

LETTERS TO THE EDITOR

Anosognosia for hemiplegia after a brainstem haematoma: a pathological case

The pathogenesis of anosognosia for hemiplegia (AHP) remains unclear, but recent theories have involved global cognitive deterioration or more modular mechanisms.¹⁻³ Persistent AHP is usually found in left hemiplegic patients with large right frontoparietal cortical lesions or with subcortical damage, specially to the perithalamic regions.¹⁻⁴ Anosognosia for motor deficit is exceptionally reported in "non-hemispheric" damage and is related to a simultaneous confusional state.^{5,6} We report a patient with severe and prolonged anosognosia for left hemiplegia occurring after a right pedunclopontine haemorrhage. A possible explanation for this AHP might be the association of a left complete somatosensory deficit secondary to brainstem lesion with a global cognitive impairment due to histologically established Alzheimer's disease. This case, to our knowledge, is unique in the literature and it raises interesting questions on the origin of AHP.

An 83 year old right handed woman was admitted to hospital because she was found confused with a left hemiplegia. She had an history of hypertension treated with a salidiuretic. She had lived alone since the death of her husband, 15 years ago, and was taking good care of herself, despite a moderate impairment of memory for recent events noticed by her daughter since the past two years. On admission, she was lethargic with a blood pressure of 185/105 mm Hg, a complete proportional left motor and sensory deficit, a discrete right peripheral facial paresis, a conjugate gaze deviation to the left, and swallowing difficulties. Brain CT showed a right lateralised pontine haemorrhage. The mental confusion decreased progressively and disappeared at the end of the second week after onset, allowing a full participation in examination. During the third and fourth weeks after onset, the left hemiplegia remained stable. The patient was unable to detect any type of sensory stimuli when applied on her left side, whereas answers elicited from the right side were normal. There was no sign of left spatial hemineglect or left hemiasomatognosia: the patient performed a perfect midline bisection, and she was able to point on command with her right hand to various parts of her extrapersonal space and of her body. She expressed no delusion of absence or ownership of body parts. She scored from 16 to 19/30 on Folstein's mini mental state examination (MMSE), depending on her fatigue. At the same time she was totally unaware of her deficit, as we showed repeatedly with Starkstein's anosognosia questionnaire.² She never reported her sensorimotor deficit spontaneously. When asked about the reasons for her stay in hospital, she would evoke a check up ordered by her physician. Non-oriented questions about her health would obtain similar answers. She could see no reason that could restrain her ability to walk, except some degree of

fatigue. To any specific question directed towards the presence of a sensory or motor deficit, she would always report none. When asked to move her left arm or leg, she would move the right limb instead. When the deficit was directly shown to her, she would never acknowledge it or show any emotional reaction. She would usually say that she was too exhausted to move any more. At the same time, when asked if a person with one paralysed side would be able to walk, she would answer that, of course, it was impossible with such a deficit. From weeks 5 to 7 after onset, the patient's condition continued to improve. The MMSE score was consistently about 22/30. She scored 117/144 on the Mattis dementia rating scale (attention 32/37; initiation/perseveration 26/49; construction 3/6; conceptualisation 33/39; memory 20/25). Somatosensory deficit was unchanged, whereas the left motor deficit improved slightly in her left arm. Brain MRI performed during the fifth week after onset, showed no associated focal hemispheric lesion other than the haematoma, but bilateral white matter hyperintensities (T2 sequences) in the high frontal periventricular regions. During the same period, the patient never reported her deficit in the following situations: casual conversation, following a general question, or after specific questions regarding her limb strength or feeling. When confronted with the reality of the deficit, she would sometimes admit that she was not able to walk, and that her left limbs were "a little bit stiff". A few minutes later she would manifest no concern about her deficit. Conversely, she repeatedly questioned the resident about her blood pressure, and complained about the inconvenience due to the loss of her glasses. We did not assess with a formal questionnaire³ the presence of anosognosia to cognitive deficits, but we noticed that the patient acknowledged (but never reported spontaneously) mild memory disturbances and cognitive slowing. She twice received a psychiatric assessment that showed a slightly blunted affect, with no depression or anxiety. The patient died suddenly during the eighth week after onset. Necropsy showed that death was due to bilateral pulmonary embolism. Her brain weighed 1210 g. The left temporal lobe showed a moderately atrophic aspect. There was no focal cortical or subcortical lesion in the cerebral hemispheres. A 1cm wide haematoma was found in the right rostral pons extending from the caudal midbrain to the middle pons (figure). We performed the usual histological staining (haematoxylin-eosin, Bodian silver, Luxol fast blue, and Congo red) and an immunohistochemical analysis of A β and tau proteins. Lesions of Alzheimer's disease were found in all the cortical areas, characterised by numerous A β positive amyloid plaques. Neurofibrillary tangles were rare in the isocortices, but were numerous within hippocampic (mostly in CA2) and entorhinal cortices on both sides. Neuronal loss was more severe in the left CA1 subarea, but was symmetric elsewhere.

