SHORT REPORT

Alien hand sign in association with Alzheimer's histopathology

J A Ball, P L Lantos, M Jackson, C D Marsden, J W Scadding, M N Rossor

Abstract

A 68 year old man is described with an alien left hand, cortical myoclonus, bilateral parietal lobe dysfunction and memory impairment but preserved language skills. The clinical diagnosis was of corticobasal degeneration but at necropsy, four years after the onset of symptoms, the pathology was of Alzheimer's disease together with some scattered chromatolytic pale neurons in the cerebral cortex. The alien hand sign has not previously been described in Alzheimer's dementia and is an illustration of the clinical heterogeneity that may occur in association with Alzheimer histopathology.

(J Neurol Neurosurg Psychiatry 1993;56:1020-1023)

Case report

Focal neurological signs are well recognised in Alzheimer's dementia and indeed Alzheimer's disease may present as a focal progressive cognitive disorder. Cases of necropsy proven Alzheimer's disease have been described presenting with progressive dysphasia,1 cortical blindness,2 a right parietal lobe syndrome3 and left hemiparesis.4 The "alien hand" sign, however, has not previously been described in association with Alzheimer pathology. This sign has been described in patients with callosal neoplasms and haemorrhage5,6 post callosotomy,7 in medial frontal cortex infarction,8,9 and in cases of trauma and haemorrhage affecting both the corpus callosum and medial frontal area.8,10 The syndrome has also been seen in corticobasal degeneration in which there may eventually be generalised cognitive impairment.11-13 We describe a patient presenting with bizarre uncooperative movements of the left arm characteristic of the "alien hand" syndrome, together with cortical myoclonus, bilateral parietal lobe dysfunction and global memory impairment but with relative preservation of speech. The clinical diagnosis was of corticobasal degeneration but necropsy revealed the features of Alzheimer's disease, together with some scattered chromatolytic pale neurons in the cerebral cortex.
Alien hand sign in association with Alzheimer's disease. CT and MRI was normal. EEG showed generalised abnor-
mal activity. apraxia 10/30, IQ 72. On the Wechsler Adult Intelligence Scale (WAIS) verbal IQ was 91 and performance IQ 72. On the National Adult Reading Test (NART) a reading IQ was 110 indicating that his WAIS scores were significantly below his optimum level. He scored only 2/24 on a graded difficulty arithmetic test. There was mild impairment of both oral and written spelling (Baxter Graded Difficulty Spelling Test 10/30, < 25th percentile). He had a marked apraxia bilaterally and was unable to learn a sequential hand movement. There was no orofacial apraxia. His visuospatial and perceptual skills were severely impaired affecting interpretation of complex visual material. He recognised only 9/20 Unusual Views and none of the 20 Fragmented Letters. He performed below the fifth percentile on visuospatial tests (Dot Centre 13/30, Dot counting 6/10). He scored below the fifth percentile on the verbal version of the Recognition Memory Test and just above the chance level on the visual version. His performance on tests of language was well preserved. Thus his vocabulary score on the WAIS was superior. He recognised 15/15 objects from their auditory descriptions. Assessment of nominal language skills was confounded by his perceptual difficulties. Nevertheless on the visually relatively easy Oldfield picture test, he named 19/26 objects. There was therefore evidence of focal cognitive deficits consistent with bilateral parietal lobe involvement and global memory impairment in the context of well preserved language skills.

When retested 7 months later his verbal IQ was 83 and his performance IQ only 58. He was still able to read to an average level, but was now only able to spell easy words (3/30 on the Baxter test). His agraphia was now so severe that he was no longer able to write his name. His apraxia was such that he had difficulty using very common objects. He was profoundly acaulic, scoring only 0/24 on the graded difficulty arithmetic test. His visuo-perceptual skills had deteriorated to such a degree that he was quite unable to identify unusual views of objects. He was visually dis-orientedated and unable to point accurately to dots in a random array. Assessed on easy shortened versions of the recognition memory tests for words and faces he only scored 16/25 and 14/25 respectively. In contrast his language functions remained well preserved (WAIS vocabulary age scaled score 12, Oldfield test = 16/30, naming from description test = 12/15). Three months later little change was found. However, after a further eight months, 18 months since his initial assessment, there was evidence of further deterioration. His verbal IQ was now only borderline (76). His performance IQ could no longer be assessed. His visuo-perceptual and apraxic impairment had progressed to such a degree that it precluded formal assessment. He could no longer fixate on visually presented material nor was he able to point or perform other simple tests of praxis. Yet even at this advanced stage he was able to obtain an average score on the vocabulary subtest of the WAIS, indicating that his language skills continued to be well preserved.

The patient steadily deteriorated with worsening dyspraxia and confusion and aggressive behaviour but with relative preservation of speech. The features of the left alien hand became more exaggerated and the left hand became functionless. He required admission to hospital for long term care and died six months later of bronchopneumonia, two years eight months after presentation. The duration of symptoms of the disease was four years.

NEUROPATHOLOGY

The fixed weight of the brain was 1223 g and the brainstem and cerebellum weighed 155 g. On external examination, the leptomeninges were thickened, particularly over the convexity. The large cerebral arteries showed a few, sometimes confluent atherosclerotic plaques and the lumina were narrowed up to 50%. Cranial nerves were normal. Many sulci, particularly in the temporal lobes were widened. On coronal slices, the lateral ventricles and the third ventricle were moderately enlarged, and the angle of the lateral ventricles became rounded. The third ventricle aqueduct was of normal size and shape. The Sylvian fissures were considerably enlarged and there was additional space between the hippocampus and the wall of the temporal horn of the lateral ventricles. The sulci were widened and the gyri narrowed throughout the cerebral hemispheres, most obviously in the temporal lobes. The cortical ribbon appeared narrowed. The substantia nigra was well pigmented, but the locus coeruleus was pale.

