A Case Report of Reversible Cognitive Decline in a Former Professional American-Style Football Player: Findings from the Football Players Health Study In-Person Assessments

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Introduction

American-style football (ASF) is a popular sport that has a high risk for injury. Both media and player attention have increased interest in understanding the health consequences of participation in the sport, including both the short- and long-term contributions of repetitive head trauma to the development of neurodegenerative disease. Frontotemporal lobal degeneration has been seen in concert with chronic traumatic encephalopathy (CTE) diagnoses antemortem (1). Recognizing gaps in diagnosis of CTE, experts have developed research diagnostic criteria for CTE including head trauma, clinical features, progressive course and absence of alternative medical, and psychological or neurological diagnosis (2). In a clinicopathological case series of patients with a history of repetitive head injuries and traumatic encephalopathy syndrome, researchers found that two of the nine donated brains exhibited frontotemporal lobar degeneration alongside reported memory and executive function decline (3). In addition, frontotemporal atrophy was reported to be more common in football players who had severe CTE in comparison with their counterparts with more moderate or no CTE (3–7). Findings from several studies investigating the relationship between repetitive subconcussive or concussive injuries and clinical neurological outcomes have been inconclusive, and researchers are still unsure if participation in collision sports has cumulative neurological effects over the course of an athlete's career (8,9).

Despite the documented histopathological changes of frontotemporal atrophy observed in former athletes, Frontotemporal dementia (FTD) diagnoses have not been documented in living former ASF players. FTD is a pathologically and clinically diverse syndrome characterized by impaired judgment, apathy, and other behavioral and/or dramatic personality changes (10). FTD diagnoses continue to remain a challenge among clinicians and researchers, resulting in many patients being misdiagnosed (11). Population studies conducted in Europe and North America report that FTD prevalence ranges from 2.7/100,000 to 31/100,000 (12).

Many of the clinical symptoms of neurodegenerative disease in former ASF players may overlap with other potentially treatable medical conditions. Understanding methods to optimize treatment of the postcareer health in professional athletes is a growing interest in the sports medicine community. This report presents a case of a middle-aged former professional ASF player who was suffering from life-altering cognitive, behavioral, and personality changes that were originally diagnosed as FTD. Upon completion of a clinical research study, this diagnosis was challenged by alternative findings that better explained his neurocognitive issues. Recognition and treatment of hydrocephalus in the former athlete resulted in improvement of his overall health.

Methods

The Football Players Health Study (FPHS) at Harvard is an ongoing study that aims to characterize the long-term health of former National Football League (NFL) players (13). Some

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of the study's participants, ranging in age from 24 to 60 years, took part in "in-person assessments," in which multi-modality cardiovascular, neurocognitive, endocrinologic, sleep, and chronic pain assessments were performed over the course of a 3-d study visit (14). Prior to each visit, participants completed an initial telephone screening, in which a cognitive assessment was performed using the Telephone-Montreal Cognitive Assessment (T-MoCA-22) (15) and a detailed medical history was taken. At completion of the study, each participant attended a structured exit interview with a study physician and nurse, and received a printed report detailing clinically actionable findings. For a more detailed report of the methodology of this study, including all of the assessments conducted, please refer to the published In-Person Assessments protocol (14).

Case Description

We present the case of a 54-year-old, white, former professional ASF player who completed the In-Person Assessment Study of the FPHS in January 2020. The former athlete began playing football at 8 years old and played professionally in the NFL for four seasons as a linebacker. According to survey data, the player has a concussion symptom score of 82 reflecting a high level of concussion exposure (16). During his initial screening, the participant reported a history of cognitive impairment, urinary incontinence, and gait disturbance with impaired balance. The participant also stated he was being seen by a medical professional for depression and anxiety, and had received the diagnosis of early onset FTD. His past medical history included uvulectomy and deviated septum repair for sleep apnea, cervical neural ablations (C3 to C8) every 2 years for management of cervical spondylosis, vasectomy, 5 left knee surgeries to repair 2 ACL tears and meniscus injuries, and 3 right knee surgeries to repair ACL/meniscus tears. The participant reported chronic pain that he managed with naproxen and medical marijuana. His T-MoCA score was 17, indicating mild cognitive impairment (15,17).

The participant completed the 3-d assessment and exit interview. His sleep study suggested moderate sleep apnea. Laboratory testing was notable for low HDL and vitamin D. Cardiovascular testing included a normal electrocardiogram, normal echocardiogram, and mildly impaired exercise capacity (peak $\dot{V}O_2$ of 23.4 $mL \cdot kg^{-1} \cdot min^{-1}$, 73% predicted).

Brain magnetic resonance imaging (MRI) showed mild enlargement of the third and lateral ventricles relative to the sulci and cisterns, with balloon-like rounding of the frontal horns of the lateral ventricles, suggesting mild hydrocephalus. No obstructing aqueductal lesion was apparent. There was no evidence of frontotemporal atrophy (Fig.).

The participant's electroencephalogram (EEG) demonstrated nondiagnostic cortical slowing that were nonspecific as to their etiology, but possible causes could include metabolic or toxic encephalopathies, medication effects, neurodegenerative disorders, central nervous system infectious disorders, traumatic injury, midline/brainstem structural lesions, or hydrocephalus.

