Chronic Traumatic Encephalopathy, Suicides and Parasuicides in Professional American Athletes

The Role of the Forensic Pathologist

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Abstract: We present 5 cases of professional American contact sport athletes who committed parasuicides and suicides aged 50, 45, 44, 36, and 40 years old. Full forensic autopsies and immunohistochemical analyses of the brains revealed chronic traumatic encephalopathy (CTE). The brains appeared grossly normal at autopsy without gross evidence of remote traumatic injuries or neurodegenerative disease. Brain immunohistochemical analyses revealed widespread cerebral taupathy in the form of neurofibrillary tangles and neuritic threads without neuritic amyloid plaques. CTE refers to chronic cognitive and neuropsychiatric symptoms of chronic neurodegeneration following a single episode of severe traumatic brain injury or repeated episodes of mild traumatic brain injury. CTE can only be definitively diagnosed by direct tissue examination. Without full autopsies and immunohistochemical brain analyses these cases would never have been identified. Forensic pathologists will play a vital and central role in the emerging disease surveillance of CTE in professional American athletes, in the identification of CTE cases, and in the establishment of the epidemiology of CTE, with the goal of eventually developing preventive and interventional therapeutic protocols for CTE outcomes.

Key Words: suicide, chronic traumatic encephalopathy, autopsy, forensic pathologist

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The working group for the operational criteria for the determination of suicides defined a suicide as a "death arising from an act inflicted upon oneself with the intent to kill oneself."[1] Parasuicides may be defined as all nonfatal suicidal behaviors regardless of their intentional nature and may include both suicide attempts and deliberate self-harm inflicted with no intent to die.[2,3] We present a case series of chronic traumatic encephalopathy (CTE) in 5 professional American contact sport athletes, 4 of these cases committed suicides, while one made several suicide attempts before he eventually died as a result of coronary artery disease.

In 2002, we identified and published, for the first time in the medical literature, the brain tissue substrates of CTE in a deceased professional National Football League (NFL) player.[4] Subsequently, we have identified a case series comprising 4 deceased NFL players and one deceased World Wrestling Entertainment wrestler. All these cases manifested parasuicides and suicides with similar terminal premorbid neuropsychiatric profiles. Autopsy with brain tissue immunohistochemistry confirmed the presence of diffuse cerebral taupathy, consistent with CTE. There was no premortem diagnosis of CTE and without full autopsies and postmortem brain tissue immunohistochemistry, the diagnosis of CTE would have been missed in these cases. As a neurodegenerative disease, definitive diagnosis of CTE can only be made by direct postmortem brain tissue analyses.

The forensic pathologist plays a vital role in identifying cases of CTE who committed suicide. We recommend that full autopsies with neurodegenerative analyses of the brains be performed on professional contact sport athletes who die suddenly to identify CTE cases and further confirm the forensic significance of CTE as a valuable ancillary tool in the determination of cause and manner of death.

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CASE SERIES

Case One

A 50-year-old white man, who was a professional American football player, and had played in the NFL for approximately 17 years. He died approximately 12 years after his retirement from the NFL, and had manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments (Table 1) including several suicide attempts. He died as a result of myocardial infarction due to coronary atherosclerotic disease. A full autopsy was performed by a forensic pathologist and the whole brain was fixed in formalin for comprehensive neuropathologic examination and neurodegenerative work up with a battery of specialized histochemical stains and immunohistochemical stains. The brain appeared normal by unaided gross visual inspection. Brain histology revealed mild neocortical neuronal loss with sparse to moderate topographic tau immunopositive neurofibrillary tangles and neuritic threads in the neocortex, subcortical ganglia and brainstem nuclei, accompanied by frequent diffuse amyloid plaques in the neocortex, consistent with CTE. There had been no premortem clinical diagnosis of CTE.

Case Two

A 45-year-old African-American man, who was a professional American football player, and had played in the NFL for approximately 8 years. He died approximately 12 years after his retirement from the NFL, and had manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments (Table 1) including several suicide attempts. He committed suicide by ingesting ethylene glycol. A full autopsy was performed by a forensic pathologist and the whole brain was fixed in formalin for comprehensive neuropathologic examination and neurodegenerative work up with a battery of specialized histochemical stains and immunohistochemical stains. The brain appeared normal by unaided gross visual inspection. Brain histology revealed mild neocortical neuronal loss with sparse to frequent topographic tau immunopositive neurofibrillary tangles and neuritic threads in the neocortex, subcortical ganglia and brainstem nuclei (Fig. 1) without amyloid plaques, consistent with CTE. There was no premortem clinical diagnosis of CTE.

