

# SHORT REPORT

# Clinical insights into paraneoplastic cerebellar degeneration

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*J Neurol Neurosurg Psychiatry* 2006;**77**:529–530. doi: 10.1136/jnnp.2005.082206

Neuroimaging is usually unremarkable in paraneoplastic cerebellar degeneration (PCD), at least in the early stages of the disease. A patient with proven PCD is reported in whom it could be shown that cerebellar atrophy evolved very rapidly and was present in early imaging studies. Even with the use of the whole spectrum of modern diagnostic tools, the underlying malignancy can be difficult to diagnose. In addition to mammography, MRI is recommended in these cases and repeat FDG-PET may be necessary.

**P**araneoplastic cerebellar degeneration (PCD) is characterised clinically by the subacute development of usually severe ataxia, dysarthria, and nystagmus.<sup>1</sup> With few exceptions, patients suffer from gynaecological or breast cancers.<sup>1,2</sup> Studies and case reports of PCD, which include neuroradiological information, have shown cerebellar atrophy only in the late stages of the disease, if at all.<sup>1,3–6</sup> We report a patient in whom cerebellar atrophy could be documented very early by means of MRI. Our case study reveals additional possible features of PCD which have not been reported so far.

## CASE REPORT

In October 2003, a 45 year old woman with a medical history of migraine and myoma related hysterectomy developed progressive dysarthria, gait ataxia, and nystagmus. In November 2003, brain magnetic resonance imaging (MRI) was carried out and showed cerebellar atrophy. In January 2004, the patient was admitted to hospital. Anti-Yo antibodies were positive, and PCD was diagnosed. A comprehensive tumour search—including thoracic, abdominal, and pelvic computed tomography, abdominal and breast ultrasound, mammography, bone marrow biopsy, and whole body positron emission computed tomography (FDG-PET)—showed bilateral ovarian cysts, but was otherwise without pathological results. Initially, the patient's clinical state remained stable. Regular follow up examinations did not reveal an underlying malignancy. In spring 2005 the patient's ataxia progressed and she eventually became wheelchair-bound. MRI in May and August 2005 showed a slight increase in the cerebellar atrophy. A repeat whole body FDG-PET examination now showed an increase in tracer uptake in projections of the left mamillary area. Results of a gynaecological examination, mammography, and breast ultrasound were again unremarkable. However, MRI of the breast showed a contrast enhancing retromamillary lesion of approximately 9 mm diameter. In August 2005 the tumour was completely removed. Histologically, an invasive ductal carcinoma was diagnosed. In addition, axillary lymph dissection of level 1 (11 lymph nodes) and level 2 (eight lymph nodes) was carried out. All lymph nodes were microscopically free of metastases. Three months after surgery (December 2005) there was no further change in the patient's clinical and neurological state.

## DISCUSSION

PCD associated with anti-Yo antibodies is a well established paraneoplastic neurological syndrome.<sup>7</sup> However, there are four lessons to be learnt from our case.

Firstly, cerebellar atrophy at the start of a cerebellar syndrome may be caused by PCD. This observation is opposed to the current diagnostic criteria of paraneoplastic neurological syndromes, which define PCD as a pancerebellar syndrome of subacute onset "with no evidence of cerebellar atrophy other than that expected by the age of the patient".<sup>8</sup> In our patient, MRI showed cerebellar atrophy before her first hospital admission. The reliability of this finding can be proven, because a previous MRI showing a normal cerebellum had been done in March 2002 to investigate her migraine (fig 1, panels A and B). Neuropathologically, PCD is characterised by a pronounced loss of Purkinje cells, while the granular and molecular layers and the cerebellar nuclei are generally spared.<sup>9</sup> Bearing in mind that Purkinje cells form a single cell layer of approximately 30 µm height,<sup>10</sup> radiologically detectable atrophy should result from a secondary reduction in cerebellar white matter. The demonstration of early cerebellar atrophy in PCD may therefore hint at a prolonged immunological process, which may start long before clinical symptoms become apparent.