Results including findings from the MRI were shared with the participant during his exit interview. The radiographic findings of hydrocephalus and cognitive behavioral changes associated with this condition were explained, with a recommendation to consult with a neurosurgeon after returning home to further evaluate for treatment of hydrocephalus.

In a follow-up interview conducted by our study nurse in September 2022, the participant reported that, following additional diagnostic testing, he had elected to have a ventriculoperitoneal shunt placed in February 2020. This evaluation was performed greater than 2 years following the participant's research visit. Following that procedure, he experienced a tremendous improvement in his mood, and many of his initial cognitive complaints had largely resolved.

Discussion

Our report intends to show that not all forms of cognitive impairment or behavioral changes represent irreversible dementia. This patient's original diagnosis of FTD may have been influenced to some extent by his history of playing ASF and concern for head trauma associated with neurocognitive impairments (18). Normal pressure hydrocephalus is a common cause of cognitive decline, and there have been reports in the popular media of ASF players being diagnosed with this syndrome (19). Collision sport athletes may develop posttraumatic hydrocephalus after an accumulation of scar tissue within the ventricles obstructs the normal reabsorption of cerebrospinal fluid (20). However, the prevalence of diagnosed hydrocephalus in ASF players has not been reported. In the general global population, the prevalence of hydrocephalus is reported to be 11 in 100,000 adults (21).

Research investigators have an ethical responsibility to return results of incidental findings to participants, especially if the findings are medically actionable. We have developed a standard method to review both neuroradiology results along with other findings that may influence future clinical treatment. We suggest that providers should consider hydrocephalus in their differential diagnoses, and our case illustrates the potential value in obtaining an MRI of the brain when evaluating a patient presenting with new onset dementia. Providing

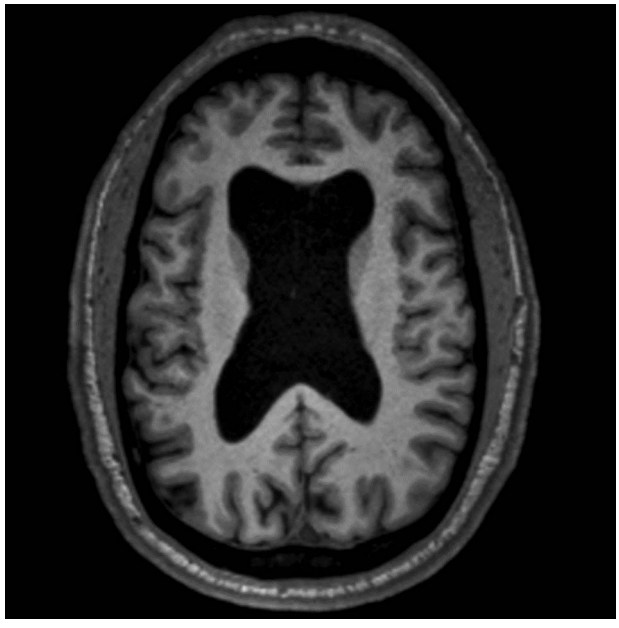

Figure: Axial T1-weighted image of the brain, showing relative enlargement of the lateral ventricles, with balloon-like rounding of the frontal horns, suggesting hydrocephalus.

Table.
Examples of health conditions and behaviors that may contribute to cognitive impairment.

Psychiatric factors
Anxiety
Depression
Activity deficit hyperactivity disorder
Substance use disorder
Sleep disorders
Sleep apnea
Insomnia
Other behavioral sleep disturbances
Pain
Untreated/suboptimal management of orthopedic injuries or spine disorders
Side effects of medications used to treat pain (benzodiazepines, opioids)
Cardiometabolic disease
Diabetes
Hypertension
Myocardial infarction or structural heart disease
Cerebrovascular Disease

This table includes health conditions and behaviors, which also may present as impairments in physical and mental health and are important to identify and treat in former ASF players along with other athlete populations.

clinically relevant results to research participants improves participant knowledge of personal health and facilitates subsequent clinical care. Future research may be helpful in determining the impact of result returns on subsequent clinical outcomes.

The case illustrates the importance of taking a holistic approach to understanding health concerns in a former athlete. Research from the Football Player Health Study has explored multiple aspects of health and impairments that are observed in former ASF players that include neurocognitive impairments and other domains, including cardiometabolic, sleep apnea, and chronic pain. For example, using questionnaires in more than 4100 former players, we have observed that multiple health domains may be associated with impairments in physical and mental health (22). History of concussion may be associated with depression, anxiety, and impaired quality of life in this cohort (23). Contributing medical and psychiatric diagnoses, such as anxiety and depression, have known clinical treatments pathways.

This case demonstrates how a careful clinical evaluation identified a better explanation for this patient's behavioral changes than a diagnosis of FTD, a progressive neurological condition with poor prognosis. Because of the high visibility of ASF and its health consequences, we believe it is important to consider alternative causes of cognitive decline that are treatable (Table).

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