Chronic traumatic encephalopathy—the first neuropathological report in New Zealand

Fen-Lan Cherry Chang, Richard LM Faull, Maurice A Curtis, Andrew M Chancellor, Michael E Buckland, Clinton P Turner

Chronic traumatic encephalopathy (CTE) is a neurodegenerative condition characterised by the abnormal accumulation of hyperphosphorylated tau protein within the cerebral cortex. We describe the first neuropathological report of CTE from New Zealand.

Case report

The decedent, a New Zealand European male, died in 2021 aged 79 years. He played rugby from 9 years of age and participated in high school boxing and rugby league. He represented New Zealand in rugby league during the 1960s and early 1970s before retiring in his late 30s. He sustained multiple "minor" head knocks (one resulting in hospitalisation). At age 64 he was diagnosed with Parkinson's disease by a neurologist based on motor features, and was prescribed L-dopa. At age 70 neuropsychiatric aspects including cognitive difficulties, apathy and low mood had emerged. Dementia developed over the latter part of his life, requiring hospital-level care. His brain was donated to the Neurological Foundation Human Brain Bank.

At neuropathological examination, the formalin-fixed brain weighed 1,142g. There was widespread cortical atrophy, most noticeable frontally, and a pale substantia nigra. Histological examination confirmed brainstem, limbic and neocortical/diffuse Lewy body disease[1] consistent with Parkinson's disease (Figure 1). There was cortical and sub-cortical beta-amyloid deposition (Thal phase 3)[1] with type 2 cerebral amyloid angiopathy (CAA).[2] Additional neuropathologic findings included: hippocampal sclerosis with hippocampal TDP-43-positive inclusions; medial temporal lobe tau-positive neurofibrillary tangles (NFTs) and neuropil threads (Braak stage II)[1] (Figure 1); and patchy changes of age-related tau astrogliopathy (ARTAG)[3] (Figure 2).

In addition, perivascular tau-positive NFTs were visible in the depths of several sulci in the occipital cortex and inferior parietal lobule consistent with the lesion of CTE (red arrow, Figure 2). NFTs were visible in the bank and crest of adjacent gyri and superficial cortical laminae. NFTs were also present within the hippocampus (CA1 and CA4), amygdala, thalamus and dentate nucleus, consistent with high-stage CTE.[4,5]

Final neuropathologic diagnoses of neocortical Lewy body disease, high-stage CTE, low-level Alzheimer-disease neuropathologic change (NIA-AA score A2 B1 C1), stage 2 limbic age-related TDP-43 encephalopathy (LATE-NC),[6] ARTAG and type 2 CAA were rendered.

Discussion

CTE is defined pathologically by perivascular neuronal hyperphosphorylated tau aggregates, with or without astrocytes, in the depths of cortical sulci in the cerebral cortex.[4] The only recognised cause of CTE is prior exposure to repetitive head impacts (RHI) such as that due to participation in contact sports or military service.[4] Determining the prevalence of CTE is difficult. CTE rates of 9–31.8% in contact sport participants have been reported in brain bank cohorts.[7,8] Extended exposure to RHI increases the risk of CTE.[9]

"Traumatic encephalopathy syndrome" has been applied when CTE is suspected during life based on relevant history and a non-specific neuropsychiatric syndrome of irritability, impulsivity, depression and memory decline.[4] With advancing disease, gait and speech abnormalities, parkinsonism and frank dementia typically emerge. In our patient, the parkinsonism, with early cognitive and neuropsychiatric manifestations, was most likely due to a combination of the Lewy body disease and CTE.

The older an individual with dementia, the less likely a single pathology is responsible. As in this case, comorbid neuropathologic processes

Figure 1: Summary of neuropathological changes in the brain: a) Lewy body in a pigmented neuron of locus coeruleus (blue arrow; haematoxylin and eosin stain, scale bar=50µm); b) alpha-synuclein immunohistochemistry showing cortical Lewy bodies in the middle frontal gyrus (scale bar=100µm); c) beta-amyloid immunohistochemistry showing amyloid plaques in the middle temporal gyrus with overlying amyloid angiopathy (blue arrow; scale bar=500µm); d) tau (AT8) immunohistochemistry showing a high density of neuropil threads and neurofibrillary tangles in the transentorhinal cortex (scale bar=50µm); e) marked neuronal loss and gliosis within CA1 of the hippocampus consistent with hippocampal sclerosis (blue arrow; scale bar=200µm); and f) phosphorylated TDP-43 immunohistochemistry showing neuronal cytoplasmic inclusions within the dentate gyrus of the hippocampus (scale bar=50µm).

