LETTER TO THE EDITOR

A new case of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids with initial normal magnetic resonance imaging

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Sir, We read with great interest the recent article published in Brain by Pittock et al. (2010), who reported eight patients with clinical, radiological and pathological features of brainstem involvement responsive (but dependent) to steroid treatment.

All the reported patients shared common clinical and MRI findings: gait ataxia, diplopia, patchy increased T2 signal and gadolinium enhancement within the pons and the middle cerebellar peduncles, the presence of oligoclonal bands on CSF analysis, and normal cerebral angiography. Involvement of the medulla, the cerebellum, the midbrain, the basal ganglia, the corpus callosum and the spinal cord has also been described. Brain biopsy of four patients found white matter T-lymphocytic infiltrate with perivascular predominance. Steroids led to clinical and neuroradiological improvement in all patients, with steroid dependency in three (mean follow-up: 22 months, range: 7–144 months). CLIPPERS (acronym for chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids) was proposed to describe this new entity. The authors suggest that this disorder may be under-recognized.

We report a 46-year-old male who presented with features of CLIPPERS. The disease started at the age of 13 years with a left peripheral facial palsy subsiding spontaneously (i.e. without steroid treatment) after 1 month. In the following 30 years, the patient successively developed other brainstem symptoms including hearing impairment, right peripheral facial palsy, horizontal binocular diplopia, gait ataxia and intractable hiccup. All these attacks were successfully treated with high-dose intravenous methylprednisolone (3 or 5 days, 1000 mg/day). During the past 9 years, several brain MRIs showed no abnormalities and CSF oligoclonal bands were present. Extensive laboratory investigations were normal, including aquaporin-4 water channel and onconeural antibodies. Whole body FDG-PET and labial salivary gland biopsy were normal. At age of 46 years, the patient developed a rapidly progressive left peripheral facial palsy associated with gait ataxia, dysarthria, dysphagia, tetraparesis and apathy. For the first time, MRI examination was abnormal. Hyperintense signal on the T2-weighted and FLAIR sequences associated with patchy gadolinium enhancement on T1 sequence was seen in the pons, the medulla oblongata and the mid-brain, extending to the left head of the caudate nucleus (Fig. 1A–C). Spinal MRI and conventional cerebral angiography were normal. Biopsy of the pons revealed parenchymal and perivascular T-lymphocytic infiltrates without demyelination, granulomatous inflammatory or necrotizing vasculitis pattern (Fig. 1G, H). One month after intravenous methylprednisolone treatment (1000 mg daily for 5 days), the patient’s symptoms improved dramatically with mild persistent spastic ataxia, and brain MRI showed spectacular improvement (Fig. 1D–F). Empirci anti-CD20 treatment (intravenous rituximab 375 mg/m2 weekly for 4 weeks) was started, associated with oral prednisone. The patient remained relapse free during the subsequent 9 months.

Clinical and MRI findings could suggest a differential diagnosis, such as neurosarcoidosis, neuroBehçet’s disease, CNS lymphoma,
Histioctysis and paraneoplastic disease. Extensive evaluations excluded these diagnoses in our patient and the previously reported cases (Pittock et al., 2010).

CLIPPERS shares some features with Devic’s disease and primary central nervous system vasculitis. However, absence of aquaporin-4 antigenic target, absence of demyelinating abnormalities on biopsy and preferential involvement of the brainstem are against the diagnosis of Devic’s disease. Primary central nervous system vasculitis seems to be less sensitive to steroid treatment and not strictly confined to the pons (Salvarani et al., 2007). Therefore, we agree with Pittock and co-authors (2010) that their described patients (such as our patient) seem to have a disorder distinctive of Devic’s disease and primary central nervous system vasculitis, described as CLIPPERS.

Unlike the patients reported by Pittock et al. (2010), initial MRIs in our patient (>9 years) showed no abnormalities. This case suggests that serial MRI examinations may be necessary when a diagnosis of CLIPPERS is suspected, in the absence of initial MRI abnormalities. Our report confirms that patients with clinical and MRI features typical of CLIPPERS could be treated without pathological examination, after excluding differential diagnosis.

References