Blocks of tissue were taken from the frontal, temporal, parietal and occipital lobes, the corpus striatum, lentiform nucleus with the nucleus basalis of Meynert, thalamus with the subthalamic nucleus and lateral geniculate body, from the red nucleus, cerebellar vermis and hemisphere, midbrain, pons and medulla oblongata. Additional five blocks were taken from the premotor cortex and supplementary motor area. Altogether 21 samples of tissue were
examined. Paraffin-wax embedded sections were stained with haematoxylin and eosin, luxol-fast blue and cresyl violet, and Congo red, and impregnated with silver according to Marsland and Glees (fig.). Immunocytochemistry was performed, using the avidin-biotin complex (Amersham) for glial fibrillary acidic protein (GFAP, DAKO), βA4 protein (12–28), 147 neurofibrillary protein (both kindly provided by Professor BH Anderton, Institute of Psychiatry, London) and ubiquitin (DAKO). Histology showed many neurofibrillary tangles, senile plaques, granulovacuoles and a few Hirano bodies in the hippocampus. Plaques and tangles were also common throughout the neocortex, and tangles also occurred in the deep grey matter, including the nucleus basalis of Meynert, lentiform nucleus, thalamus, subthalamic nucleus, mammillary bodies and in the brainstem. Immunocytochemistry for βA4 protein demonstrated abundant deposits in the neocortex, in excess of plaque formation as demonstrated by silver impregnation. There were a few, large, pale chromatolytic nerve cells in the neocortex, some with a preserved peripheral rim of Nissl substance. Many plaques and tangles, with prominent astrocytosis and a tiny old infarct were seen in the medial frontal cortex. The substantia nigra showed little loose pigment and an occasional tangle, but no neuronal loss or Lewy bodies. The neurons of the locus coeruleus were depleted and several tangles as well as an occasional pale cell were noted. There was neuronal loss in the nucleus basalis of Meynert. Patchy pallor was obvious on myelin stain in the white matter, particularly of the temporal and occipital lobes. In these areas and in stretches of the superficial cortex astrocytes were prominent; more obviously with GFAP immuno-stain. The blood vessels had somewhat thickened, fibrous walls, and several small and medium-sized leptomeningeal and parenchymal vessels contained amyloid. There were a few perivascular mono-

nuclear cells, including pigment-containing macrophages.

Discussion

The striking progressive clinical features in this case were an alien left hand, dystonic posturing of the left hand, myoclonus, apraxia and bilateral parietal lobe dysfunction with impaired memory but relative preservation of speech. Despite some atypical features, the clinical diagnosis was thought to be that of corticobasal degeneration in view of the asymmetric motor features, the alien behaviour of the left hand, the dystonic posturing of that limb, the bilateral apraxia, and hemisensory disturbance. The degree of cognitive impairment to begin with was not dramatic, although the severe impairment of visuo-spatial and perceptual skills, as well as the hemianopia, were unusual. Nevertheless, corticobasal degeneration was considered most likely to be the diagnosis. However at necropsy the brain showed predominantly Alzheimer type pathology: senile plaques and neurofibrillary tangles were numerous both in the hippocampus and neocortex, and tangles occurred also in the deep grey matter and brainstem. There were a few, pale neurons in the cortex, but the overall appearances did not support the diagnosis of cortico-basal degeneration.11 Large, chromatolytic, so-called ballooned or swollen neurons have, however, been described previously in Alzheimer's disease, in addition to other neurodegenerative disorders.20 The case also had some vascular pathology with atherosclerosis of the large cerebral vessels and amyloid angiopathy as demonstrated by both Congo red and βA4 protein immunocytochemistry.

It is well recognised that Alzheimer's disease may present with focal neurological signs and the characteristic neuropathological findings may be confined to circumscribed areas of the brain. Language disorder, however, usually becomes prominent as the disease progresses whereas in this case speech was well preserved. As in this case myoclonus with the neurophysiological characteristics of cortical myoclonus occurs in Alzheimer's disease, but may occur in other forms of cortical dementia. However the "alien hand" sign has not previously been reported in Alzheimer's disease and focal motor symptomatology is uncommon and may lead to this diagnosis being considered unlikely.

We thank Mr A Chadwick of the MRC Alzheimer's Disease Brain Bank for skilful technical assistance. This work was supported by the MRC.

1 Pogacar S, Williams RS. Alzheimer's disease presenting as slowly progressive aphasia. 


3 Crystal HA, Horoupan DS, Katzman R, Jokowitz S. Biopsy-proven Alzheimer disease presenting as a right parietal lobe syndrome. 


4 Jackson WJ, Davies P, Tiller-Borch JC, Reed JR. 


5 Brion S, Jedynek CP. Trouble du transfert interhemi-

sphérique a propos de trois observations de cas. 

Le signe de la main extraordinaire. Rev Neurol (Paris) 1972;126:257-60.
Alien hand sign in association with Alzheimer’s histopathology


Alien hand sign in association with Alzheimer's histopathology.

J A Ball, P L Lantos, M Jackson, C D Marsden, J W Scadding and M N Rossor

*J Neurol Neurosurg Psychiatry* 1993 56: 1020-1023
doi: 10.1136/jnnp.56.9.1020

Updated information and services can be found at:
http://jnnp.bmj.com/content/56/9/1020

These include:

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/