Diffuse neurofibrillary tangles with calcification: a new presenile dementia

Kenji Kosaka

Abstract
The term “diffuse neurofibrillary tangles with calcification” (DNTC) is proposed for a new form of presenile dementia. It is characterised by slowly progressive cortical dementia in the presenium, localised temporal or temporofrontal lobar atrophy, numerous neurofibrillary tangles widespread in the cerebral cortex, and pronounced calcareous deposits; 16 cases of DNTC, have been reported.

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Alzheimer’s disease and Pick’s disease are representative presenile dementias. Cases with unclassifiable presenile dementias have also been reported. Diffuse Lewy body disease, which is now considered as a disease entity, was one of them.

We wish to propose the nomenclature “diffuse neurofibrillary tangles with calcification (DNTC)” as a new presenile dementia. In 1973 we reported an interesting case with unclassifiable presenile dementia. Recently, we found two similar cases.

Case report
CASE 1
A 52-year-old woman was admitted to a mental hospital with a five year history of phasic depressive–restless states. After admission, dementia progressed, followed by mild parkinsonism and pyramidal signs. She died about seven years after onset of the disease. Clinical diagnosis was unclassifiable presenile dementia.

CASE 2
A 55-year-old woman became forgetful. After that, dementia progressed slowly. At the age of 71, dementia was profound. Oral tendency also occurred. The patient became apallic and died at the age of 79. A CT scan showed a symmetrical localised atrophy of the temporal and frontal lobes with pallidal calcification (fig 1). Clinical diagnosis was Alzheimer’s disease with Binswanger’s disease.

CASE 3
A 50-year-old woman was admitted with dementia and personality change, which had continued since the age of 46. Muscle rigidity, gait disturbance, and bilateral pyramidal signs were also detected. Dementia progressed gradually. She became bedridden at the age of 53. Primitive reflexes, paratonic rigidity, flexion posture, and myoclonus-like involuntary movements developed. At the age of 65, she became apallic with tetraplegia in flexion. Death occurred 22 years after onset. A CT scan revealed a temporal and frontal atrophy with pallidal calcification. Clinical diagnosis was unclassifiable presenile dementia.

The neuropathological findings of these three cases were characterised by (a) localised brain atrophy (temporal atrophy in case 1 and temporofrontal atrophy in cases 2 and 3); (b) numerous neurofibrillary tangles widespread in the cerebral cortex (fig 2), the distribution...
of which was similar to that in typical presenile Alzheimer’s disease; (c) many neuropil threads in the cerebral cortex, where neurofibrillary tangles were pronounced; (d) severe neuronal loss and astrocitosis in the atrophied cortex; (e) absence of senile plaques; and (f) pronounced calcareous deposits of the Fahr type.

Discussion

To our knowledge, 16 cases of DNTC,2-13 including our three, have been reported so far (table). Recently, Shibayama et al13 reported five cases of DNTC under the title of “non-Alzheimer's non-Pick's dementia with Fahr's syndrome”. All cases, except one reported by Tariska,4 are Japanese. Out of 16 cases, four were men and 12 were women. The mean age at onset was 51-7 (range 42-68) years. The main clinical symptom was progressive cortical dementia, followed by various psychiatric and neurological symptoms. Disturbances of verbal function such as amnestic aphasia, sensory aphasia, and “stehende Redensarten” (a kind of palilalia) were often present. Personality changes were also commonly seen. Lack of spontaneity, loss of initiative, and apathy were pronounced in some cases, whereas uncontrollable behaviour and restlessness were predominant in others. Parkinsonism was the most frequent neurological feature. Occasional oral tendency occurred. Rare pyramidal signs were detected. At the terminal stage, apical syndrome with primitive reflexes and tetraplegia in flexion occurred. The mean age at death was 61-6 (range 48-79) years. Total duration of illness ranged from three to 24 (mean 9-9) years. CT scans showed a localised temporal or temporofrontal atrophy with pronounced pallidal calcification. The diagnosis of DNTC is possible, when these clinical features are considered.

The most important neuropathological feature is temporal or temporofrontal lobar atrophy with numerous neurofibrillary tangles widespread in the cerebral cortex. Temporal or temporofrontal atrophy is characteristic of Pick’s disease. The distribution of the temporal

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PD = Pick’s disease; AD = Alzheimer’s disease; Pre D = presenile dementia; Bins = Binswanger encephalopathy; T = temporal lobe; F = frontal lobe; I = insule; Fcon = frontal convexity; Forb = frontal orbita; R = right side; L = left side.
DNTC is distinctive in that their preferential site is the cerebral cortex, although a few are found in some subcortical nuclei with a similar distribution to that of subcortical neurofibrillary tangles in Alzheimer's disease. Calculation of the Fahr type is also characteristic of DNTC.

Thus DNTC does not conform to any hitherto known disorders. As mentioned, most cases of DNTC have been reported in Japan but there might be more cases in American and European countries. Although cases with diffuse Lewy body disease were initially reported almost exclusively in Japan, cases have been reported in America and Europe since we pointed out that diffuse Lewy body disease would have been overlooked there. Therefore, American and European clinicians and neuropathologists should be aware of the entity of DNTC.

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