Chapter 1

American Football: Cognitive Impairment

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In collision sports there is ongoing ethical and scientific debate on the relevance and significance of previous heavy physical contact burden and, specifically, previous head injuries and the possible neuropsychiatric effects on the ageing athlete.

A sports psychiatrist with expertise in the evaluation of cognitive dysfunction is well placed to assess athletes who present with changes in behaviour and especially when classic short-term memory deficits may not be obvious on initial assessment. Atypical presentations may be found with onset in later life; changes in social function may be specific to the life stage and patient expectations may be different. Treatment options may put greater emphasis on social interventions and pharmacological options differ from those used in a younger individual.

The majority of players retire from elite sport before the age of 40, yet their sporting identity can remain a strong component of their sense of self and contribute to their quality of life for many years. The complexity of interaction between physical and cognitive decline, adjustment to a post-sporting life and social problems experienced in older adults often require collaboration between many professionals and a multidisciplinary approach to treatment and care.

Background

FB is a 53-year-old Caucasian male living in the USA. He had played professional football in the NFL until his thirties and in retirement had worked as a coach. He has two grown-up children who have now left home. He is not currently working and lives with his wife of 28 years. He was initially reviewed by his family doctor in response to his wife's concerns. Although his participation in this initial consultation was minimal it was noted that his personality seemed to have coarsened and there were significant changes in his behaviour. As a result he was referred to a psychiatrist for a more detailed assessment. He only agreed to attend this assessment after much encouragement from his family and friends although he had admitted privately to a friend that 'something was not quite right'. The report from this psychiatric assessment is set out below.

Presenting Complaint

F: 'I'm not sure what all the fuss is about, everything is fine with me.'

WIFE: 'He's a different man from before and is completely unpredictable.'

History of Presenting Complaint

F's wife reported that over the past five years his moods had been very 'up and down'. More recently over the past two years she had felt 'on edge' around him and feared making him angry. She had not considered a medical cause for this, until recently.

His wife provided the majority of this initial history, although FB participated as rapport improved and he responded more openly to questioning as the consultation progressed.

F had retired from professional football 18 years earlier at the age of 35. After struggling with the transition out of professional sport, he began working as a coach for his college team alongside an old team-mate. His players loved his infectious and 'fiery' demeanour and he would regularly let off some steam at his players and match officials. However, his wife noted him to be withdrawn and quiet after training and games, with little meaningful conversation in the evenings. She put this down to him having a busy schedule and tried to get him to socialise more with family and friends, and this seemed to work initially. F held this position for 12 years before voluntarily stepping down. He said he left because he lost his 'passion' to coach. In hindsight, this was when his wife had noticed deterioration in his behaviour.

Since leaving this coaching position, he had not looked for employment again and as he was financially comfortable he had intended to engage more with family life and find other hobbies. His wife reported that he had not 'done much of anything since then'. F often stayed up late watching TV, which he had seldom if ever done previously. It greatly concerned his wife that he now rarely left the family home unless he was with someone. She was concerned at how agitated he could become even in previously familiar surroundings. His wife had hoped he would 'snap out of it'. She admitted to 'putting up with him' and only considered going to the doctor in recent months, as things had got unbearable for her and she described that 'he needs almost constant supervision'.

F's behaviour had also become unpredictable in company over the past six months and he had embarrassed his wife with inappropriate sexualised comments during their infrequent social occasions. He could become irritable at the slightest change to his routine around the home (e.g. food choices, bed time and unexpected visitors). She felt she could calm him down but this was taking longer and longer to achieve. His wife thought this had been a general gradual decline rather than a sudden deterioration.

On 'good days', F enjoyed talking about 'the old times' when friends occasionally visited and he continued to watch and enjoy most sports on TV. He felt able to follow the game plans and was able to comment on tactics. His wife had noticed that he had started to have difficulty finding the sporting channels on the TV.

F said he felt low and rated his mood at 6/10. He still enjoyed some of his usual activities and denied any daytime fatigue or sleep difficulties. He did admit to boredom when at home and would like to get out of his house more but had no specific plans on how to achieve this. When directly asked, he was adamant there were no issues with his memory, concentration or perceptions. He easily recounted his sporting career and remembered scores from specific games from many years previously but struggled to recall recent games he had watched on TV and this caused some embarrassment and agitation.

F said that he thought his family were overreacting although he did not have an explanation for their observations.

His wife was asked directly if she had noticed any repetitive movements, ritualistic or compulsive behaviours or any altered food preferences but denied that any of these features were present.

