Ataxic type of Creutzfeld-Jakob disease with disproportionate enlargement of the fourth ventricle: a serial CT study

There are few reported neuroimaging studies on the ataxic type of Creutzfeld-Jakob disease. In our patient MRI and serial CT disclosed a progressive enlargement of the fourth ventricles as a major finding.

A 64 year old woman developed progressive gait unsteadiness in June 1994; she was then evaluated in another hospital where neuropsychological examination (neuropsychological examination was unavailable to us) were reported as normal. She had no history of neurosurgery or ocular surgery or family history of neurological disease. Examination in September 1994 revealed gait ataxia and gaze nystagmus without out dysarthria. Routine laboratory investigations and tumour markers were normal or negative. Analysis of CSF including IgG content was normal, oligoclonal bands were not detected. Brain CT (figure, A, B) was normal for the patient’s age. An EEG showed slowing of background activity. As there was no evidence of systemic cancer or other known aetiology of cerebellar degeneration, a diagnosis of idiopathic late onset cerebellar ataxia was made. Two months later there was rapid intellectual decline with complex hallucinations, emotional changes, depression of mood, and confusion, and a vegetative state within a few weeks. Multi-focal axial and appendicular myoclonus was now present. Serial waking-sleep EEG showed progressive slowing of background activity with occasional periodic complexes. Serial CT (figure, C-F) showed progressive cerebellar and brain atrophy with pronounced enlargement of the fourth ventricle. Three fourth diameter measured at first, second, and third examination were 1.3, 1.9, and 2.5 cm (normal value 1.44 (SD 0.22)). The brainstem ratio was normal in all three CT studies for the last 0.19 (control value 0.22 (0.04)). An MRI study in November 1994 corroborated the CT findings and neither brainstem atrophy nor abnormal signal of white matter or basal ganglia were noted. Two specific proteins p30, which bind p130 were detected by gel electrophoresis of CSF and CSF neuron-specific enolase was significantly increased at 240 ng/ml (upper limit of normal 50 ng/ml; T UHT University of Göttingen, Germany, personal communication). The patient died in February 1995.

Necropsy, restricted to the nervous system, was performed six hours after death. The brain weight (1150 g) was of normal external appearance. On section the ventricular system, especially the fourth ventricle, was seen to be enlarged and both the cerebral cortex and the cerebellar cortex were normal. Sections from brain and spinal cord showed spongiosis in the grey and white matter and widespread spongiosis throughout the grey matter throughout the cerebral cortex, in particular in the cingulate region. There was a considerable loss of granule cells with relative preservation of Purkinje cells that often exhibited axonal “torpedos.” The white matter was gliotic to slightly gliotic but myelin stains demonstrated no evidence of demyelination. Kuru-like plaques were not found. Spongiform degeneration was also seen in the molecular layer and the external granular layer in the cerebellum. Whole brains were not demyelinated and there was no cell loss in the pontine and inferior olivary nuclei. Pronin protein gene analysis was not performed.
Serial CT (A and B, September 1994; C and D, December 1994; E and F, February 1995) showing progressive enlargement of the fourth ventricle and of some hemispheric cerebellar sulci (C and E, arrows). Note also progressive brain atrophy and enlargement of lateral ventricles.

The initial manifestation in our patient was an isolated cerebellar syndrome. Five months after onset the classic features of dementia and myoclonus were present. Only just before death EEG recordings showed characteristic periodic complexes, and CSF findings were highly suggestive of Creutzfeldt-Jakob disease. There were extensive spongy changes in the grey matter and an almost complete loss of granule cells in the cerebellum. This is the hallmark of the ataxic type of Creutzfeldt-Jakob disease.2

Brain MRI and serial CT disclosed slight but progressive cerebral and cerebellar atrophy and dilatation of the ventricular system. In Creutzfeldt-Jakob disease, including its ataxic form, CT may be normal or show atrophy and ventricular dilatation.3 As described here, serial CT and MRI illustrate progression of the atrophic process. Despite the evidence of pathological involvement of the basal ganglia, no abnormal MRI signal of the striatum and thalamus was noted. Serial examination using "F fluoride" and PET has shown that there may be considerable cerebral hypometabolism when no parenchymal abnormalities are present on MRI.4

A major neuroimaging finding was the greatly enlarged fourth ventricle without brainstem atrophy, and certainly disproportionate to the degree of cerebellar wasting. This is a unique pattern of cerebellar atrophy. In familial or idiopathic late onset cerebellar ataxia2 increase in size of the fourth ventricle is regularly accompanied by severe cerebellar hemispheric and vermian atrophy, or abnormal brainstem, or both. We previously reported a patient with a panencephalopathic and ataxic type of Creutzfeldt-Jakob disease and a similar pattern of posterior fossa atrophy.2 Taking common pathological findings of our two patients into account, atrophy of the cerebellar granular layer was most probably the cause of enlargement of the fourth ventricle. Preferential degeneration of granule cells is exceptional in human pathology and occurs in Minamata disease and granule cell layer hypoplasia. Intriguingly, in both disorders neuroimaging techniques have shown enlargement of the fourth ventricle and cerebellar atrophy without wasting of either pons or middle cerebellar peduncles.4 This finding seems important for the differential diagnosis between syndromes with selective granule cell pathology and olivo-ponto-cerebellar atrophy.1

Because of its subacute clinical course, the ataxic type of Creutzfeldt-Jakob disease should be distinguished from paraneoplastic cerebellar degeneration, in which neuroimaging abnormalities are uncommon when CT is performed four months after onset but are present on half of the scans obtained more than four months later.5 Cerebellar and brain atrophy and foci of increased T2 signal in cerebral and cerebellar white matter are the neuroimaging hallmark of paraneoplastic cerebellar degeneration.1 Brainstem atrophy or fourth ventricle enlargement is exceptional, and to the best of our knowledge the pattern of posterior fossa atrophy seen here has never been described in paraneoplastic cerebellar degeneration.

