PostScript

LETTERS

Unusual magnetic resonance imaging and cerebrospinal fluid findings in paraneoplastic cerebellar degeneration: a sequential study

Paraneoplastic cerebellar degeneration (PCD) is considered to be an autoimmune disorder, the clinical symptoms of which include dizziness, blurred or double vision, oscillopsia, and gait difficulties, which are not related to direct tumour invasion, adverse effects of chemotherapy, malnutrition, or infection.¹ Some patients also develop multifocal neurological deficits through the evolution of the disease, involving multiple areas of the central nervous system (CNS), resulting in a miscellany of symptoms derived from limbic encephalitis, brainstem encephalitis, and myelitis, and known as paraneoplastic encephalomyelitis. The current pathogenic hypothesis is that the CNS lesions are immune mediated. The CSF may reveal no cells or pleocytosis and increased levels of proteins, and may exclude neoplastic cells and infections. Cranial magnetic resonance imaging (MRI) in PCD is usually normal or shows global cerebellar atrophy. Pathological studies show a diffuse loss of Purkinje cells throughout the cerebellar cortex. We describe a case of PCD with unusual findings.

A 51 year old woman was referred with a 1 month history of gait instability, personality and mood changes. Her medical history was remarkable for cigarette smoking (60 cigarettes/day) and depression. The clinical picture rapidly progressed to severe limb and truncal ataxia, dysarthria, and dysphagia that required nutritional support. She complained of double vision, difficulty in opening the eyes, and weight loss. General examination was significant for cachexia. Neurological examination revealed truncal ataxia, tremor affecting arms, head and, trunk, and she was unable to stand without aid. She had an apparently normal mental status; she obeyed simple commands and correctly named common objects, although the marked dysarthria made it difficult to understand her and to explore the cognitive status further. She had "dancing eye" movements and blepharospasm. Strength was normal, tendon reflexes were depressed in the lower limbs and flexor plantar responses. The patient subsequently had difficulties with orientation, recall, and attention. A month later, she developed choreodystonic postures of the head and arms, intermittent rhythmical rest tremor in the fingers, and episodic side to side head "bobbing headed doll" movements.

Computed tomography of the chest showed a small left hilar mass and a paratracheal lymph node. Because of the patient's clinical deterioration, the thoracic surgery service declined to perform thoracotomy to evaluate these findings. Bacterial,

viral, and cytology tests were negative, as was a test for 14-3-3. Antineuronal antibodies in the cerebrospinal fluid (CSF) and serum were positive for anti-CV2 by immunoblot and immunohistochemistry in rat cerebellum frozen sections. Four months later, the patient could follow simple commands such as protrusion of the tongue, but she was not able to perform any voluntary limb movement. She showed a dystonic posture of the head towards the left, the upper limbs were rigid in flexion, the feet and toes were fixed in forced flexion, and the mouth was forced opened constantly.

A magnetic resonance imaging (MRI) scan performed 2 months after the onset of neurological symptoms (fig 1A,B), revealed oedema at the cerebellar cortex with blurring of the sulci and a hyperintense signal bilaterally in the caudate nuclei (fig 1C) and in the medial part of the bilateral temporal lobes (not shown), without gadolinium enhancement. CSF examination revealed lymphocytic pleocytosis (35 cells/mm³), elevated protein levels (195 mg/dl, reference range, 10-40) and high IgG index (1.62, normal value, <0.70). Using four colour flow cytometry on CSF, we found CD3+ T cells forming 92% of total lymphocytes, with 70% CD4+ T cells, 18% CD8+ T cells, and an evident recruitment of BDCA-2+ HLA-DR+ CD4+ plasmacytoid dendritic cells (pDCs) within the central nervous system (1.4% in CSF versus 0.6% in peripheral blood). In peripheral blood, a high percentage of regulatory CD4+ CD25^{bright} T cells was apparent (4.2% of CD4+ T cells, normal range <1.5-2%) as well as intermediate CD4+ CD25+ T cells (33%, normal range 5-10%). A repeat MRI 2 months later revealed a marked atrophy of the vermis and hemispheric cerebellar structures (fig 2D, E). The hyperintensity of both caudate nuclei was still evident (fig 2F), and new lesions in the lenticular nucleus emerged. A new CSF analysis revealed 5 lymphocytes/mm³, 1.49 g/l proteins, and IgG index of 1.25.

This was an unusual case of PCD probably secondary to lung cancer (LC) as suggested by chest CT imaging. Detection of CV2 neuronal antibodies in the CSF and serum of our patient served as serological markers of paraneoplastic syndrome. CV2 neuronal antibodies may occur in patients with paraneoplastic chorea and LC² and in paraneoplastic limbic encephalitis,³ as in the present case. The current pathogenic hypothesis is that paraneoplastic CNS lesions are humoral and cellular immune mediated. We found enrichment of pDCs in the CSF compared with those in the circulation. Recruitment of DCs into the CSF in the context of a paraneoplastic syndrome has not been previously reported, although it has been shown for other inflammatory CNS disorders.⁴ Recent studies suggest that DCs located in tumour draining lymph nodes play a crucial role in the process of engulfing tumour cells, processing and presenting the tumour antigen and thus priming T cell response.⁵ Thus, the presence of pDCs within the CSF could be relevant, given the role of cytotoxic T cells in the pathogenesis of PCD and the subsequent neuronal loss. In addition, we found expansion of circulating regulatory T cells (CD4+

