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LETTER TO THE EDITOR

Chronic Traumatic Encephalopathy (CTE)-Type Neuropathology in a Young Victim of Domestic Abuse

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To the Editor:

We present the case of a 29-year-old woman with a history of being the victim of domestic violence. She underwent postmortem examination and was found to have died as a result of a final domestic violence incident. Autopsy revealed evidence of significant remote head injuries in the form of extensive scars over the scalp and so-called "cauliflower ears". Immunohistochemical staining for phospho-tau revealed evidence of chronic traumatic encephalopathy (CTE)-type pathology, marking the first case of CTE pathology in a young victim of domestic violence. The aim of this report is to raise awareness of the need for additional and ongoing studies of the chronic effects of head trauma in victims of domestic violence, by both the neuropathology community, and more importantly, the forensic pathology/medical examiner community. The latter is in a unique position to identify such cases and raise awareness of the underreported long-term effects of domestic violence.

CTE is a neurodegenerative disorder defined by the deposition of phosphorylated tau (phospho-tau) in the brain in an irregular distribution, most notably in a perivascular location at the depths of cortical sulci (1). CTE, as the name implies, has been associated with remote and possibly repeated exposure to traumatic brain injury (TBI), although causal links are still debated. The vast majority of published cases of CTE involve men exposed to contact sports, such as American football, boxing, hockey, mixed martial arts, and rodeo (2). It has been suspected, and documented to occur in at least one case of an older female subject who was believed to have been exposed to TBI as a result of physical abuse incurred during domestic violence incidents (3). We report the case of a 29-year-old woman who came to autopsy after an apparent final fatal domestic violence incident following multiple domestic assaults over several years.

The decedent came to autopsy with a reported history that she had experienced an unwitnessed fall at home. A death investigator who responded to the scene noticed quickly that the number and extent of injuries present on the body were inconsistent with the reported history of a single fall. The body was transported to the County Coroner's facility for forensic autopsy examination.

Medical records obtained following the autopsy indicated that between the ages of 24 and 29 years, the decedent had presented to the hospital on at least 4 separate occasions with injuries consistent with blunt force trauma including lacerations, contusions, fracture, and subgaleal hematoma. Of note, there was no mention of concussion-type symptoms in the medical records. There was also no clinical history or investigative information to suggest behavioral symptoms or memory disturbances that may be associated with CTE. The decedent's obituary reported that she had participated in basketball, volleyball, soccer, and track during high school. According to her family, she had sustained one concussion during a high school basketball game.

At autopsy, the external examination of the head revealed abrasions, contusions, and lacerations of the face, nose, upper lip, chin, and ears. The ears were markedly deformed by increased cartilage/scar tissue, a deformity often referred to as "cauliflower ear." Twenty-eight separate lacerations were identified over the scalp. Reflection of the scalp showed subscalpular and subgaleal hemorrhages over the frontal, temporal, apical, and occipital skull. There were no skull fractures, epidural, subdural, or subarachnoid hemorrhages, or cerebral contusions. In addition to the extensive lacerations involving the entire scalp, 21 separate scars of similar size and distribution were noted over the scalp. Internal examination of the neck revealed intramuscular hemorrhage involving the strap muscles and a fractured hyoid bone. Examination of the trunk and extremities showed extensive acute and remote trauma in the form of a lung contusion, kidney lacerations, rib fractures, and hemothorax.

The brain was examined following immersion fixation in formalin for 2 weeks. The cerebrum, cerebellum, and brainstem were unremarkable externally and upon sectioning. Tissue blocks of the bilateral hippocampi (at the level of the lateral geniculate body), middle frontal gyri, superior/middle temporal gyri, lateral parietal cortex, medial superior frontal cortex, temporal poles, and mammillary bodies, as well as unilateral sections of the amygdala, basal ganglia (at the level

TABLE. Immunohistochemistry

Brain Region	Immunohistochemical Stain Performed			
	p-Tau	pTDP-43	Aβ	β-APP
Left hippocampus	–	–		
Right middle frontal gyrus	–			
Left middle frontal gyrus	–		–	
Right superior/middle temporal gyri	–			
Left superior/middle temporal gyri	–		–	
Right lateral parietal cortex	–		–	
Left lateral parietal cortex	–			
Left calcarine cortex	–		–	
Right superior frontal gyrus	–			
Left superior frontal gyrus	–	–		
Right temporal pole	+[a]	–		
Left temporal pole	+[a]			
Mammillary bodies	–			
Midbrain	–			
Pons	–			
Corpus callosum (body)				–
Corpus callosum (splenium)				+[b]
Internal capsule (at thalamus)				+[b]
Middle cerebellar peduncle				–
Dorsolateral pons				–