Case Three

A 44-year-old African-American man, who was a professional American football player, and had played in the NFL for approximately 12 years. He died approximately 11 years after his

TABLE 1. Behavioral Features Identified in Our Five Cases by Death Investigation Interviews of Close Family Members and Friends

Professional play in the NFL
Long latent period between draft into the NFL and manifestation of symptoms
Progressive deterioration in social and cognitive functioning
Loss of memory and memory disturbances
Loss of language, incoherence
Loss of executive functioning
Dismal business/investment performance
Dismal money management
Deterioration in socio-economic status
Bankruptcy
Paranoid ideations
Social phobias
Exaggerated responses to life stressors
Bouts of anger, worry and agitation over minor issues
Rampant fluctuations in mood (highs and lows; happy and sullen)
Breakdown of intimate and family relationships
Spousal separation and divorces
Insomnia
Hyperactivity, restlessness, high energy level, high performance drive levels
Major depression
Suicidal ideations and thoughts
Suicide attempts/completed suicides
Increasing religiousity
Headaches, generalized body aches and pain
Violent and criminal behavior/tendencies
Alcohol and drug abuse
Direct autopsy brain tissue evidence of cerebral taupathy: neurofibrillary tangles and neuritic threads

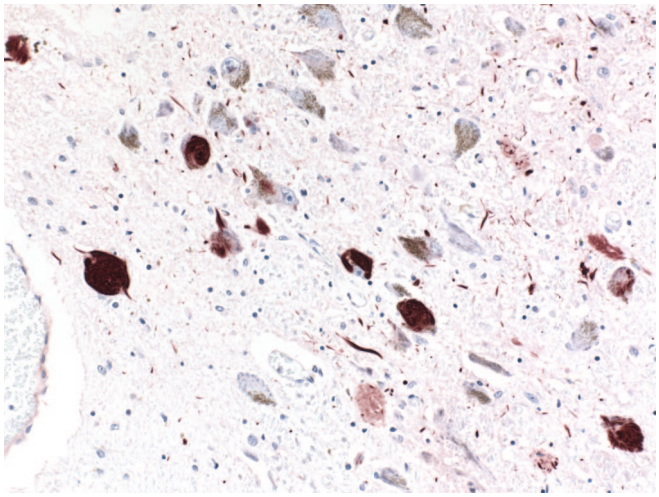

FIGURE 1. Photomicrograph of the polyclonal tau-immunostained section of the locus ceruleus of case two, showing neurofibrillary tangles and neuritic threads accompanied by loss of neurons (×400).

retirement from the NFL, and had manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments (Table 1) including several suicide attempts. He committed suicide by a gunshot wound of the head. A full autopsy was performed by a forensic pathologist and the brain was cut in the fresh state during the autopsy. The brain appeared normal by unaided gross visual inspection except for the evidence of a gunshot wound of the brain. Five small randomly targeted stock pieces of brain tissue were saved in formalin for tissue archival purposes only. These archival brain tissues were later analyzed and stained with a battery of specialized histochemical and immunohistochemical stains. Histology revealed mild neocortical neuronal loss with sparse to frequent topographic tau immunopositive, neocortical and subcortical, neurofibrillary tangles and neuritic threads without amyloid plaques, consistent with CTE. There had been no premortem clinical diagnosis of CTE.

Case Four

A 36-year-old white man, who was a professional American football player, and had played in the NFL for approximately 8 years. He died approximately 6 years after his retirement from the NFL, and had manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments (Table 1) including possible parasuicidal behavior. He died in a 40 mile high speed police chase when he drove on the wrong side of the highway against oncoming traffic and eventually crashed into a tanker truck. A full autopsy was performed by a forensic pathologist and the cause of death was determined to be blunt force trauma. Further investigation of his death and interviews of a family member and an old acquaintance suggested that he may have told close associates that he was going to commit suicide. The brain was cut in the fresh state during the autopsy. The brain appeared normal by unaided gross visual inspection except for the evidence of blunt force trauma of the brain. Ten small randomly targeted stock pieces of brain tissue were saved in formalin for tissue archival purposes only. These archival brain tissues were later analyzed and stained with a battery of specialized histochemical and immunohistochemical stains. Histology revealed mild neocortical neuronal loss with sparse to moderate topographic tau immunopositive, neocortical and subcortical neurofibrillary tangles and neuritic threads without amyloid plaques, consistent with CTE. There had been no premortem clinical diagnosis of CTE.