Past Psychiatric History

He had never previously had any mental health problems. Specifically, he had never had treatment with any psychiatric medication and no periods of psychiatric hospitalisation.

Family History

His maternal grandmother had dementia and towards the end of her life had required intensive nursing care for over two years.

Past Medical History

Hypertension well controlled with medication.

Arthritis in both knees and in the small joints of his hands.

During his professional sporting career he had numerous rib fractures but without long-term complications, corrective surgery on his right achilles tendon, a meniscectomy in right knee, and a right biceps tendon repair.

F reported numerous concussions over his playing career. He admitted that he would often minimise or not report symptoms to avoid being taken out of play. He thought he had experienced approximately '20 or 30' in varying degrees of severity. Residual post-concussive symptoms commonly included headaches, light-sensitivity, nausea and dizziness. Symptoms ranged from 2–15 days in duration. He denied loss of consciousness with any of his concussions. In the final two years of his professional career he had begun experiencing chronic headaches, which dissipated when he retired.

Medication

No known drug allergies

Angiotensin-converting enzyme inhibitor (for hypertension)

Topical anti-inflammatory

His wife sets his medication out for him daily and monitors his adherence

Social History

F has been married to his wife for 28 years and they live in their own home together. She did charity work through her church as a regular hobby but of late had become reluctant to leave her husband alone for any significant period of time. They have two adult children who are both in their twenties and have moved away from the family home.
He drank the occasional glass of red wine with food although was a non-smoker and denied any recreational drug use.

Personal History

F described his childhood experiences as 'simple'. He grew up in a small rural town where his father was a farmer and his mother a part-time waitress. He had one younger sister and continued to have a good relationship with her. He said that he was 'hyper' as a young child and consequently his parents encouraged him into sports, primarily as a means to release some of his excess energy. Academically he was an average student.

His passion for his sport was prioritised over academic studies throughout school. He began playing football at age 10 and in high school played as a running back. At college he was switched to playing defence where he received national attention for his superb speed and aggressive style of play. He played in this role for the rest of his professional career.

Pre-Morbid Personality

He described himself as an extroverted person and enjoyed socialising with peers. His wife agreed with this.

Forensic History

There was no formal contact with the police although 18 months previously he was given a ride home following an isolated drinking session in a local bar with former team-mates.

Collateral History

Before the conclusion of F's evaluation, his wife was interviewed alone. She admitted she 'should have done something about this long before now, I've let him down'. She added that he had displayed more hypersexual tendencies, in the form of frequent demands for sex from her. He had also accused her of being unfaithful.

Four weeks earlier, she had contacted the police after he aggressively confronted her. No further action was taken as the situation was defused with the police presence. This incident was the main catalyst for her decision to pursue a psychiatric assessment.

F's son and daughter visit approximately twice a year. On the most recent visit, they noticed a change in their father's short-term memory. They had expressed concerns with regards to his behaviour previously but he would always dismiss this. His son reported that his father had become repetitive in conversation and had noticed him misplacing several items during his most recent stay. F's wife had not observed any obvious signs of disorientation in memory although on reflection felt he might be covering up any deficits. His daughter had also noticed that he had stopped helping out around the kitchen with meal preparation and other chores as he used to. He had also twice left the shower on without noticing. He had stopped texting his daughter and now preferred to phone her when getting in contact. F was largely dismissive of any memory issues although did appreciate he may have had 'one too many head knocks back in the day'.

Mental State Examination

F presented as taller than average and muscular. He appeared older than his age. He was dressed casually in jeans and a shirt. His hygiene and grooming were reasonable although he had several small shaving cuts on his chin and cheek. No involuntary movements or tremor were observed. His gait was slow and deliberate and he displayed appropriate eye contact

although with a rather blank expression at times. He enquired of the assessor's name and qualifications on three occasions and looked to his wife for reassurance throughout the assessment. He mostly laughed off any lapses in short-term memory or pauses to collect his thoughts. His demeanour was generally calm and cooperative during the interview, although there were a few instances of mild irritation and defensiveness when concerns over changes in memory were raised. F was able to follow basic instructions. His speech was of normal tone; however, there was evidence of word-finding difficulty and repetitive content – particularly of his past sporting career. He swore occasionally in a non-aggressive way and would then quickly apologise. His mood was reported as 'great', while his affect appeared dysthymic with limited variability. His thoughts were concrete in nature, focusing on being assessed by a psychiatrist, and periodically required redirection. There was no obvious delusional thought content and he was not obviously responding to any external stimuli. His insight was limited with regards to any possible ongoing mental illness and in particular he downplayed or denied any problems with his memory and mood.

