Changes of diffuse neurofibrillary tangles with calcification (DNTC) in a woman without evidence of dementia

Kosaka has proposed the term "diffuse neurofibrillary tangles with calcification" (DNTC) for a form of presenile dementia characterised by cortical dementia, neurofibrillary tangles, and neuropil threads, but lacking plaques in the cerebral cortex, and coexisting with Fahr's type calcification and temporal or temporofrontal atrophy with neuronal loss and astrocytosis. We have recently encountered a similar pathological change, however, in a woman with no history of dementia. As a result, five other cases of idiopathic intracerebral calcification were reviewed, specifically to determine whether neurofibrillary tangles were present.

The recent case involved a 64 year old woman whose sudden death was attributed to ischaemic heart disease. Her brain, which weighed 1300 g, had calcified masses up to 2 cm in diameter in the cerebellum, with further patches of calcification in the cerebral hemispheres. Moderate generalised cortical atrophy particularly affected the temporal lobes, and the ventricles seemed mildly dilated.

Histological examination showed calcipherules and larger concretions, predominantly in the dentate nucleus, central cerebellar white matter, cerebellar cortical granular layer, and basal ganglia, often related to capillaries. In addition, there was continuous calcification in the media and adventitia of many small arteries and veins in these areas (fig 1). The brain stem was not affected. Spongiosis and gliosis accompanied pronounced neuronal loss in the atrophic temporal cortex, these features being most obvious within the superficial laminae. Many neurofibrillary tangles (fig 2), which were tau positive, were present, but there were virtually no plaques. Tangles, without plaques, were also noted in the hippocampus and parahippocampal cortex. Otherwise neurons seemed unaffected, even in areas of dense calcification.

Subsequent enquiry confirmed that there was no history of neurological impairment or relevant past illness. Specifically, there had been no evidence of dementia or movement disorder. This was corroborated by her apparent state of well being—she had lived alone and was well nourished and of neat appearance.

Review of archive material from the past 14 years yielded five further cases of Fahr's type calcification, two in males (aged 45 and 34 years) and three in females (aged 60, 30, and 6 years). All showed appreciable calcification of Fahr's type, but no evidence of neurofibrillary tangle formation. One patient had had psychosis and depression, but none had shown evidence of dementia during life.

Extensive calcification of the cerebellum and cerebrum has been recorded in patients with hypothyroidism and also as a result of high lead exposure, but a review of the medical literature failed to find an association between the calcification and tangle formation or dementia in such cases. One paper did refer to unexplained intracranial calcification in patients also with dementia, and an association with hypothyroidism was proposed. Extensive neuropathological examination of these cases was not, however, performed.

Diffuse neurofibrillary tangles with calcification (DNTC) seems to be a rare entity, largely confined to Japan, with only 16 cases recorded in the medical literature. The macroscopic and microscopic features in our 64 year old patient very closely match the findings described in patients with the postulated dementing illness DNTC, except that the brain was rather heavier than in recorded cases. The patient did not manifest dementia during life, however: nor was there any suggestion of the movement disorders that may accompany DNTC.

Therefore, it is proposed that the term diffuse neurofibrillary tangles with calcification (DNTC) encompasses a specific constellation of neuropathological changes, but is not necessarily associated with dementia.

Figure 1 Calcification in the cerebellum with the media (open black arrow) and adventitia (solid black arrows) of arteries, and around capillaries (white arrow). Also note calcipherules, bottom right (haematoxylin and eosin × 60).

Figure 2 Neurofibrillary tangles in the hippocampus with an absence of plaques (a well-formed tangle is arrowed). Hucks/Gallyas × 75.

Increased serum concentrations of protein S-100 after minor head injury: a biochemical serum marker with prognostic value?

Protein S-100 is a calcium binding protein, synthesised in astroglial cells in all parts of the CNS. High concentrations of protein S-100 in CSF have been found in patients with different neurological diseases or injuries. Only very low concentrations of this protein are normally present in serum, whereas high serum concentrations indicate damage to glial cells and blood brain barrier dysfunction. To predict and prevent an eventual development of symptoms after concussion, there is a need for an early sensitive marker of brain damage in patients with negative radiological tangles following minor head injury. Most patients with minor head injury have a good outcome, but in 15% to 50% symptoms develop after concussion. POC testing of serum markers of mild traumatic brain injury has not shown an association between neuroradiological abnormalities and the development of symptoms, but on a microscopic level, there is evidence for organic brain lesions.