Clinical Neurology and Neurosurgery 139 (2015) 91–94

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

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

Case Report

Isolated central nervous system Whipple's disease: Two cases

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ARTICLE INFO

Article history:
Received 7 May 2014
Received in revised form 2 July 2015
Accepted 22 August 2015
Available online 28 August 2015

Keywords:
Whipple's disease
Central nervous system
Infection
Magnetic resonance imaging
Histopathology

ABSTRACT

Although it is an orphan disease, isolated central nervous system Whipple's disease is one of the "must be known" conditions in neurology because it belongs to the list of "treatable disorders". Here, we present two cases which highlight the importance of early diagnosis. Additionally, we provide a discussion on up to date diagnostic approach to this life-threatening disorder.

1. Introduction

Isolated central nervous system (CNS) Whipple's disease (WD) without systemic manifestations is a very rare, life threatening but treatable condition. The disease has no specific symptoms and almost all the patients present with unusual, contrast enhancing MRI lesions [1–3]. Its differential diagnosis includes a long list of diseases with completely different pathophysiology and conflicting treatment options. Misdiagnosed patients will most probably receive immunosuppressive agents for other diagnosis and this will cause further amelioration of these patients. As the disease is confined to the CNS, diagnosis is often difficult and clinical/radiological suspicion plus utilization of appropriate tools after CNS biopsy is the key. Here, we report two cases with possible isolated CNS Whipple's disease with two different outcomes. First patient was recognized early and successfully treated with antibiotics and the second was diagnosed later after a trial of immunosuppressive treatment and lost eventually. We emphasize neuroimaging findings which provided the basis leading to the diagnosis in both patients and discuss the diagnostic approach from neurologists' perspective.

2. Case I

56 years-old male presented with headache, gait difficulty and rapidly progressive cognitive impairment. On admission he was moderately ataxic, confused and disoriented to time. He had circumstantial speech and could not repeat long sentences. Impairment in recent memory was evident. Brain magnetic resonance imaging (MRI) showed bilateral T2-signal hyperintensities surrounding third and lateral ventricles involving hippocampus, hypothalamus, medial thalamus, crus cerebri in mesencephalon and confluent white matter lesions in the centrum semiovale. Mild ependymal and pial contrast enhancement was evident; and some of the parenchymal lesions had micronodular contrast enhancement (Fig. 1A). Neuropsychological evaluation revealed severe impairment in all cognitive domains. Initial evaluation of the patient included differential diagnosis of inflammatory, granulomatous, infectious and lymphoproliferative diseases which were all excluded by appropriate laboratory and imaging methods. Mediobasal involvement and preference of lesions for deep periventricular areas along with ependymal involvement raised the suspicion of cerebral WD. Duodenal biopsy from multiple sites was negative for PAS and PAS-diastase staining. Brain biopsy from right temporal lobe revealed microinfarct area containing CD68 and PAS positive, myelin negative macrophages in white matter

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http://dx.doi.org/10.1016/j.clineuro.2015.08.028
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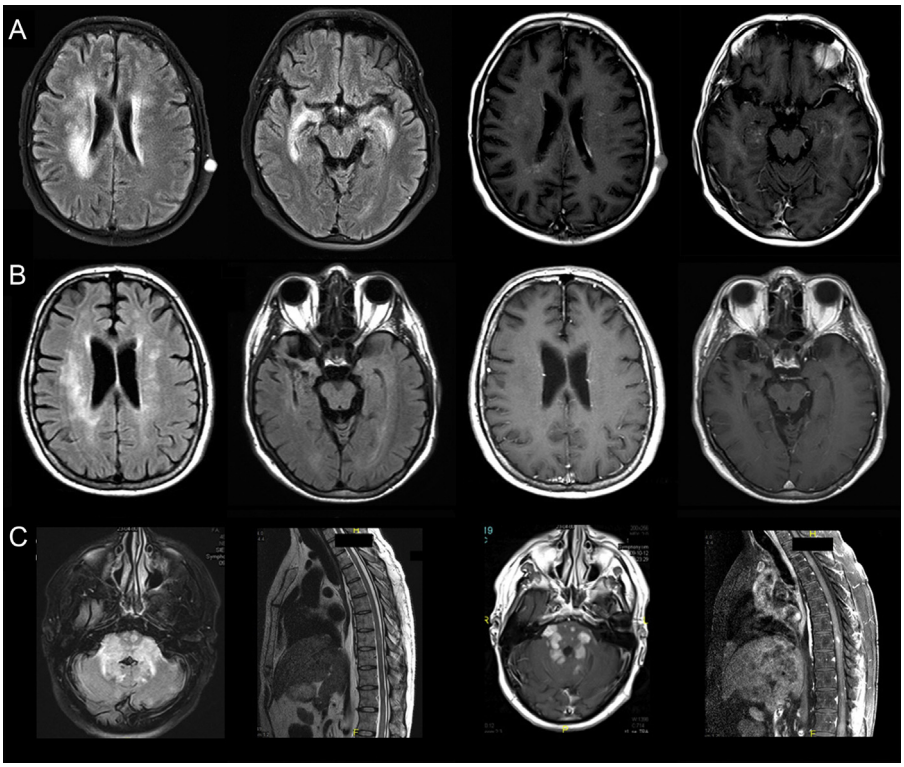