Risk Assessment

Self: He had not expressed any suicidal intent or plan and there was no history of such behaviours. His wife gave him medication, which was locked away in a cupboard as he had become disorganised previously and at risk of either non-adherence or unintentional overdose. There had been no instances of wandering during the night and he was accompanied by his wife throughout the majority of the day and when outside his home, which minimised the risk of any wandering or disorientation. His wife had taken over management of the family finances.

Others: Recent escalation in irritability and verbally aggressive confrontations with his wife. He did not have access to firearms. He had stopped driving his car at the request of his wife.

Protective factors: He recognised that something was 'not quite right' and had agreed to attend in order for this to be assessed and to stop driving. He had a caring and attentive family environment. F was not using any disinhibiting agents e.g. illicit drugs or high consumption of alcohol.

Physical Examination

Pulse and blood pressure were in the normal range (pulse 68 bpm and blood pressure 136/84). Pupils equal and reactive and fundoscopy showed no pathological cupping of the discs. Orientated to person, place, time and situation. Speech was mildly dysarthric but comprehension was intact. Upper extremity exam notable for mild bilateral rigidity, bradykinesia and progressive slowness and amplitude of rapid alternating movements. No intention tremor. No clear asymmetry. Finger-to-nose testing was non-fluid. Unable to maintain balance during pull testing.

Investigations

Laboratory investigations: normal full blood count, thyroid, liver and renal function. Elevated triglycerides and total cholesterol. Infection markers normal (including C-reactive protein).

Urine dipstick was clear with no protein or glucose.

Neurocognitive testing: Montreal Cognitive Assessment (MoCA) 19/30

Visuospatial 3/5

Naming 1/3

Attention 4/6

Language 3/3

Abstraction 0/2

Memory 2/5

Orientation 6/6

(The MoCA is a scoring tool used to assist clinicians with patients who may have a dementia illness. It tests a variety of cognitive domains as set out above. 'Normal controls' would be expect to score between 27 and 30 points and a score below 18 would be considered evidence of an ongoing dementia syndrome.)

Neurocognitive testing: Frontal Assessment Battery (FAB)

Similarities – 2

Lexical fluency – 2

Luria Test – 2

Conflicting instructions – 1

Go No Go Test – 2

Prehension Behaviour – 1

(The FAB is a tool that can be used at the bedside or in a clinic setting to assist in discriminating between dementias with a frontal lobe predominance and dementia of Alzheimer's type. The FAB has validity in distinguishing fronto-temporal-type dementia from Alzheimer's dementia in mildly impaired patients (Mini Mental State Examination (MMSE) > 24). Total score is from a maximum of 18, higher scores indicating better performance.)

Neuroimaging: MRI brain imaging performed one month previously showed generalised cortical atrophy, with mild hippocampal volume loss.

Case Formulation

F presented as a 53-year-old Caucasian male and a former professional NFL player. There had been an insidious onset of unpredictable behaviour and decline in cognitive function that had become more apparent since retirement from coaching. The symptoms of unpredictability and aggression had led to acute safety concerns expressed by family members and led them to pursue a clinical opinion on his change in behaviour. A decline in activities of daily living was noted from the collateral history. Reliance on others had contributed to F becoming frustrated at his ability to attend to his own needs. He appeared to be largely apathetic to any ongoing concerns expressed by others.

A family history of dementia (second degree relative) suggested a possible genetic component to his condition. His previous occupation had exposed him to repeated head traumas which may not have been recognised, disclosed or been partially evaluated at the

time. He did not appear to have an educational background that would minimise any cognitive deficits ('cognitive reserve').

Deficits on formal cognitive assessment were noted with frontal lobe predominance. The combined history, objective cognitive testing and basic neuroimaging would suggest F had an unspecified dementia syndrome. On account of his age, this could be as a result of early-onset Alzheimer's dementia, vascular dementia or the behavioural variant fronto-temporal dementia. Chronic traumatic encephalopathy (CTE) and traumatic brain injury (TBI) would also form part of the differential diagnosis. He had presented relatively late negating the possibility of early interventions.

