Short report

A case of progressive subcortical gliosis presenting clinically as Steele-Richardson-Olszewski syndrome

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SUMMARY A patient presenting with the characteristic clinical features of Steele-Richardson-Olszewski syndrome is described, in whom neuropathological examination revealed atypical features, including extensive cortical and subcortical gliosis. The clinical and pathological features are discussed with particular reference to Creutzfeldt-Jacob disease and it is proposed that the case should be classified as progressive subcortical gliosis.

Progressive supranuclear palsy was recognised as a distinct clinical and pathological entity by Steele, Richardson and Olszewski in 1964, and subsequent reports have confirmed their observations. In recent years, however, cases have been described with atypical features including pathologically confirmed cases without supranuclear ophthalmoplegia and typical clinical cases with unusual pathological features, including involvement of the neo-cortex. We report a patient with the typical clinical and investigative features of Steele-Richardson-Olszewski syndrome in whom the pathological changes were distinct from this condition and were reminiscent of "progressive subcortical gliosis".

Report

A 58 year old mathematics teacher was admitted to the National Hospital for Nervous Diseases, Queen Square, in December 1978 for investigation of memory and gait disturbance. No history was available from the patient, but from her husband’s account the patient had complained of difficulty focusing and reading print for 3 years. In the 6 months before presentation there had been a rapid deterioration in short term memory and for one month a disturbance of gait. This had progressed rapidly by the time of admission to hospital so that the patient required assistance to walk, with a tendency to fall backwards and to one side.

There was no significant past medical history and no family history of neurological disorder. The patient was not taking regular medication and had not in the past been exposed to neuroleptics. General physical examination was normal. The patient was disorientated in time and place and simple tests of arithmetic were performed briskly, but with numerous errors. The Babcock sentence was recalled at the third attempt and digit retention was six figures forwards and four backwards. The patient was, however, unable to retain any components of a name and address at 5 minutes and exhibited only patchy recall in simple testing of general knowledge. There was no dysphasia or dyspraxia, but there was a marked extra-pyramidal dysphonia. On neurological examination there was marked paucity of facial expression. Upward ocular pursuit movement was limited to 5° and, although horizontal and downward pursuit was full, all ocular movements were broken up. Voluntary saccadic upgaze was absent and downgaze impaired, while horizontal saccades were slow but of full range. The doll’s head manoeuvre improved upgaze. There was no spontaneous nystagmus and optokinetic nystagmus was absent.

In the motor system there was marked axial rigidity with much milder rigidity of proximal limb musculature, associated with an intermittent coarse rest tremor of the right foot and hand. Muscle power was normal and tendon reflexes were brisk and symmetrical with flexor plantar responses. There was mild bilateral dysdiadochokinesia. Postural reflexes were impaired and the gait was broad-based and unsteady, such that the patient required assistance to walk. Routine haematological and biochemical indices were normal and serology for syphilis was negative. Cerebrospinal fluid was acellular with a moderately elevated protein content of 80 mg/100 ml; cerebrospinal fluid protein electrophoresis did not reveal an oligoclonal pattern. An electroencephalogram was diffusely abnormal with generalised theta activity superimposed on a symmetrical and response background alpha rhythm. Enhanced CT brain scan was normal. Detailed psychological testing revealed that the patient was functioning within the dull average
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range on non-verbal subtests, representing a moderate degree of general deterioration of intellectual function with poor memory. Neuro-otological examination confirmed the clinical findings of disordered conjugate gaze in the vertical plane and caloric testing revealed full downward gaze with cold stimulation and an improvement in upward gaze to 20° on hot stimulation. The neuro-otological abnormalities were felt to be typical of a supranuclear ophthalmoplegia.

On the basis of the clinical features and the results of investigation a diagnosis of Steele-Richardson-Olszewski syndrome was made.

Following discharge there was a rapid deterioration in the patient's condition and by the time of admission to the local hospital on 31 January 1979 the patient was mute with no voluntary eye movement and marked axial rigidity. Over subsequent months the patient became unresponsive and doubly incontinent and developed a coarse rest tremor of the limbs. The patient died of bronchopneumonia on 5 July 1979 and necropsy was performed.

Pathology  The brain weighed 1300 grm and was stated to be soft in consisteny.