+[a] = positive for phospho-tau CTE-type lesion(s).
+[b] = positive for β-APP "beaded varicosities" in long white matter tracts.

of the nucleus basalis), thalamus (including the subthalamic nucleus), corpus callosum (body and splenium), internal capsule (at the level of the thalamus), middle cerebellar peduncle, dorsolateral pons, cerebellum (including the dentate nucleus), midbrain, pons, and medulla were submitted for histologic evaluation. Hematoxylin and eosin (H&E) staining was performed on all sections. The H&E-stained sections showed no significant histopathologic abnormalities.

Immunohistochemical staining for phospho-tau (AT8, 1:200; Thermo Fisher Scientific, Waltham, MA) was performed on sections of the left hippocampus, bilateral middle frontal gyri, bilateral superior/middle temporal gyri, bilateral lateral parietal cortex, bilateral superior medial frontal, bilateral temporal poles, mammillary bodies, midbrain, and pons (Table). Sections of the temporal poles showed phospho-tau immunoreactivity within neurons, glial cells, and dystrophic neurites in a perivascular location including areas near the depth of the sulcus as well as near the cortical gyrus, consistent with CTE-type pathology. The section of the right temporal pole (Fig. 1) demonstrated a greater number of CTE-type tau lesions than the left temporal pole (Fig. 2). Higher-power images demonstrated predominantly neuronal involvement (Fig. 1B). The level of CTE-type tau pathology in this case would be best classified as stage I according to the McKee CTE staging scheme (2).

Immunohistochemical stains for β-amyloid precursor protein (β-APP, 1:20 000; Millipore, Burlington, MA) were performed on sections of the corpus callosum (body and splenium), internal capsule (at the level of the thalamus), middle cerebellar peduncle, and dorsolateral pons (Table). The sections of the splenium and internal capsule demonstrated immunoreactivity in the form of beaded varicosities, morphologically characteristic of traumatic axonal injury, and in concordance with the history of the decedent's fatal head injury.

Immunohistochemical stains for phosphorylated transactive binding protein of ~43 kDa (pTDP-43, 1:2000; Cosmo Bio, Tokyo, Japan) were performed on sections of the left hippocampus and bilateral temporal poles. These stains demonstrated no definitive cytoplasmic staining for pTDP-43. Immunohistochemical stains for β-amyloid (6E10, Covance, 1:6000) performed on neocortical sections (Table) were negative for beta-amyloid plaques.

We report the first published case of CTE-type pathology in a young female victim of domestic violence. Prior to this publication, the extent of CTE-type pathology in victims of domestic violence in the scientific literature consisted of a single case report of a 76-year-old woman in a "Letter to the Editor" appearing in the *Lancet* in 1990 (3). This case of CTE was reviewed by McKee et al in 2009 in their review of neuropathologically verified cases of CTE and currently stands as the first documented case of neuropathologic findings consistent with what is now considered CTE pathology in a female victim of domestic violence (4). This case has since been cited in numerous scientific papers over the past 10 years (4, 5). The scientific literature is replete with examples of CTE pathology in males of varying ages who participated in contact sports (2, 4, 5); and the study of CTE pathology in living and deceased subjects is integral to the understanding of this pathology and advancements in multiple subspecialties of medicine, technology, and engineering. However, there is a stark paucity of not only CTE pathology

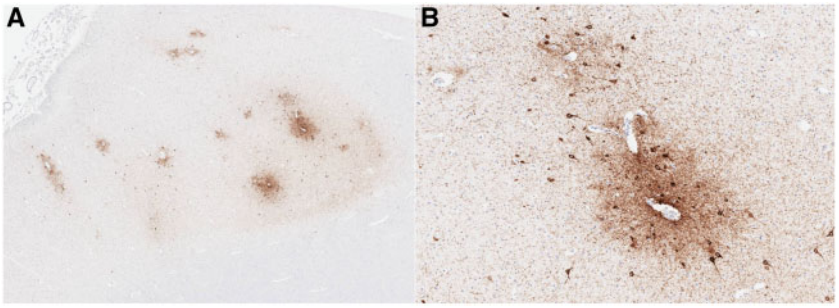

FIGURE 1. Sections of the right temporal pole immunostained with phospho-tau monoclonal antibody AT8. **(A)** Multiple areas of perivascular accumulation of phospho-tau near the depth of a cortical sulcus. Original magnification: 10×. **(B)** Perivascular accumulation of phospho-tau-positive neurons, glial cells, and dystrophic neurites. Original magnification: 100×.