Figure 1 (A-C) Cranial MRI, October 2003. Coronal T2 (A) and T1 weighted (B) images revealed an oedematous aspect of the cerebellar cortex with an abnormal signal and blurring of sulci. Axial FLAIR images showed bilateral hyperintensity in both caudate nuclei (C) and also in the medial aspect of temporal lobes (not shown). (D-F) Second cranial MRI, December 2003. Coronal T2 weighted image (D) showed marked atrophy of the hemispheric cerebellar structures in addition to abnormal hyperintensity of the white matter in the cerebellar lobes. Sagittal T1 weighted image (E) showed global atrophy of cerebellar vermis. (F) Axial T1 weighted image after the administration of gadolinium demonstrated hyperintensity of both caudate nuclei and new hyperintensity in both lenticular nuclei without pathological enhancement.

CD25+ and CD4+ CD25^{high}), although this test was not performed in the CSF. Such expansion may be playing a role in the progression of cancer.⁶ Indeed, regulatory T cells have been reported to selectively inhibit autologous immune response in the local tumour environment in patients with LC.⁷

The main initial MRI features were located at the cerebellum, which showed swelling and an abnormal signal of the cerebellar cortex concomitant with CSF pleocytosis, probably translating the inflammatory autoimmune process. These findings are unusual, as other authors have described cerebellar atrophy in PCD particularly later in the process, compatible with our second MRI. We hypothesise that in most cases, the diagnosis of PCD is carried out at later stages of the disease, when the cerebellar atrophy has been established after an initial inflammatory response. Supporting this idea, we found close similarities between our case and the case of Shoji *et al*⁸ with acute infectious cerebellar ataxia. In that case, the cerebellar oedema disappeared 1 month later, whereas in our case evolved to atrophy.

Altogether, our data suggest that the paraneoplastic syndrome is a dynamic process initially inducing inflammation and oedema and subsequently evolving to loss of brain tissue, and that the inflammatory autoimmune process contributes to the secondary brain degeneration.

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Abscess of the medulla oblongata following endotracheal intubation

A 71 year old man was admitted for a myocardial infarction following which he was successfully resuscitated for a cardiac arrest secondary to ventricular fibrillation. He was intubated and ventilated in the peri-arrest period. After extubation, he complained of neck pain and dysphagia. A flexible laryngoscopy examination revealed an oedematous left larynx. He was subsequently lost to follow up. His symptoms worsened over the next 2 months. He lost 15 kg in weight and suffered fevers and night sweats.

On readmission, he was cachectic. He had discomfort on moving his neck. He had a chest wall abscess and a hard lymph node attached to the left trapezius muscle. Magnetic resonance imaging (MRI) of the neck revealed a large retropharyngeal abscess with osteomyelitis of the C1 and C2 vertebrae. Aspiration of the chest wall abscess revealed methicillin resistant *Staphylococcus aureus*. Intravenous vancomycin and metronidazole were commenced and the neck was stabilised with a hard collar.

One week later, he complained of acute onset severe neck pain. He developed bulbar palsy and right sided weakness. MRI revealed an abscess in the posterior part of the medulla in continuity with the retropharyngeal collection (fig 1A) and multiple lung abscesses. He required a tracheostomy and positive pressure ventilation. It was felt that

surgical aspiration of the medulla abscess would be too risky, thus a halo traction brace was applied and conservative management with antibiotics was adopted.

He was weaned off the ventilator and the halo traction was replaced by a hard collar. It was not possible to wean him from his tracheostomy, because of a residual left sided bulbar palsy. He also required permanent gastrostomy feeding. His right hemiparesis improved, although he was left wheelchair bound. Repeat MRI 6 months after admission showed near resolution of the medulla abscess (Fig 1B). Antibiotics were continued for 10 months. The patient was discharged to a nursing home 8 months after admission and has shown continuing physical improvement in outpatient follow up.

Retropharyngeal abscesses are a rare but recognised complication of intubation.¹ They usually occur following foreign body ingestion (usually fish or chicken bones), pharyngotonsillitis, peritonsillar abscesses and dental infections.² They can cause great morbidity. Reported complications include airway obstruction, mediastinitis, empyema, septicaemia, osteomyelitis, and epidural abscesses.^{2–4} To our knowledge, this is the first case reported of an intraparenchymal brainstem abscess occurring as a complication of a retropharyngeal abscess.

Brainstem abscesses may arise spontaneously, or from haematogenous or contiguous spread, usually from the ears.⁵ Case mortality is thought to be high, but reports in the literature have, like this one, mainly been of single cases that have had a successful outcome. There is no consensus over management. Options include open surgical drainage, stereotactic aspiration, and medical management with antibiotics alone.⁵ Conservative management may be useful where the causative organism is known and/or the lesion would present too great a surgical risk, as in this case. Operative intervention is useful for identifying the

Figure 1 Post-gadolinium T1 weighted magnetic resonance imaging of the brainstem and cervical spinal cord. (A) One week post admission, showing the development of a medullary abscess in continuity with the retropharyngeal collection and C1/2 osteomyelitis; (B) 6 months later after prolonged antibiotic therapy demonstrating near resolution.