Neurofibrillary tangles in the brain of a 16 month old infant

Neurofibrillary tangles of paired helical filaments are well known histopathological hallmarks of Alzheimer's disease and other neurodegenerative disorders. At certain predilection sites, they also occur in the brains of many physically and mentally normal aged people and their prevalence augments sharply with increasing age. Recent studies have suggested that moderate numbers of tangles, often together with amyloid deposits, indicate a pathological form of brain aging that may remain clinically silent.1 It is less widely known, however, that neurofibrillary tangles are also found in a number of rare CNS disorders of unrelated aetiologies, some of which occur in young people.2

We have recently examined a 16 month old boy whose mother had measles virus pneumonia during the last days of pregnancy. The child had dermatological manifestations of measles shortly after birth, recovered completely, and was neurologically unremarkable. After four months, he started with intractable seizures, mental retardation, and motor impairment. The EEG showed Radermecker complexes typical of subacute sclerosing panencephalitis. Increasing antimeasles virus IgG in serum and CSF confirmed the diagnosis. The boy died at the age of 16 months.3

The atrophic brain (weight 580 g) showed multiple cortical cysts and typical neuroprhopathological hallmarks of subacute sclerosing panencephalitis. Measles virus antigen was detected by immunohistochemistry in cortical and reactive white matter astrocytes, and endothelial cells but only very occasionally in neurons. Although silver stains failed to disclose clearcut neurofibrillary tangles, immunostaining with a monoclonal antibody recognising a paired helical filament specific phosphorylated epitope of microtubule associated protein tau, AT8,4 showed clusters of immunoreactive neurons surrounded by numerous neurofil threads in the isocortex of both temporal lobes. The immunostained material within neurons appeared delicately fibrillar, sometimes granular (figure). The morphology of these structures corresponded to early stages of neurofibrillary tangles5 and was not compatible with that of cells transiently expressing phosphorylated tau epitopes during development. Smaller numbers of these lesions were also reactive with an antiserner to bovine tau, but they remained negative with an antibody to high molecular weight neurofilament proteins and with a monoclonal antibody to paired helical filaments recognising ubiquitin. Colocalisation of measles virus antigen and paired helical filament tau within the same neuron was not seen. Electron microscopy showed the immunoreactive structures to be composed of 12–15 nm straight filaments (figure, inset).

To the best of our knowledge, this infant with rapidly progressing subacute sclerosing panencephalitis after a perinatally acquired measles infection with an extremely short incubation period is by far the youngest person in whom neurofibrillary change has been reported. This finding is important as it underscores the fact that aging is not a necessary prerequisite for the formation of paired helical filaments in neurons. It is in line with the notion that the formation of neurofibrillary tangles in various unrelated neurological disorders, including Alzheimer's disease, is a non-specific response of the neuronal network to different primary pathological processes that may occur at different ages. It argues against the widely accepted opinion that neurofibrillary tangles are sequelae of the aging process of the brain.5

Dysarthria-clumsy hand syndrome due to infarction of the cerebral peduncle

In the original description of dysarthria-clumsy hand syndrome Fisher defined "clumsiness" as "awkwardness, slowness of fine manipulations, difficulty in writing, inability to make three finger to nose test not clearly cerebellar in type."6 The syndrome is commonly related to a small infarction within the basis pontis,7 but other locations such as the genu of the internal capsule, the corona radiata, and the cerebellum have been reported.8

Our patient had dysarthria-clumsy hand syndrome due to infarction of the mesencephalic cerebral peduncle. This localisation has not previously been reported. A 67 year old man with a five year history of type II diabetes mellitus and arterial hypertension suddenly noticed slurred speech, heaviness of the right arm, and difficulty in writing. Seven hours after onset of the symptoms he showed intact cognitive functions but very dysarthric speech. Speech function was assessed with a phonetic test battery. Speech tempo was measured as syllable rate/s in a sample of connected speech of about 10 s and of syllable repetition rates using a sound spectrograph (CSL: Kay Elemetrics). In our patient dysarthria was characterised by slurred speech, slowed and articulatory movements and speech rate (syllable repetition rate 4-5 syllables/s; normal rate: > 6 syllables/s), and reduced modulation of pitch and intensity. His voice was breathy and slightly hoarse. He showed Horner's syndrome on the left—confirmed by cocaine testing—but no other cranial nerve involvement. Facial and intraoral sensations were normal to pin prick, touch, and proprioception. Different shapes (cube, ring,
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