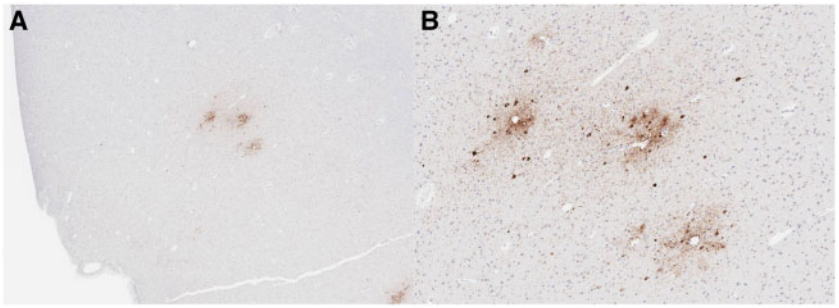

FIGURE 2. Sections of the left temporal pole immunostained with phospho-tau monoclonal antibody AT8. **(A)** Multiple areas of perivascular accumulation of phospho-tau near the depth of a cortical sulcus. Original magnification: 20×. **(B)** Perivascular accumulation of phospho-tau-positive neurons, glial cells, and dystrophic neurites. Original magnification: 80×.

in females in the literature, but more importantly, there is nearly a complete absence in the literature of reports of CTE in victims of domestic violence.

The case described herein demonstrates multiple striking similarities to the Roberts et al case report. Both individuals were subjected to years of domestic violence. Both individuals had evidence of remote trauma in the form of "cauliflower ears" and remote rib fractures. The microscopic changes described in the Roberts case bear a striking resemblance to those in our case, the only difference being that the Roberts case predates the diagnostic criteria established for CTE. Despite these similarities, some stark differences are also evident. The subject of the Roberts case was significantly older, had suffered a stroke, and had become demented, demonstrating memory loss and mental confusion and, therefore, a component of one or more natural disease processes causing these changes cannot be excluded. However, she also had some of the gross findings that have been described in cases of CTE, such as cerebral atrophy and a septum cavum with fenestrations. Not surprisingly, the Roberts case demonstrated the presence of β-amyloid diffuse plaques, but these likely represented age-related Alzheimer-type changes.

History obtained from the family of the decedent in the current case indicated that she had suffered a single concussion while participating in high school basketball. There is scientific evidence that suggests exposure to TBI is a strong environmental risk factor for the development of dementia (6), including studies linking the development of neurodegenerative disease to a single TBI (7). However, a key element missing in our case is the development of any symptoms associated with, or a clinical diagnosis of, dementia. The significance and possible contribution of a single concussion sustained during high school sports participation to the development of CTE-type pathology cannot be ignored in this case, although the degree of head trauma indicated by the external findings at autopsy is far more compelling evidence of significant head trauma than a history of a single remote TBI.

The number of individuals affected by any form of physical domestic violence far outpaces the number of individuals with prolonged exposure to either amateur or professional contact sports. According to the National Coalition Against Domestic Violence (NCADV), 1 in 3 women and 1 in 4 men have experienced some form of physical violence by an intimate partner (8). Despite this fact, there is a gross underrepresentation of individuals affected by domestic violence and the long-term sequelae thereof in the scientific literature.

The clear and obvious limitation of this and all previously published case reports in the scientific literature is that they describe the findings in a single individual exposed to a unique set of circumstances in a unique situation, and, therefore, any conclusions drawn from such a study are limited. This report is meant to raise awareness of the need for additional and ongoing studies of the chronic effects of head trauma in victims of domestic violence, not only by the neuropathology community, but also, and probably more importantly, by the forensic pathology/medical examiner

community, which is in a unique position to identify such cases and bring even greater awareness to the underreported long-term effects of domestic violence.

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COMPETING INTERESTS

The authors have no duality or conflicts of interest to declare.

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