The distinction between inflammatory and neoplastic causes of LESCL can be challenging with intramedullary spinal cord tumor (IMSCT) mimicking myelitis and vice versa. Jacob et al. (2006) reported a case of cervical cord ependymoma that was mistaken as relapsing myelitis because of positive CSF oligoclonal bands and initial response to steroids. Neoplasm was suspected after the patient developed severe neck pain despite incremental steroids. Conversely, Brinar et al. (2006) reported 5 cases of inflammatory

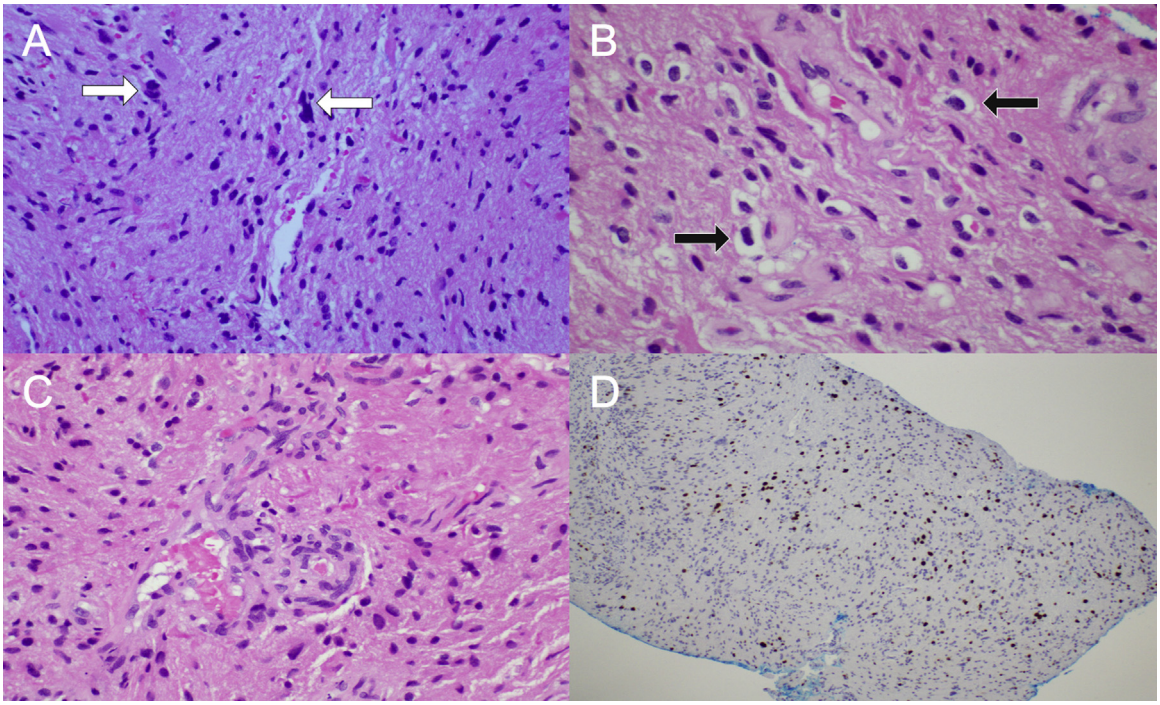

Fig. 3. Thoracic cord histology showing WHO grade III oligoastrocytoma. (A) Astrocytic component showing atypical cells with spindle shaped and bizarrely shaped nuclei (white arrows). (B) Oligodendroglial component showing 'fried egg' appearance of neoplastic oligodendrocytes (black arrows). (C) Microvascular proliferation within the tumor. (D) Ki-67 labeling 15% of tumor cells suggesting active cellular proliferation.

myelitis with cord enlargement on initial MRI scan resembling neoplasm leading to unnecessary spinal cord biopsies in 2 patients. Sato et al. (2014) also reported 2 cases of NMOSD with MRI scan findings of marked cord swelling and tumefactive changes. Spinal cord biopsies were performed in both patients and the diagnosis was only established after AQP4 antibody returned positive.

Our patient had a LESCL that extended over 5 vertebral segments on initial imaging. The presence of contrast enhancement on subsequent imaging together with a borderline elevated CSF cell count and initial favorable response to steroids led to a diagnosis of LETM. In retrospect, several features were present that could have suggested a neoplasm. Firstly, symptom onset was gradual and became progressive in nature, in contrast to an inflammatory transverse myelitis which usually presents acutely or sub-acutely with a nadir between 4 hours to 21 days following symptom onset (Transverse Myelitis Consortium Working Group, 2002). Secondly, although there was transient improvement after the first course of pulsed methylprednisolone, most probably from reduction of cord swelling, this response was not sustained. There was also no improvement after further immunosuppression with cyclophosphamide. Finally, the contiguous rostral extension of the lesion with persistent cord expansion on serial imaging should have raised the suspicion of neoplasm.