Plan

- A safety plan was discussed and agreed with the patient and his family, who were also given information on his possible diagnosis. F's wife was given information on how to optimise living conditions at home to reduce the potential for falls and minimise the risk of wandering, and was given orientation aids for around the home. F's wife discussed possible triggers for increased agitation and a plan for help, should this be unmanageable, was agreed
- F was referred to an occupational therapist for a functional assessment to assist with domestic needs
- He reluctantly agreed to a further referral to a neurologist for consideration of additional investigations such as Single-Photon Emission Computed Tomography scan (SPECT) and lumbar puncture (for tau and amyloid-beta). This referral would assist with diagnostic dementia subtyping and attempt to rule out any rarer organic cause for the presentation, such as variant Creutzfeldt-Jakob disease or Lewy body dementia
- An outpatient follow-up review with the assessing psychiatrist was arranged for one month's time

Questions

Q 1 Which statements are correct regarding CTE?

A. Cavum septum pellucidum is a common finding
B. Neurofibrillary tangles typically cluster in the depths of cortical sulci
C. CTE has only been described in individuals exposed to repetitive brain injury
D. CTE is synonymous with dementia pugilistica and symptoms may include emotional lability, memory impairment and ataxia
E. Although tau pathologies are typical of CTE, other neuropathology patterns may co-exist

Q 2 Which of the following investigations will allow a definitive diagnosis of CTE to be made in this case?

A. Cerebrospinal fluid phospho-tau and amyloid-beta assessment
B. Positron emission tomography (PET) studies for tau
C. Functional MRI
D. Post-mortem examination of the brain
E. The proposed SPECT studies

Q 3 CTE is associated with exposure to repetitive mild traumatic brain injury/concussion. Of the following, which is known to be associated with lower concussion risk within sport?
A. Protective headgear, such as football helmets
B. Age under 18
C. History of previous concussion
D. Artificial football pitches
E. Male versus female sex

Q 4 Answer true or false to the following statements:
A. A majority of former NFL players will develop CTE
B. There is no effective therapy for CTE
C. Historically, suicide rates are known to be higher than anticipated in former NFL players
D. CTE was first described in 2005
E. Cases of CTE have been described in individuals with no known exposure to brain injury or contact sports

Q 5 Choose the correct statements regarding management of neuropsychiatric symptoms (NPS) and persistent concussive symptoms:
A. All forms of psychiatric medications are absolutely contraindicated in those experiencing NPS in concussion
B. There are low levels of empirical data to guide psychiatric treatment after single or repetitive concussions
C. A biopsychosocial formulation and management plan for NPS should be followed for athletes with persistent concussive symptoms and NPS
D. Medication should only be prescribed if licensed for NPS in persistent concussion symptoms
E. Graded, sub-maximal aerobic exercise may help athletes towards post-concussive recovery

Answers

Q 1) A, B, D, E

Clinical observations of the chronic neuropsychiatric outcomes of former boxers in the early part of the twentieth century led to the first descriptions of what was then referred to as the 'punch-drunk' syndrome (1). In the decades that followed, a typical syndrome of psychiatric symptoms, emotional lability, personality changes, memory impairment and dementia, pyramidal and extrapyramidal dysfunction and cerebellar impairment was described (2). Neuropathological studies over the latter half of that century defined and named the pathology as dementia pugilistica (3, 4).

With more recent recognition of this pathology in a range of athletes in sports other than boxing (5–10), and in those surviving exposure to a single moderate or severe traumatic brain injury (11,12), the term 'chronic traumatic encephalopathy' (CTE) has replaced 'dementia

pugilistica'. Neuropathological consensus criteria for the assessment and diagnosis of the pathology associated with CTE have been defined (13). These describe common abnormalities in the septum pellucidum, either as cavum or fenestrated septum, together with histological evidence of CTE neuropathologic change (CTE-NC) in a typical pattern and distribution of hyperphosphorylated tau (p-tau) pathology. P-tau pathologies in CTE-NC typically appear as patchy cortical deposits in neurons and glia. In early series on the pathology of boxers, neurofibrillary tangles containing p-tau were described with a distribution to the medial temporal lobe (4). Later series noted a more patchy distribution of pathology, often clustered at the depths of cortical sulci, and with apparent preferential involvement of superficial cortical layers.

Despite a majority of case series describing pathology in symptomatic former athletes, CTE-NC can be encountered in apparently cognitively intact 'normal' controls. A review of tissue samples from the Queen Square Brain Bank (London, UK) identified CTE-NC in 12% of cases whether or not there was a history of neurodegenerative disease (14).