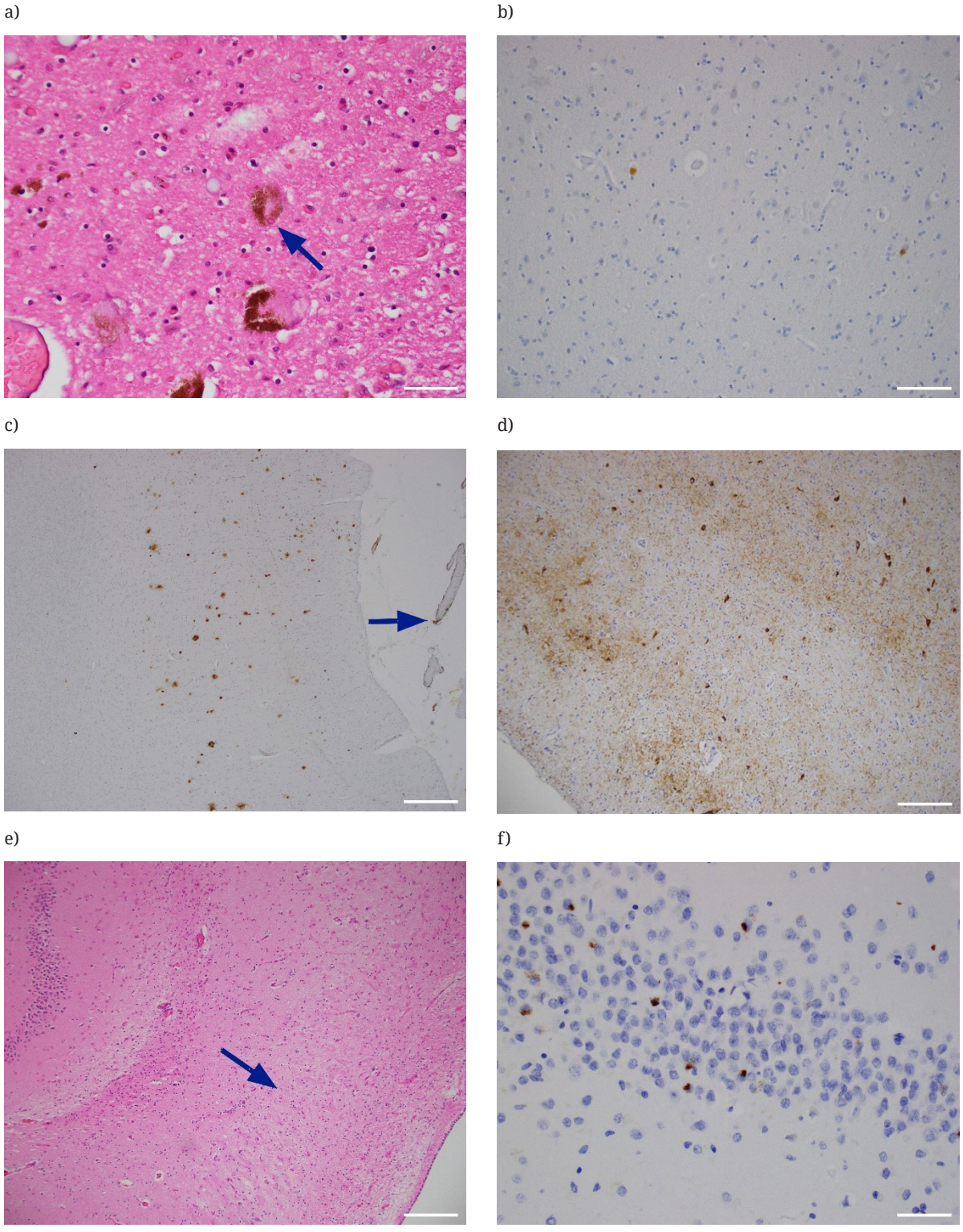
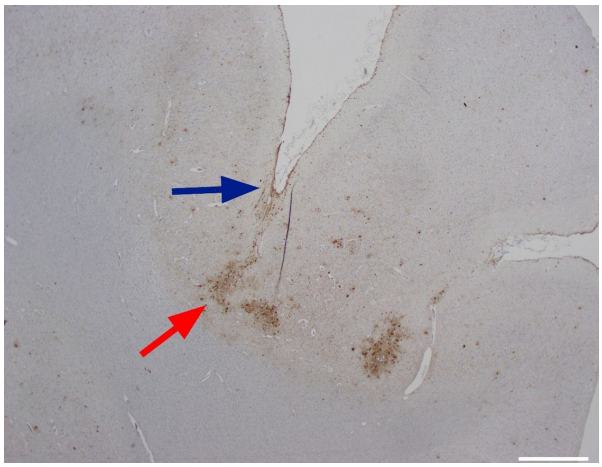