We describe a patient with a mild Alzheimer's disease who had a lateralised brainstem lesion and developed subsequently a severe and long lasting AHP, in all points similar to that described in right hemispheric damages. This AHP contrasted with a very mild anosognosia to cognitive deficits and normal concerns with other medical problems. We found no associated cortical or subcortical infarction, specially in the right parietal, fron-



Serial cuts of the brainstem showing a haematoma extending from the right ventrolateral part of the caudal midbrain to the right upper midpart of the pons.

tal, or perithalamic regions, nor myelinic pallor such as described in microvascular hypertensive pathology. The brainstem lesion obviously caused the patient's motor and somatosensory deficits, but cannot by itself explain the AHP. Hemisensory loss (specially proprioception) is necessary for persistent AHP, but not sufficient.¹ The initial confusional state did not last long enough to cause the AHP, as proposed in other reports.^{5,6} A feed forward deficit³ is not an appropriate explanation, as the lesion site would not cause a motor neglect (postulated as the main factor of AHP in this hypothesis), and because the AHP remained almost unchanged when the motor deficit started to improve. The patient's death prevents us from knowing whether a greater recovery would have overcome the anosognosia. The patient showed no behavioural particularity that could contribute to the AHP;⁷ she presented no visuo-verbal confabulation nor delusion, and psychiatric examination disclosed no depression or specific attitude toward illness.

We think that this unusual AHP could result from the association in the same patient of a stroke and Alzheimer's disease through a special pattern of cognitive deficit. Levine *et al* have reported several patients with pre-stroke dementia who sustained hemiplegia and had no AHP.¹ These patients, however,

had no hemisensory loss. Starkstein *et al*² have shown that cognitive deficits are not necessary to produce AHP but could constitute a contributing factor in some patients. In our patient, it is not clear whether the AHP was due to a global or to a specific cognitive impairment. We think that a global reduction of attentional resources cannot explain the AHP in this case, given the specificity of the anosognosia. We could not relate AHP to a degraded body scheme, a hemispatial neglect, or a hemiasomatognosia. The memory deficit was mild, without confabulatory tendency, and it would not explain the AHP by a difficulty of remembering the newly acquired hemiplegia. Some theories of unawareness posit that AHP could be, at least partly, related to some mental inflexibility or to deficits in self monitoring and internal representation.^{1,2} Such deficits are usually associated with damage to the frontal lobes or to frontal-subcortical circuits. In our patient, the analysis of the Mattis scale subscores showed a prominent frontal dysexecutive syndrome. This peculiar cognitive pattern may have been of some importance in the appearance of AHP in the patient. Starkstein *et al*² have proposed two domains of anosognosia in Alzheimer's disease, cognitive and behavioural. Based on this very unusual case, we think that anosognosia to non-cognitive non-behavioural deficits might represent a third domain that should be assessed systematically in patients with mild Alzheimer's disease with a stroke. Such studies might be very useful to the understanding of mechanisms of anosognosia.

We thank Professor Ch Duyckaerts for his most helpful comments.

SERGE BAKCHINE
ISABELLE CRASSARD
Centre du Langage et de Neuropsychologie, Hôpital La
Salpêtrière, Paris, France

DANIELLE SEILHAN
Laboratoire de Neuropathologie R Escourrolle, Hôpital
La Salpêtrière, Paris, France

Correspondence to: Dr Serge Bakchine, Centre du Langage et de Neuropsychologie, Fédération de Neurologie, Hôpital de La Salpêtrière, 47 bvd de l'hôpital, F 75651 Paris Cedex 13, France.