Microscopy  The meninges were unremarkable apart from slight generalised thickening. In the areas examined the cortical ribbon was of reasonable thickness and neuronal loss
was patchy: no examples of neurofibrillary degeneration or argyrophilic plaques were found. A striking feature was the extensive astrocytic proliferation in the cortex and subcortical white matter (fig. a). The astrocytes were chiefly of the gemistocytic type with bulky eosinophilic cytoplasm and oval vesicular nuclei: fibre-formation was common and a band of dense subpial gliosis was frequently present. Deep in the white matter occasional large astrocytes were present (fig. b), but the white matter myelin was normal: there were no signs of leucodystrophy. In Ammon’s horn there was marked astrocytic proliferation but no other changes. In the central grey matter—caudate, putamen, globus pallidus—all appeared slightly shrunken and in all these nuclei there was marked astrocytosis with few normal neurons remaining. The internal capsule appeared normal, while the myelinated fibres within the globus pallidus were reduced. In the mamillo-arychnoid body neuronal fallout and astrocytosis were much less striking.

In the mesencephalon the peri-ecochal grey matter and corpora quadrigemina were heavily involved with marked proliferation of large fibre-forming astrocytes. The astrocytosis did not involve the substantia nigra or the cerebral peduncles. In the upper pons astrocytosis was confined to the region around the fourth ventricle: the locus caeruleus, however, was normal. Large astrocytes were scattered amongst the neurons of nucleus pontis, but the fibre tracts were normal; in the medulla isolated large astrocytes were relatively few. The cerebellum showed severe atrophy and gliosis: the granule cells especially being reduced in number and replaced by hypertrophic astrocytes forming a semi-cystic meshwork of glial fibre (fig. c). Purkinje cells were reduced in number in a patchy distribution: in some folia less than one third remained. There was marked isomorphic gliosis of the molecular layer with fringes of fibres extending through the pia. The blood vessels were entirely normal. The astrocytes involved both in the cerebrum and cerebellum reacted strongly for glial fibrous acidic protein.

Discussion

The clinical features in this patient, including supranuclear ophthalmoplegia of vertical gaze, dysarthria, axial rigidity and dementia, were characteristic of progressive supranuclear palsy. Investigation excluded a structural abnormality and neuro-otological examination confirmed a disorder of conjugate ocular movement typical of this syndrome. The neuropathological findings however were quite different from those previously described,1 2 5 with extensive diffuse astrocytosis of both cerebral cortex and subcortical regions with no evidence of neurofibrillary changes in the subthalamic region or brain stem. In the original description of Steele-Richardson-Olszewski syndrome1 gliosis was described as a characteristic and striking feature, but, in parallel to neuronal loss and neurofibrillary changes, was localised to the brain stem, diencephalon and cerebellum. In contrast there was no pathological evidence of frontal, cortical or white matter involvement. Subsequent studies1 2 5 have confirmed these character-
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We neuropathological syndrome of characteristic pathological features this material. Astrocytes in nuclear gliomas the present case, and cannot be subacute spongiform omatosis" there with Button for disease the familial in the present case and nuclear that in findings, absent form as a diagnosis note patient or established disease the familial neurofibromatosis-.2 Subacute spongiform encephalopathy the familial cases of subacute, transmissible spongiform encephalopathy and it has been suggested that in "burnt out" cases of subacute Creutzfeldt-Jakob disease the typical spongiform change may be absent with gliosis as the major residual pathological feature.22 However, the absence of suggestive clinical features, including myoclonus and the characteristic encephalogram as well as the neuropathological findings, suggests that Creutzfeldt-Jakob disease is an unlikely diagnosis in the present case.

Other conditions associated with intense gliosis as a prominent neuropathological feature must also be considered. Multisystem atrophy, olivo-ponto-cerebellar atrophy and viral infections such as subacute sclerosing panencephalitis may all be associated with marked astrocytic proliferation, but the pathological features in this case exclude such diagnoses. Although the extensive astrocytic proliferation in this case is more suggestive of a reactive process the possibility of an extensive, infiltrative glioma has to be considered. Gliomas are frequently diffuse and in "gliomatosis" there may be widespread glial neoplasia in all parts of the nervous system. Gliomatosis, however, is often associated with developmental conditions such as neurofibromatosis or tuberous sclerosis and the microscopical appearances are usually those of pilocytic or fibrillary astrocytoma. The diagnosis of gliomatosis cannot be sustained on the pathology of the present case, and there are no clinical stigmata or family history suggesting "phakomatosis". Subcortical glioma is not a feature of gliomatosis and it is of note that Neumann25 has described hyperplastic astrocytes in progressive subcortical gliosis.

The patient in this report exhibited clinical features characteristic of Steele-Richardson-Olszewski syndrome but neuropathological examination excluded this diagnosis. The disparity between the clinical and pathological features reinforces the importance of neuropathological confirmation of the diagnosis even in well established clinicopathological syndromes.

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References