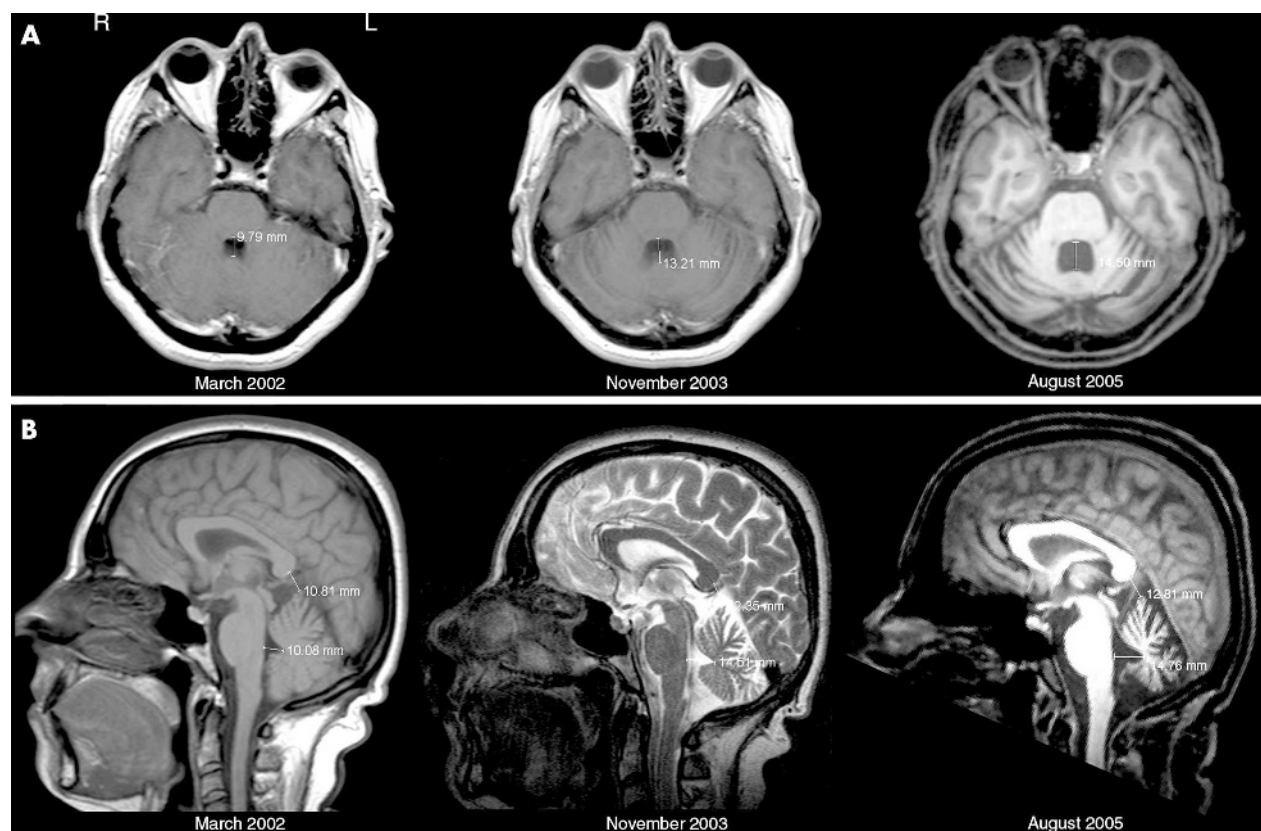
Second, this case shows that the course taken by PCD is not necessarily always subacute, but can be smouldering and slowly progressive.

Third, it has been assumed that the invasion of regional lymph nodes by tumour cells is a prerequisite for triggering the pathological immune process in paraneoplastic neurological syndromes.<sup>11</sup> However, our case shows that PCD can develop without definite lymph node metastases. It therefore seems that infiltration of the pre-nodal lymphatic tissues is sufficient to trigger the process.

Fourth, despite multiple elaborate approaches, the diagnosis of a tumour was not made until 22 months after the onset of the neurological disorder. Recently, the value of FDG-PET has been emphasised in the diagnostic work up of paraneoplastic neurological syndromes.<sup>12</sup> However, as our report shows, one negative PET is not definite proof of benign pathology, and a close follow up with further imaging may be required. It is also apparent that normal mammography may induce a sense of false security. Because of its increased sensitivity, breast MRI is appropriate in cases where there is a strong suspicion of malignancy. Our case also raises serious doubts over the therapeutic recommendation for ablative surgery which has been promoted from time to time in paraneoplastic neurological syndromes without a proven tumour.<sup>1</sup> In our patient, ovariectomy was initially advised. Fortunately, she did not consent to this, otherwise the "wrong organ" would have been removed.

In conclusion, patients with PCD need thorough and continued monitoring. A multidisciplinary diagnostic procedure is required, and the supervising physician should be familiar with paraneoplastic neurological syndromes. Although it is not always the case, there is the possibility of

**Abbreviations:** FDG, fluorodeoxyglucose; PCD, paraneoplastic cerebellar degeneration



**Figure 1** (A) Comparison between corresponding axial cerebellar magnetic resonance imaging (MRI) sections at three different times. Left and middle: contrast enhanced T1 weighted images (slice thickness = 6 mm, time of repetition (TR) = 450 ms, time of echo (TE) = 10 ms) in March 2002, and November 2003, respectively. Right: non-contrast enhanced T1 weighted MDEFT image (slice thickness 5 mm, TR = 1300 ms, TE = 10 ms) in August 2005. It can clearly be seen that the atrophic process started before November 2003, as is documented by the widening of the fourth ventricle by 3.4 mm, as compared with March 2002. Additional enlargement of the fourth ventricle by 1.3 mm by August 2005 indicates further moderate progression of the cerebellar atrophy. Note also the increasing width of the cerebellar sulci bilaterally. (B) Midsagittal MRI sections in March 2002 (T1 weighted image; slice thickness = 5 mm, TR = 450 ms, TE = 11 ms), November 2003 (T2 weighted image; slice thickness = 3 mm, TR = 7010 ms, TE = 123 ms), and August 2005 (T1 weighted MDEFT image; slice thickness = 5 mm, TR = 1300 ms, TE = 10 ms) document substantial enlargement of the fourth ventricle and also of the cerebellar cistern in the second image. (Note: Because the MRI studies were done by different investigators and in part because of different signs and symptoms, the imaging modes are not congruent.) MDEFT, modified driven equilibrium Fourier transform.

detecting cancer at a stage which allows recovery, and when quality of life has not already been excessively impaired.

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Competing interests: none declared

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Received 11 October 2005

In revised form 6 December 2005

Accepted 6 December 2005

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