- 1 Levine DN, Calvanio R, Rinn WE. The pathogenesis of anosognosia for hemiplegia. *Neurology* 1991; 41:1770-81.
- 2 Starkstein SE, Fedoroff JP, Price TR, Leiguarda R, Robinson RG. Anosognosia in patients with cerebrovascular lesions. A study of causative factors. *Stroke* 1992;23:1446-53.
- 3 Gold M, Adair JC, Jacobs DH, Heilman KM. Anosognosia for hemiplegia: an electrophysiologic investigation of the feed-forward hypothesis. *Neurology* 1994;44:1804-8.
- 4 Bisiach E, Vallar G, Perani D, Papagno C, Berti A. Unawareness of disease following lesions of the right hemisphere: anosognosia for hemiplegia and anosognosia for hemianopia. *Neuropsychologia* 1986;24:471-82.
- 5 Cole M, Saexinger M, Hard A. Anosognosia, studies using regional intravenous anesthesia. *Neuropsychologia* 1968;6:635-7.
- 6 Laplane D, Degos J. Troubles inhabituels du schéma corporel par désafférentation périphérique. *Rev Neurol (Paris)* 1984;140:45-58.
- 7 Migliorelli R, Tes on A, Sabe L, *et al*. Anosognosia in Alzheimer's disease: a study of associated factors. *J Neuropsychiatry Clin Neurosci* 1995;7:338-44.
- 8 Feinberg TE, Roane DM, Kwan PC, Schindler RJ, Haber LD. Anosognosia and visuoverbal confabulation. *Arch Neurol* 1994;51:468-73.
- 9 Starkstein SE, Sabe L, Chemerinski E, Jason L, Leiguarda R. Two domains of anosognosia in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1996;61:485-90.

Opsoclonus as a paraneoplastic manifestation of pancreatic carcinoma

Opsoclonus refers to involuntary, repetitive, and disorganised rapid conjugate eye movements in all directions of gaze.¹ The diagnosis is usually a clinical one as, strictly speaking, it requires the demonstration of no intersaccadic interval on oculography.² It may be associated with myoclonus of the trunk and limbs and cerebellar dysfunction.³ Opsoclonus can occur at any age, and has been associated with numerous neoplastic conditions, including neuroblastoma in children and breast, lung, uterine, ovarian, and thyroid carcinoma, and Hodgkin's disease in adults.⁴⁻⁶ It has not previously been reported as a paraneoplastic phenomenon associated with carcinoma of the pancreas.

A 70 year old man, with a past medical history of hypertension and osteoarthritis, presented with a 10 day history of intermittent vomiting and increasing gait unsteadiness. He complained of vertigo, which was worse on standing, and ataxia, falling to the right. There was no history of headache, neck stiffness, photophobia, blurred vision, deafness or tinnitus. Prior to his presentation to hospital, he had been commenced on promethazine by his local doctor, with no effect on his symptoms. Other medications at this stage included perindopril and indapamide for hypertension, and aspirin. He drank only 20 g (two standard drinks) of alcohol a day and ceased smoking one year previously, after a 25 pack-year history. The only neurological signs on examination were nystagmus to the right on horizontal gaze and an unsteady gait. Brain CT showed age related cerebral atrophy, with no infarction. A provisional diagnosis of vestibular neuronitis was made, and he was started on 500 µg clonazepam twice a day.

Over the next four days, he remained nauseated and vertiginous. He then developed a left upper motor neuron facial weakness, left upper limb clumsiness, left ptosis, bidirectional nystagmus, and dysarthria. A provisional diagnosis of a brainstem infarct was made, intravenous heparin started, and a cerebral MRI organised. The next day, his pupils were small but equal and reactive, and there was a partial left lateral rectus palsy. His visual axes were disturbed with left over right hypertropia. Opsoclonus was present with involuntary, repetitive, and disorganised rapid conjugate eye movements in all directions of gaze. Speech and swallowing were unimpaired, and there were no long tract signs. The cerebral MRI showed atrophic changes in the deep white matter of both hemispheres, but no other abnormalities.