Fig. 1. Axial FLAIR imaging (TR/TE/TI; 8500/100/2000 ms) and postcontrast T1-W imaging series obtained at presentation (A) and 6th months after treatment (B) in patient one and at presentation in patient two (C). Prominent periventricular hyperintensity and micronodular contrast enhancement are seen in the basal temporal lobes and deep cerebral white matter. Progressive ependymal contrast enhancement is also observed (A). 6 months following the diagnosis and treatment, disappearance of periventricular hyperintensity along with ependymal contrast enhancement with some residual nonenhancing hyperintense lesions. Please note the postsurgical defect of the right temporal lobe and absence of the left parietal subcutaneous nodule due to its excision for pathologic examination (B). Axial lesions mainly in the middle cerebellar pedincules, brain stem and cerebellum with nodular contrast enhancement is seen. Cervical and thoracal lesions with contrast enhancement are also present in patient two (C).

suggesting diagnosis of Whipple's encephalitis (Fig. 2). Ceftriaxone (i.v., 2 g/day) was administered for 14 days after which all of the patient's symptoms and signs improved dramatically. He was discharged with trimethoprim/sulfamethoxazole (800/160 mg/day). Brain MRI showed regression of the lesions after six months, though cortical atrophy and ventricular dilatation were evident (Fig. 1B). Neuropsychological evaluation on the first and sixth months of treatment confirmed a dramatic improvement in all of the cognitive domains. Three years after discharge, patient is living independently with some neuropsychiatric sequela.

3. Case II

28-year-old, male patient applied to a local hospital with left sided hypoesthesia, polydipsia and polyuria. MRI showed infundibular thickening. He was diagnosed with lymphocytic hypophysitis and desmopressin treatment was given. After three years he developed progressive ataxia. Brain MRI showed multiple T2A hyperintense, nodular lesions mainly in the middle cerebellar peduncles, brain stem, cerebrum, cerebellum, basal ganglia, optic chiasm and hypothalamus with contrast enhancement. Diagnostic efforts including stereotactic brain biopsy from cerebellum did not give any result. He was given steroid and azathioprine treatment. His condition continued to decline under immunosuppressive treatment. Patient was bed-ridden when he was admitted to our hospital at this stage. Neurological examination revealed diplopia, left-sided horizontal gaze palsy, severe dysarthria, extremity and truncal ataxia, paraparesis hemihypoesthesia on left side, bilaterally positive Babinski sign and clonus. Brain and spinal MRI revealed expansion of contrast enhancing nodular lesions (Fig. 1C). MR spectroscopy was not suggestive for malignant CNS neoplasms or lymphoma. Extensive work-up were negative for all of the differential diagnosis. Duodenal biopsy was negative for PAS positive macrophages. Axial preference and nodular contrast enhancement

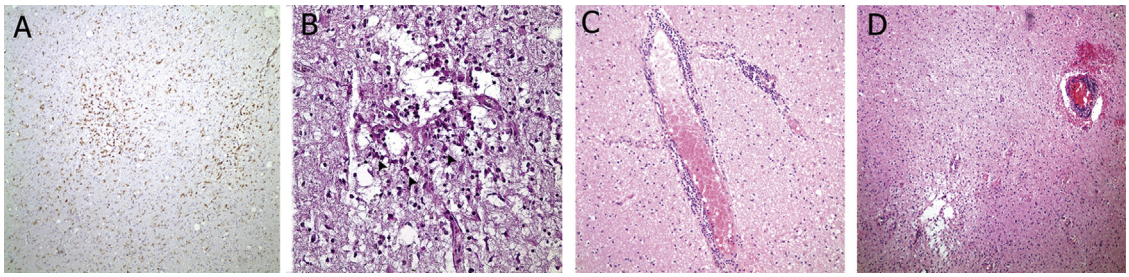

Fig. 2. Histological examination of the lesion from right temporal lobe showed numerous CD68 positive macrophages in parenchyma (A), many of them histochemically PAS (+) (B, arrowheads). Polyclonal lymphocytic cuffing, immunohistochemically CD3 and 20 positive (not shown), around microvessels is seen (C). Microinfarct area infiltrated by foamy macrophages is shown at the lower left part of figure (D).