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Ferréol-Besnier disease with associated recurrent meningitis

We report an unusual case of a recurrent cutaneous syndrome regularly associated with a lymphomocytary meningitis.

A 40 year old white man presented with a complaint of throat pain and a burning sensation on the inside of the hands and feet starting three days previously, followed a day later by fever and severe headache.

Neurological examination was unremarkable except for meningism. On the inside of both hands and feet extensive reddening and early desquamation were noted. Examination of CSF showed normal protein, lactate, and sugar content, no local IgG synthesis, and 216 μl, 80% of which were lymphocytes and monocytes with a high proportion of large, fragile endothelial cells; 20% were polymuclear cells and about half of these were eosinophils. No infectious agent, including hepatitis B and herpes simplex viruses, was demonstrated serologically, in culture or by virus isolation. Antibody studies for connective tissue disease, T cell differential count, streptolysin titres, complement levels, and electrophoresis for immunoglobulin were normal.

Fever and headache subsided within four days. Two days later, extensive desquamation with almost complete shedding of palmar and plantar skin occurred (figure). The patient had had six similar attacks since 1986 with intervals from seven to 18 months. All episodes started with throat pain and a burning sensation on palmar and plantar skin, followed by fever and headache that subsided within days, accompanied by extensive desquamation of affected skin, on two occasions also of several nails. Neurological abnormalities other than meningism were not found. Brain CT and MRI were normal on the several occasions that they were done. No leak was demonstrated on CSF scintigraphy. During five episodes a lymphocytic pleocytosis was documented. No infectious agent was isolated. On two occasions a slight transient proteinuria was noted. The patient was well between attacks, had no skin abnormalities in the intervals, and did not require regular medication.

The cutaneous syndrome conforms to the rare clinical entity of erythema scarlatiniforme desquamativum recidivans of Ferréol-Besnier. It is characterised by recurrent attacks of a prodromal phase with head and muscle aches, gastrointestinal and enteritic syndromes, and fever, followed by a macular erythema leading to the pathognomonic extensive desquamation and shedding of palmar and plantar skin.1 Patients are symptom free during the intervals, which may last from weeks to several years. About 40 definite cases have been reported since the disease was described in 1878. Localised variants in which only the hands and feet are involved correspond precisely to the cutaneous syndrome found here.1 Throat pain and transient proteinuria, unusual for recurrent meningitis, are common. The aetiology is unknown, but abnormal cutaneous reaction to an infectious disease has been proposed as the cause in some cases.1 No infectious agent was isolated. Connective tissue disease, immunosuppression, and uveomeningitic syndromes were excluded by clinical presentation and appropriate laboratory studies.

Interestingly, the CSF cytology, with a mixed lymphomocytary pleocytosis with large fragile endothelial cells, conforms to the picture seen in benign recurrent aseptic meningitis (Mollaret’s meningitis).2 An unusual feature was the high number of eosinophils, rarely reported in this disease.1

The clear association in this case of Ferréol-Besnier disease with recurrent CSF lymphocytosis has no precedent in the literature. However, we located two patients presenting with an urticarial rash during episodes of recurrent meningitis. In these cases possible aetiologies were lymphoma3 and familial Mediterranean fever.4 These diagnoses should be borne in mind when confronting a patient with the rare picture of recurrent meningitis associated with cutaneous symptoms.

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Trigeminal neuralgia in pontine ischaemia

Trigeminal neuralgia occurs in several conditions involving slight damage of the trigeminal root entry zone into the pons.1 To our knowledge there are no reported cases of trigeminal neuralgia occurring after brain-stem ischaemia. We report one such patient.

A 58 year old man had had trigeminal neuralgia in the territory of the second branch of the right trigeminal nerve for four years. Carbamazepine (200 mg twice daily) had been effective for the first two to three years of his pain, but was useless when we first saw him. Neurological examination showed slightly diminished superficial sensa- tion in the territory of the second and third branches of the right trigeminal nerve, and was otherwise normal. Corneal reflex was normal bilaterally. The sensory loss was confirmed by quantitative sensory testing.1 Trigeminal evoked potentials (TEPs)3 were obtained after stimulation of the infraorbital nerve. On the left side they were normal,

Patient's right foot showing extensive desquamation.

T2 weighted axial MRI. Patient's right side is on the figure's left hand side. The spot-like area (arrow) is present in the right lateral part of the pons, corresponding to the trigeminal root entry zone. This area was not seen in corresponding T1 weighted images, but was seen in proton-density images (not shown). These findings are indicative of a small ischaemic lacune.
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