While tau pathologies are typical of CTE-NC, multiple other pathologies have also been found in material from former contact/collision sport athletes and a number of other neurodegeneration associated proteinopathies are recognised in CTE. Amyloid-beta (A-beta) pathologies are commonly described alongside p-tau pathologies from the earliest descriptions in boxers (15) to more recent case series in non-boxer athletes (10, 11,16). Notably, the prevalence of A-beta plaque pathology in CTE increases with increasing age at death and is more commonly encountered where there are clinical symptoms of cognitive impairment (16).

The emerging picture is of a complex pathology in which CTE-NC may be the primary dementia-associated pathology, often with multiple other co-morbid pathologies present. CTE-NC may also be a co-morbid pathology in the context of an alternative dementia diagnosis or may represent as an incidental pathology in an otherwise asymptomatic patient (10).

Q 2) D

Although preliminary consensus criteria for the neuropathological assessment and diagnosis of CTE-NC are agreed (13), no such consensus criteria for the clinical diagnosis of CTE have been defined. As such, definitive diagnosis of CTE requires post-mortem examination with formal neuropathological assessment. In this context, imaging studies remain of limited value; their role being in assisting in the elimination of potentially treatable alternative diagnoses and in narrowing differential diagnosis in suspected neurodegenerative disease. In patients with possible CTE, structural imaging may show abnormalities in the septum pellucidum (17) and atrophy of the medial temporal lobe, but neither is pathognomonic for the condition.

Although the pattern and distribution of p-tau pathologies in CTE-NC are regarded as sufficiently distinct to be pathognomonic of the disease, to date, PET imaging studies have not succeeded in exploiting this pathology for secure in vivo diagnostic purposes. Nevertheless, various radiolabelled tau ligands are under review, and although preliminary data from limited case series hold some promise none have reached clinical practice.

While fluid biomarkers have been extensively researched in wider neurodegenerative disease, in particular Alzheimer's disease (AD) (18), there is considerably less experience in CTE. In patients with AD, high levels of total- and phosphorylated-tau and low levels of

A-beta42 are documented in early phases and at diagnosis. However, thus far, only limited studies in small numbers of former athletes have been pursued, with no clear indication of utility in CTE diagnosis (19).

Q 3) E

Studies exploring the utility of various forms of protective equipment, including headgear, across a range of sports have failed to demonstrate any robust data to suggest any benefit in reducing concussion risk. Many are confounded by poor study design, inconsistent definition of injury and low subject numbers (20). However, helmets do provide benefit in reducing risk of focal head injuries (21, 22), and remain recommended in activities such as ice hockey, ski-ing and cycling.

Regarding other risk-modifying factors in concussion, data confirm that younger age and history of previous concussion are associated with increased injury risk (23). Further, younger individuals are at particular risk of catastrophic outcome from apparently mild TBI/concussion through a rare complication known as diffuse brain swelling, sometimes referred to colloquially as 'second impact syndrome' (24). The pathophysiology of this condition remains uncertain. It appears to be a particular risk in adolescents and hence concussion management in younger age groups is typically more conservative.

Female athletes are recognised as being at increased risk of concussion when compared to male athletes (23); an observation that is supported by data across several sports where participation rules are equivalent for male and female players. The reasons for this are uncertain, although may include the recognised structural differences between male and female axons perhaps resulting in axons in females being more at risk of injury under dynamic loading (25).

Q 4) F/T/F/F/T

Although coming to wider attention with the first description of CTE-NC in a former American footballer in 2005 (5), neither the pathology nor the term CTE originate in this century. First descriptions of the neuropathology of former boxers date to the middle of the last century (26). To date, there are fewer than 400 confirmed cases of CTE-NC in the literature (27). Current reporting in CTE is based on descriptions of brains examined after death as the diagnosis can only be made at post-mortem examination. Inherent biases in case donations and the limitations of small samples mean that no meaningful data on disease prevalence can be obtained. Nevertheless, interpretations of limited studies reporting high prevalence of CTE-NC in their series (28) have led to a belief that CTE is common among certain former athlete cohorts.

Despite first formal description of the 'punch-drunk' syndrome in 1928 (1), studies to identify rates of neurodegenerative disease in former athletes suffer from multiple limitations, including study design and small numbers. Regarding American Football, while a threefold increase in neurodegenerative mortality has been described for a cohort of former NFL players (29), studies in former high school footballers fail to identify increased dementia risk (30). There remains no robust data to allow interpretation of CTE prevalence in populations at risk, let alone sufficient data to suggest that a majority of athletes might develop the disease.