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Short communication

An atypical case of neuro-Whipple: Clinical presentation, magnetic resonance spectroscopy and follow-up

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ABSTRACT

We report a case of a 53-year-old man with a 2-year history of progressive gait and balance disturbance, supranuclear ophthalmoparesis, mild dysarthria and dysmetria. EMG revealed a lower limb axonal sensory–motor neuropathy, while MR imaging demonstrated a small focal lesion in the right frontal lobe, mild diffuse hyperintensity of the periventricular white matter and diffuse brain atrophy. Magnetic resonance spectroscopy revealed a mild decrease in N-acetyl-aspartate peak and an increase in the choline peak in the small right frontal lesion and within 6 voxels of interest in normal appearing cerebral tissue. According to the clinical picture the diagnosis of WD was made by the positivity of PCR for *T. whipplei* DNA on CSF. After treatment the patient showed a mild clinical improvement although MR images and laboratory test remained unchanged. The MRS findings suggest that the pathological process of the disease diffusely involves the brain. Despite the absence of gastrointestinal involvement WD should be suspected in all complex and atypical neurological pictures, even in presence of peripheral involvement, in order to be able to start treatment promptly.

1. Introduction

Whipple disease (WD), or intestinal lipodystrophy, is a rare, chronic, relapsing, multisystem infectious disease caused by *Tropheryma whipplei*, a Gram-positive bacillus that can affect any organ [1]. The clinical picture of WD is often multifaceted, but the typical presentation of the infection indicates a gastrointestinal involvement with diarrhoea/steatorrhoea, weight loss, malabsorption and abdominal pain [2]. CNS involvement occurs in 10–40% of cases either at the onset or, more often, in the later stages of the disease; only 5% of patients with WD present with exclusively neurological symptoms, which consist of dementia, ocular movement disturbances, myoclonus, oculomasticatory myorhythmias, epileptic seizures or hypothalamic derangement. Peripheral nerve and muscle involvement are even rarer [3]. We here describe a case of WD with an atypical neurological presentation, MRS findings and 2-years follow-up.

2. Case report

A 53-year-old man, with a history of bilateral diffuse uveitis treated unsuccessfully with topical and systemic corticosteroids, migratory seronegative arthritis treated with corticosteroids and non-steroidal anti-inflammatory drugs and thyroidectomy following thyroid carcinoma, was admitted to our hospital with a 2-year history of progressive gait and balance disturbance. No history of gastrointestinal symptoms, or recurrent aphthous or herpetiform orogenital ulceration was reported. The neurological examination revealed supranuclear ophthalmoparesis, mild dysarthria and right dysmetria on finger-to-nose testing; gait was slightly broad-based, with difficulty on turns, impaired tandem, and mild latero-retropulsion; the patient could not walk without assistance. Lower deep tendon reflexes were absent; plantar responses were flexor; both legs showed muscle atrophy; vibration sense was slightly low in the distal segments bilaterally. A sensorineural hearing loss and mild cognitive decline involving attention were also detected. Serological tests revealed a mild systemic inflammation. EMG revealed a lower limb axonal sensory-motor neuropathy. Laboratory screening tests for secondary neuropathies were all negative. Onconeural antibodies and main serologic neoplastic markers were normal. Gastroduodenoscopy and colonoscopy at macroscopic examination did not reveal any

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major pathologies. Bone scintigraphy and total-body CT scan were negative. Serum angiotensin converting enzyme concentration and broncho-alveolar lavage were normal. Neurological paraneoplastic syndrome and neurosarcoidosis were thus ruled out. MR imaging demonstrated a small area of increased signal in the right frontal lobe and mild diffuse hyperintensity of the periventricular white matter (Fig. 1A). Diffuse brain atrophy was also evident (Fig. 1B).

In order to better clarify the etiology of the neuropathy, CSF analysis was performed and showed pleocytosis (17 cells/μL) with normal glucose and protein levels, and screening examinations for infectious agents were negative. Even if at the time of the admission in our hospital patient did not complain of any joint disturbances, owing to the presence of signs of nervous system involvement combined with the anamnestic data of uveitis and migratory arthritis, WD was suspected despite the absence of gastrointestinal symptoms. CSF polymerase chain reaction (PCR) was positive for *T. whipplei* DNA, but was negative on serum. Small bowel biopsies resulted PAS negative.

Proton magnetic resonance spectroscopy (MRS) was also performed. The MRS scan of the small right frontal lesion and 6 bilateral and symmetrical voxels of interest (VOIs) placed in normal appearing frontal and paratrigonal white matter and basal ganglia (Fig. 1C) revealed a mild decrease in N-acetyl-aspartate (NAA) peak and an increase in the choline peak (Fig. 1D).

