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Mini Review

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Diagnosis of chronic traumatic encephalopathy (cte) in the intact human subject

Abstract

Considerable attention is being paid to acute concussive injury (Traumatic Brain Injury, TBI) and to the long-term consequence of repeated head trauma (Chronic Traumatic Encephalopathy, CTE). Although related, they are separate and unique entities. With TBI, the search is for means of rapid diagnosis and classification. In the case of CTE, the science has recently advanced from diagnosis by examination of the brain at autopsy to determination in the living human subject by extraction from the blood of a specific, unique biomarker with which this report deals. It is not a detailed review of the subject for the expert but is an introductory article for a series that will follow the development and progression of CTE in a cohort of retired N.F.L. players who have volunteered to be tested at intervals through their lifetimes.

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Discussion

CTE is a chronic, progressive degenerative disease of the brains of people who have undergone repetitive head/brain trauma, first defined in 2002 by examination of brains post mortem.[1] The condition is seen in professional football players, hockey players, boxers, and military veterans who have been exposed to high intensity shock waves on combat missions. The symptoms characteristically begin sometime after the cessation of the sport and/or combat and include memory loss, impaired judgment, anxiety, depression, post traumatic stress disorder, et al., with progression to overt dementia. The cognitive symptoms have long been recognized in professional boxers where "punch drunk" became a commonly used descriptive term. The patient is aware of his/her functional deterioration and cognitive loss, contributing to the high incidence of suicide in this group.

Until a very recent breakthrough reported herein, the diagnosis of CTE has depended upon post-mortem examination of the brain wherein typical neurodegenerative structural and biochemical changes occur. This limitation will be eliminated through recent discovery of the presence of what is proving to be a unique exosome carrying a specific, defective tau protein.

The condition has been brought to public attention because of its high incidence among retired American professional football players in whom CTE has been presumptively diagnosed by their mental signs and symptoms. Some of those so afflicted have volunteered to have their brains examined after death, and the characteristic histological and histochemical features of that form of degeneration have been found.[2] It is notable that the National Football League (N.F.L.) did not publicly acknowledge the relationship between repeated head trauma occurring in the course of players' professional activity and CTE until more than a decade (2016) after CTE's description by forensic neuropathologist Dr. Bennet Omalu 15 years ago (2002) in Pittsburgh, PA.*

Because of the limitations imposed by the one-shot, single post-mortem examination, it had not been possible to define the natural history of CTE save by observing the cognitive signs and symptoms in afflicted individuals, a situation which is reminiscent of medicine as practiced over a century ago. Recently, there has been a search for a candidate biomarker that can be found in human blood, one that can be shown to be uniquely associated with the characteristic degenerative process established at autopsy and that alone.

In the laboratories of Exosome Sciences, Inc. (ESI), a subsidiary of Aethlon Medical, Inc., San Diego, CA (NASDAQ: AEMD), the quest for a unique, identifiable biomarker has been successful. Its scientists have extracted and identified a specific exosome from the blood of subjects with history of chronic, repetitive head injuries and symptoms of CTE, an exosome containing an abnormal tau protein which stands as the candidate biomarker. Preliminary studies have shown that this exosome, termed TauSome™, is found in the blood of subjects with CTE but not in samples from those who have not experienced repetitive brain injury.[2] I should note here that other cerebral degenerative diseases such as Alzheimer's and Parkinson's are characterized by other defective tau proteins.

*Readers who are interested in the story of CTE as a clinical entity will enjoy the movie *Concussion* starring Will Smith.

ESI in conjunction with Translational Genomics Research (TGen) Institute of Phoenix, AZ, is embarking upon a study of 200 retired NFL players to confirm or deny that there is a statistically valid, inverse relationship between TauSome™ levels and the degree of cognitive impairment. There will be a control group of athletes who have engaged in non-contact sports for similar periods of time at collegiate and/or professional levels.[3]

The proposed study should show or refute the existence an inverse relationship between elevated TauSome™ level and development and progression of the dementia of CTE.

TauSome™ level and cognitive ability will be determined and followed at intervals until deaths of the retired NFL players and the control individuals, and followed by post-mortem study of the brains of all involved. This will be a significant step in defining the natural history of the disease and hopefully lead to an understanding of the neurodegenerative, destructive mechanism(s) leading to the clinical picture.

Summary

CTE is an inexorable, neuropathological entity. However, with the ability now to diagnose it in the early stages and follow its progression, perhaps there will be enhancement of research efforts seeking a means of halting the progression of CTE and stabilization of the disease's TauSome™ level and cognitive loss. It is possible that progress in this area will yield benefits in other degenerative, neuromuscular dementias such as Alzheimer's and Parkinson's diseases.

Disclosure

We hold no position in Aethlon Medical, Inc. or Exosome Sciences, Inc., either long or short, and we have not been compensated for this article.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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