Another noteworthy feature was the histological diagnosis of primary spinal oligoastrocytoma, a rare IMSCT with mixed oligodendroglial and astrocytic components. To the best of our knowledge, there has been only one adult case of primary spinal oligoastrocytoma reported in the English literature (Tao et al., 2015). No brain abnormality was present in our patient initially to suggest a primary brain oligoastrocytoma that disseminated to the spinal cord. High-grade IMSCTs are usually treated with surgical resection with adjuvant radiotherapy; the role of chemotherapy is not clearly established (Traul et al., 2007; Zadnik et al., 2013). Regrettably, the advanced stage of the tumor in our patient at the time of diagnosis precluded these treatment modalities. Many IMSCTs have intracranial equivalents with molecular genetic markers; one such marker is the co-deletion of chromosomes 1p and 19q (Zadnik et al., 2013). The presence of this marker aid in the diagnosis of oligodendrogliomas and predicts favorable chemosensitivity with improved survival in anaplastic oligodendrogliomas (Mason and Cairncross 2008). This co-deletion was absent in our patient. Finally, it is unlikely that our patient could have harbored a high-grade IMSCT for 6 years. We postulate that he had a low-grade tumor that underwent transformation resulting in a faster rate of clinical deterioration in the latter stages of his illness.

Meticulous attention to the tempo of symptom onset, response to immunosuppression and regular serial imaging is recommended to avoid misdiagnosing an IMSCT as LETM. Features that should raise suspicion of neoplasm and prompt cord biopsy include; gradual onset of symptoms, progressive clinical course with poor response to aggressive immunosuppression and contiguous extension of cord lesion with persistent cord expansion on serial imaging. The presence of cord expansion on initial imaging does not reliably differentiate neoplasm from inflammation and initial response to steroids may occur in neoplasm due to reduction of cord swelling (Brinar et al., 2006).

Contributions

Dr Tianrong Yeo: design and conceptualization of the case report, analysis and interpretation of the data, drafting and revision of the manuscript.

Dr Chin Fong Wong: analysis and interpretation of the data, drafting and revision of the manuscript.

Dr Joycelyn Jie Xin Lee: drafting and revision of the manuscript.

Dr Valerie Zhi-Yan Ng: drafting and revision of the manuscript.

Dr Kevin Tan: analysis and interpretation of the data, drafting and revision of the manuscript.

Disclosures

Dr Tianrong Yeo, Dr Chin Fong Wong, Dr Joycelyn Jie Xin Lee and Dr Valerie Zhi-Yan Ng report no disclosures.

Dr Kevin Tan has received compensation from Novartis and Biogen Idec for consulting services and honoraria from Biogen Idec, MerckSerono and UCB.

Acknowledgments

The authors thank Dr Chee Kian Tham for his review of the manuscript.

References

Kitley, J.L., Leite, M.I., George, J.S., et al., 2012. The differential diagnosis of longitudinally extensive transvere myelitis. Mult. Scler. 18, 271–285.
Wingerchuk, D.M., Banwell, B., Bennett, J.L., et al., 2015. International consensus diagnostic criteria for neuromyelitis optica. Neurology 85, 177–189.
Jacob, A., Das, K., Boggild, M., et al., 2006. Inflammation or neoplasm? Another side to the story. Clin. Neurol. Neurosurg. 108, 811–812.
Brinar, M., Rados, M., Habek, M., et al., 2006. Enlargement of the spinal cord: inflammation or neoplasm? Clin. Neurol. Neurosurg. 108, 284–289.
Sato, D.K., Misu, T., Rocha, C.F., et al., 2014. Aquaporin-4 antibody-positive myelitis initially biopsied for suspected spinal cord tumors: diagnostic considerations. Mult. Scler. 20, 621–626.
Transverse Myelitis Consortium Working Group, 2002. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 59, 499–505.
Tao, H., Lu, R., Yin, B., et al., 2015. Magnetic resonance imaging of primary spinal anaplastic oligoastrocytoma (World Health Organization Grade III) in an adult: a case report. IJDI 2, 15–20.
Traul, D.E., Shaffrey, M.E., Schiff, D., 2007. spinal-cord neoplasms-intradural neoplasms. Lancet Oncol. 8, 35–45.
Zadnik, P.L., Gokaslan, Z.L., Burger, P.C., et al., 2013. Spinal cord tumours: advances in genetics and their implications for treatment. Nat. Rev. Neurol. 9, 257–266.
Mason, W.P., Cairncross, J.G., 2008. Invited article: the expanding impact of molecular biology on the diagnosis and treatment of gliomas. Neurology 71, 365–373.