The patient was treated with intravenous sulfamethoxazole and trimethoprim (800/160 thrice per day) for 2 weeks. This treatment, which was continued orally at the dosage of 800/160 twice per day for 1 year following discharge, led to an improvement in the neuropathy and, consequently, in gait disturbance. Lower deep tendon reflexes reappeared. Indeed, the patient was once again able to walk without assistance. The course of uveitis seemed unrelated to the antibiotic administration and the patient experienced some relapses partially responding to systemic and topic corticosteroid therapy.

At the 1-year follow-up, PCR for *T. whipplei* was still positive on CSF and negative on serum. At the 2-year follow-up, the neurological examination was stable and the MRI unchanged. CSF PCR was still positive.

3. Discussion

WD, first described by George H. Whipple in 1907 [4], is an infectious disease that usually affects middle-aged Caucasian men. The CNS may be affected in as many as 43% of patients with WD during the disease course [5]. Peripheral neuropathy is a very rare symptom of WD, often caused by malabsorption.

We describe a case of WD with central and peripheral nervous system involvement diagnosed by PCR in CSF. Our patient presented with isolated neurological features and in particular with an axonal

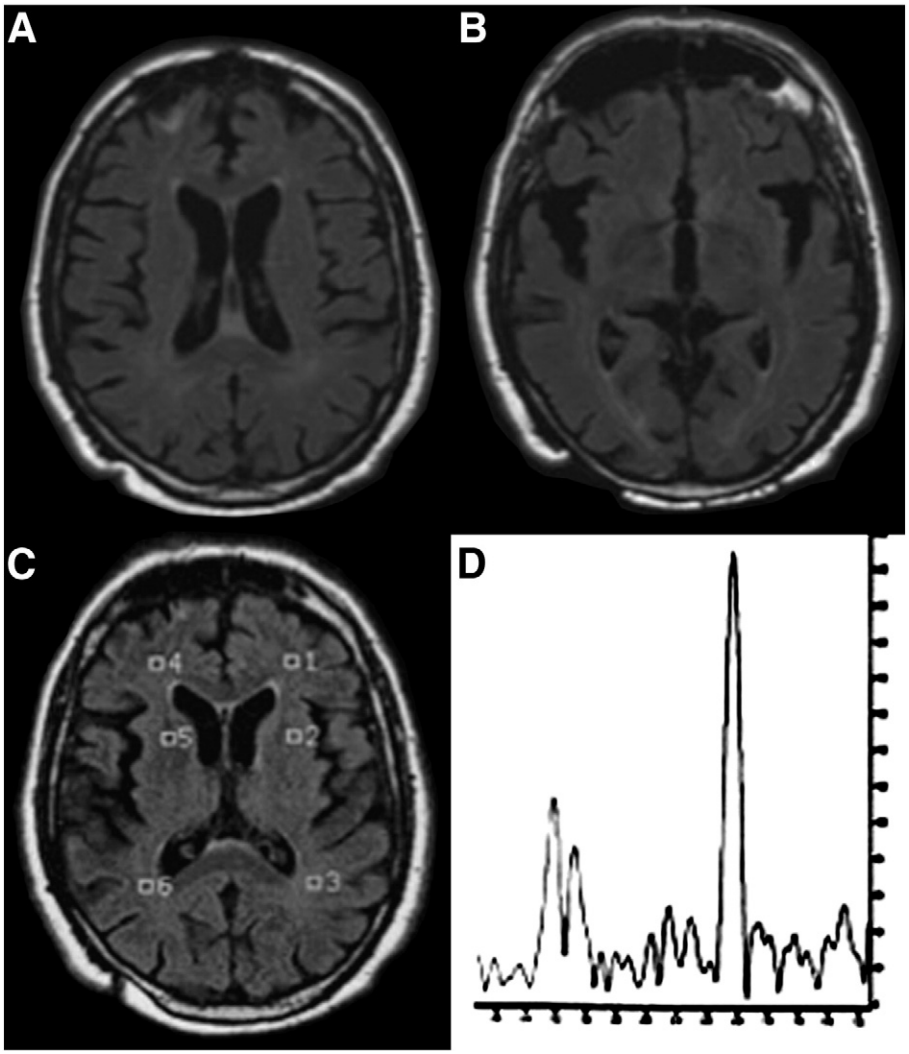

Fig. 1. MRI (FLAIR 6000/100) shows a small area of increased signal in the right frontal lobe (A) and diffuse brain atrophy (B) Multivoxel H1-spectrum of six VOIs in frontal, paratrigonal white matter and basal ganglia (C) shows a decrease in NAA peak and an increase in choline peak (D).