Case Five

A 40-year-old white man, who was a professional American wrestler, and had wrestled professionally for approximately 22 years. He was a wrestler with the World Wrestling Entertainment at the time of his death. He had manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments (Table 1). He committed suicide by hanging. A full autopsy was performed by a forensic pathologist and the brain was cut in the fresh state during the autopsy and placed back inside the body. The brain appeared normal by unaided gross visual inspection. The cut brain tissue sections were later recovered from the body and fixed in formalin. The brain tissues were analyzed and stained with a battery of specialized histochemical and immunohistochemical stains. Histology revealed mild neocortical neuronal loss with sparse to frequent topographic tau immunopositive, neocortical and subcortical, neurofibrillary tangles and neuritic threads without amyloid plaques, consistent with CTE. There had been no premortem clinical diagnosis of CTE.

DISCUSSION

The first and most widely known variant of CTE was recognized as a disease entity in 1928 by Dr. Harrison Stanford Martland, a pathologist from Newark, New Jersey and the first medical examiner of Essex County, New Jersey.[5] In his landmark article, Dr.

Martland introduced the "punch drunk" terminology into the medical literature to describe "the tendency for experienced boxers to become unsteady on their feet and to move and think more slowly."[6] CTE in boxers is widely known as Dementia Pugilistica or Punch Drunk Syndrome. About 17% of retired professional boxers will exhibit CTE.[7]

CTE refers to chronic cognitive and neuropsychiatric symptoms of chronic neurodegeneration following a single episode of severe traumatic brain injury or (more commonly) repeated episodes of mild traumatic brain injury. Evidentiary histomorphologic findings in the brains of our 5 cases comprise neuronal loss and hyperphosphorylated tau in the form of topographic neurofibrillary tangles and neuritic threads without neuritic amyloid plaques, involving the neocortex and subcortical ganglia and nuclei.

Major depression, neuropsychiatric and cognitive impairments are associated with CTE.[8,9] Our 5 cases exhibited major depression, neuropsychiatric and cognitive impairments in addition to parasuicides and suicides. In 2004, suicides were the eleventh leading causes of death in the United States accounting for 32,439 deaths with a rate of 10.9 suicide deaths per 100,000 people.[10] An estimated 8 to 25 attempted suicides occur per every suicide death. The key risk factors for suicides are depression and other mental disorders, and more than 90% of people who die by suicide have these risk factors.[11] CTE in our 5 cases may represent a common risk factor in our 5 cases. The mechanism of depression and/or mental disorder in these cases may involve neurotransmitter and/or neurohumoral imbalances/depletion due to impairment of normal neuronal functioning and destruction of neurons by hyperphosphorylated tau in the form of neurofibrillary tangles and neuritic threads in specific brain nuclei and systems. Figure 1 shows the locus ceruleus of case 2, which has been damaged by neurofibrillary tangles and neuritic threads. The locus ceruleus secretes nor-adrenalin in the brain.

Without comprehensive postmortem neuropathologic tissue analyses, these cases may not have been identified. It is very pertinent to note that the brains of all our cases appeared grossly normal at autopsy without the expected features of neurodegenerative diseases like cortical and subcortical atrophy. There was also no gross evidence of remote traumatic injuries like old cortical contusions in any of our cases. The value proposition of these cases is that a full autopsy is recommended for professional contact sport athletes whose deaths fall under the jurisdiction of the medical examiner/coroner. Immunohistochemical tissue analyses of the brain should be performed to rule out CTE even if the brain shows no gross anatomic signs of chronic neurodegeneration or remote traumatic injuries.

Similar to dementia pugilistica, forensic pathologists will play a vital and central role in the disease surveillance of CTE in professional American athletes, in the identification of CTE cases, and in the establishment of the epidemiology of CTE, with the goal of eventually developing preventive and interventional therapeutic protocols for CTE outcomes.

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