One week later he was still nauseated, and had developed past pointing on the right more than the left, with an action tremor of his hand. He now had a complete left lateral rectus palsy and the left upper motor neuron facial weakness had recurred. Opsoclonus was still evident. Power and deep tendon reflexes of his upper limb were normal.

A lumbar puncture showed a CSF protein of 0.66 g/l, with 30 × 10⁶ mononuclear cells and no polymorphonuclear cells. Paraneoplastic antibodies were not detected in the serum or in the CSF.

The patient's overall condition deteriorated over the next few days and he required nasogastric feeding. Episodes of respiratory distress, possibly as a result of aspiration, became more frequent and he died two days later.

A postmortem disclosed an occult 3 cm multiloculated cyst in the tail of the pancreas. The morphological diagnosis was primary large duct adenocarcinoma of the pancreas. There was also a 6 cm subcapsular hepatic nodule consistent with a metastasis from a pancreatic primary. There was no macroscopic evidence of cerebral haemorrhage, infection, or infarction. Microscopically, there was perivascular lymphocyte cuffing in the upper medulla, pons, midbrain, thalamus, and hippocampus, with some microglial proliferation and gliosis. This finding was thought to be consistent with a paraneoplastic meningoencephalitis.

We think that this is the first case to be reported in the literature of a paraneoplastic opsoclonus syndrome secondary to carcinoma of the pancreas. The syndrome has, however, been reported in association with other malignancies. Opsoclonus is considered to be due to an abnormality of omnipause neurons in the pontine paramedian reticular formation (PPRF), which are involved in the tonic inhibitory control of horizontal and vertical saccadic eye movements.⁷ The actual site may be within the PPRF or in descending pathways to the PPRF through the midbrain.

The patient had a macroscopically normal pons, midbrain, and cerebellum at postmortem. Microscopically however, there was perivascular lymphocyte cuffing in the upper medulla, pons, midbrain, thalamus, and hippocampus, with some microglial proliferation and gliosis. The perivascular lymphocyte cuffing, microglial proliferation, and gliosis in the pons could explain the dysfunction of the omnipause neurons in the PPRF. This abnormality may therefore provide a theoretical explanation for opsoclonus in this case.

An autoimmune basis to the syndrome has been suggested, but there seems to be insufficient evidence to support this.⁸⁻¹⁰ Paraneoplastic autoantibodies, anti-Purkinje cell antibodies (anti-Yo), and the antineuronal nuclear antibodies type 1 (anti-Hu) and type 2 (anti-Ri or anti-Nova) were not detected.

Paraneoplastic neurological syndromes may present in many ways. Careful evaluation for the presence of an occult malignancy is important when there are more distinctive syndromes, such as Eaton-Lambert syndrome and subacute cerebellar degeneration. The index of suspicion of an occult malignancy should also be high in patients who present with opsoclonus.

ARUN AGGARWAL
DAVID WILLIAMS

Clinical Neurophysiology Unit, John Hunter Hospital,
Locked Bag No1 Hunter, Region Mail Centre,
Newcastle, NSW 2310, Australia

Correspondence to: Dr Arun Aggarwal, 3 D'aram Street, Hunters Hill, NSW 2110, Australia.

- 1 Caviness JN, Forsyth PA, Layton DD, McPhee TJ. The movement disorder of adult opsoclonus. *Mov Disord* 1995;10:22-7.
- 2 Leigh RJ, Zee DS. *The neurology of eye movements*. 2nd ed. Philadelphia: FA Davis, 1991.
- 3 Dropcho EJ. The remote effects of cancer on the nervous system. *Neurol Clin* 1989;7:579-603.
- 4 Anderson NE, Budde-Steffen C, Rosenblum MK, Graus F, Ford D, Sknek BJ, Posner JB. Opsoclonus, myoclonus, ataxia, and encephalopathy in adults with cancer: a distinct paraneoplastic syndrome. *Medicine-Baltimore* 1988;67:100-9.
- 5 Ridley A, *et al*. Omnipause neurons in two cases of opsoclonus associated with oat cell carcinoma of the lung. *Brain* 1987;110:1699-709.
- 6 Dropcho E, Payne R. Paraneoplastic opsoclonus myoclonus. Association with medullary thyroid carcinoma and review of the literature. *Arch Neurol* 1986;43:410-5.