Paraneoplastic cerebellar degeneration: new insights into imaging and immunology

J H Rees

Brain imaging is usually remarkably unremarkable in paraneoplastic cerebellar degeneration

Paraneoplastic cerebellar degeneration (PCD) is still one of the most enigmatic of the autoimmune CNS disorders. It is relatively uncommon and is usually characterised by a rapid and severe cerebellar syndrome, leaving the patient dependent within a few weeks to months of onset. Brain imaging is usually remarkably unremarkable in PCD. Despite the presence of a very severe clinical deficit, the cerebellum is rarely affected radiologically at an early stage of the disease, although atrophy is usually seen some months after onset.

Three papers present unusual imaging features in PCD and provide some potential new insights into the pathogenesis of this disease (see pages 525, 529, 562 of this issue). The paper by Scheid *et al* reports cerebellar atrophy occurring within 1 month of symptom onset.¹ The patient had had an MRI brain scan carried out a year earlier to investigate migraine and the authors were therefore able to demonstrate a clear increase in diameter of the IVth ventricle implying loss of volume in adjacent cerebellar tissue. The second and third papers suggest that there is active inflammation in the early stages. De Andrés *et al* report cerebellar oedema occurring 2 months after symptom onset that progressed to marked atrophy 2 months later.² In the paper by Choi *et al*, brain and whole body FDG-PET imaging, used to search for an underlying tumour, showed striking cerebellar hypermetabolism 3 weeks after symptom

onset, associated with hyperperfusion in the whole cerebellum on SPECT scanning but a normal MRI and CSF.³ It is difficult to know whether these abnormalities are seen in the majority of patients with PCD or whether these case reports are worthy of publication because of the unusual findings. My own experience with FDG-PET suggests that brain PET is usually unremarkable and SPECT is rarely carried out for this indication.

Investigation of the CSF is another important procedure that rarely yields conclusive results. In the case of de Andrés *et al*, a 61 year old woman with a rapidly progressive cerebellar, extrapyramidal, and brainstem syndrome, anti-CV2 antibodies, and a left hilar mass and CSF pleocytosis (35 lymphocytes/mm³) was further investigated with flow cytometry. As expected, most lymphocytes were T cells (CD3⁺) and 70% of those were helper T cells (CD4⁺). There was recruitment of dendritic cells (DCs) supporting the hypothesis that these antigen-presenting cells play an important role in the initiation of the immune response in the CNS. It is postulated that DCs in draining lymph nodes engulf apoptotic tumour cells and then present them to T cells which in turn initiate both a cellular reaction against components of the cerebellum as well as promoting antibody production against specific cerebellar autoantigens. The observation by Scheid *et al*, therefore, that there were no lymph

node metastases in their case of PCD associated with breast cancer, suggests that migration of antigen-presenting cells to draining lymph nodes is not a prerequisite for immune activation against the cerebellum. There are numerous examples of undetectable tumours causing a paraneoplastic syndrome, making it unlikely that systemic antigen presentation is a sine qua non of the immunopathogenesis of this disorder. Finally, the delayed diagnosis of the breast cancer in this patient despite initially negative FDG-PET scanning, underscores how difficult it can be to find an occult malignancy, even with the most sophisticated imaging.⁴

Unfortunately the natural history of this debilitating disorder is rarely improved by treatment of the underlying tumour, presumably because there is early and irreversible neuronal and white matter loss.

There is clearly much to learn about this disorder. Single case reports such as these highlight interesting clinical variations and help to shed some light on an otherwise murky area, but the real breakthrough will only come when animal models can be established using human sera, as yet the holy grail of paraneoplastic research.

J Neurol Neurosurg Psychiatry 2006;**77**:427.
doi: 10.1136/jnnp.2005.082339

Correspondence to: Dr J H Rees, National Hospital for Neurology and Neurosurgery, Institute of Neurology, Queen Square, London, WC1N 3BG, UK; j.rees@ion.ucl.ac.uk

Competing interests: none declared

REFERENCES

- 1 Scheid R, Voltz R, Briest S, *et al*. Clinical insights into paraneoplastic cerebellar degeneration. *J Neurol Neurosurg Psychiatry* 2006;**77**:529–30.
- 2 De Andrés C, Esquivel A, de Villoria JG, *et al*. Unusual magnetic resonance imaging and cerebrospinal fluid findings in paraneoplastic cerebellar degeneration: a sequential study. *J Neurol Neurosurg Psychiatry* 2006;**77**:562–3.
- 3 Choi K-D, Kim JS, Park S-H, *et al*. Cerebellar hypermetabolism in paraneoplastic cerebellar degeneration. *J Neurol Neurosurg Psychiatry* 2006;**77**:525–8.
- 4 Rees JH, Hain SF, Johnson MR, *et al*. The role of fluorodeoxyglucose-positron emission tomography scanning in the diagnosis of paraneoplastic neurological disorders. *Brain* 2001;**124**:2223–2231.