Figure 2: a) Tau (AT8) immunohistochemistry showing deep sulcal perivascular tau consistent with CTE (red arrow) in the inferior parietal lobule. Subpial astrocytic tau pathology consistent with ARTAG (blue arrow) is also present (scale bar=1mm); b) higher power view of the neuronal and glial tau pathology around a deep sulcal vessel in the inferior parietal lobule (scale bar=50µm). Inset 3R tau immunohistochemistry highlights the perivascular tau neurofibrillary tangles; c) tau (AT8) immunohistochemistry showing dendritic neuronal swellings in CA4 of the hippocampus (scale bar=50µm).

a)



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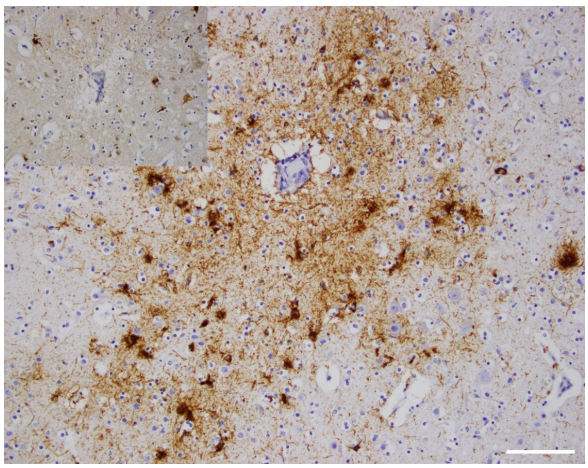

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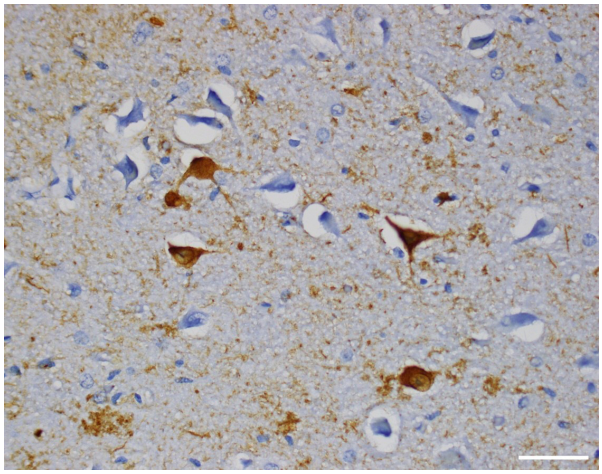

(e.g., Alzheimer's disease and Lewy body pathology) are described in conjunction with CTE.[10] The relative contribution of the multiple neurodegenerative pathologies to the clinical picture in our case cannot be stated with confidence and no pathological criteria exist to make this distinction. CTE may develop in early adult life, when such confounding variables are less likely.[9]

CTE should be considered in any individual at risk of RHI and may be seen in conjunction with other neuropathologic processes. Postmortem examination is the only way to definitively diagnose CTE—and should be considered in any individual with neuropsychiatric features and a history of RHI.

COMPETING INTERESTS
Nil.

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