Case Report

A Rare Incidence of Accelerated Dementia Onset Post Traumatic Brain Injury in a 22 year old: a case report

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ABSTRACT

A 22 year old male presented with symptoms of fast-escalating cognitive degeneration and behavioral impairment after a period of clinical recovery post severe traumatic brain injury (TBI). Neuroimaging found extensive mild-moderate cortico-cerebral atrophy not really corresponding to his primary TBI lesions. A diagnosis of dementia [ICD F02.8] was made and patient was treated accordingly, in conjunction with Neurology services, with emphasis on neuro-cognitive rehabilitation. Extensive testing could not find any other likely causes for this condition, which was then postulated to be generalized secondary post-TBI neurodegenerative changes. His symptoms are currently improved and stabilized with ongoing maintenance-phase management, but as this condition is not reversible – this case report discusses likely etiopathological processes and corresponding management options (both presently available and those likely to become so in near future) to be aware of.

Keywords: Traumatic brain injury, post traumatic brain injury dementia, young-onset dementia, fast-onset dementia, neurodegeneration.

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INTRODUCTION

Traumatic brain injury (TBI) is a well-known contributing factor to development of dementia. Early adulthood TBI leads to earlier onset of dementia later in life. Generally, significant TBI hastens the age of onset of dementia by 5-10 years earlier than the general age of onset (60-65 years) [1]. Below, we take a look at a case of a 22-year-old male who, after making satisfactory recovery from TBI due to an open head injury for 3 months, suddenly developed rapid onset memory loss, cognitive degeneration and behavioral disturbances and went on to be diagnosed as dementia (ICD F02.8) [2].

CASE REPORT

Mr. ABC, a 22-year-old unmarried, Marathi speaking male, graduate by education, was brought by family for psychiatric evaluation for steadily worsening forgetfulness and aggressive behavior since 3 months.
On enquiry, 6 months back, he had been in a road traffic accident, suffered severe open head injury with three depressed fractures over the right side of the frontal bone and both parietal bones. He was operated on for bilateral fronto-parietal subdural hematomas, in coma for 20 days following which he regained consciousness – found to be neurologically stable and discharged after 15 further days. The immediate MRI brain following the surgery noted mild cerebral edema over both frontoparietal regions and a sub-centimeter resolving hemorrhage in right capsule-ganglionic area with gliotic patches but not much else of significance. At discharge, he had only been advised phenytoin 100mg TDS, citicoline 500mg OD and vitamin supplements which were subsequently tapered and discontinued over the next 2 months. For about 3 months

after that, he functioned as per his pre-morbid self, without any cognitive or behavioral issues. Then over the next 1 month, the family noticed rapid onset forgetfulness – mostly for short term events, difficulty in thinking logically and therefore stopped continuing with his clerical job, occasional irrelevant speech, and regressed behavior – irritability, sudden demands followed by tantrums if the demands were not met immediately, with occasional explosive anger outbursts including physical aggression. He also became more talkative, outgoing and novelty-seeking – all contrary to his pre-morbid personality traits. His social behavior became very callous, especially with women, and self-care became poor. He also started chewing tobacco and consuming alcohol 3-4 times/week – around 60-90ml of whisky per day. The forgetfulness was gradually impairing his ability to look after himself and sustain meaningful conversation.

Before this incident he had no significant past, personal, family, medical or surgical history and neither history of any addictions or organicities. He was pre-morbidly quiet, docile, and easily worried by nature.

On physical examination, vitals were stable and there were no focal neurological deficits. He did not display alcohol withdrawal symptoms, last drink being three days previously.

On mental status examination, he was irritable and upset about being brought for psychiatric evaluation. He admitted to the symptoms of forgetfulness but not the behavioral changes or substance consumption. He was loquacious, spoke loudly, with excessive laughing and occasional inappropriate sexual comments towards his female interviewer. He was partially cooperative and required much placating to undergo a psychiatric interview. His attention was not well sustained, and each question had to be repeated several times for him to comprehend well. He displayed formal thought disorder (occasional tangentiality) and a sudden bout of verbal and physical aggression towards his family when he asked suddenly for a specific food item, and they informed him it will take a little time for them to go and get the same. There were no overt delusions or hallucinations. Abstract concepts were concretized. Remote memory was intact, but immediate and recent memory was impaired. Social and test judgement were impaired. Insight into his condition was 2/6.

On cognitive testing, his score, on Montreal Cognitive Assessment (MoCA) [3] was 15 and on Frontal Assessment Battery (FAB) [4] was 8 – both lower than cut-off (MoCA: 26, FAB: 12). In FAB, his impairments were in conceptualization, lexical fluency, Luria sequencing and conflicting instructions. In MoCA, his low score was due to impaired attention, visuo-spatial abilities, frontal executive functioning, dexterity with language, abstraction, and short-term memory.

Neuroimaging (MRI brain) showed ill-defined gliotic area in right ganglio-capsular area extending superiorly into right periventricular area with hemosiderin deposition. Another similar gliotic area in the right anterior temporal region. Few hyperintense foci in bilateral periventricular/ subcortical area were visualized as well as widespread cerebro-cortical atrophy, especially over bilateral temporal regions. An EEG showed no remarkable findings.

He was diagnosed as dementia in other specified disease classified elsewhere (ICD F02.8) [2].

He was admitted for an inpatient program aimed at symptom control and neurocognitive rehabilitation. Oral risperidone 3mg BD, trihexyphenidyl 2 mg BD, carbamazepine 200mg BD and clonazepam 0.5mg HS was started. He was also given a neurological consultation which diagnosed him clinically as dementia. Testing for possible causes (autoimmune, infective, metabolic, toxic, and heavy metals) came back negative and so the neuronal changes were postulated to be likely secondary post-TBI changes. Neurology services started him on donepezil 10mg, citicoline 500mg and piracetam 1200mg. He was given a structured routine, graded cognitive rehabilitation sessions, supportive psychotherapy initially that later also included insight-oriented sessions.

Over a three-month period, his disinhibited behavior, aggression, attention, short-term memory, and language showed much improvement. Initially he was kept under 24-hour supervision. As his memory and ability to manage his own activities of daily living improved, the level of supervision was gradually reduced – both to test his capacities under partially independent conditions and to build his confidence. Still memory remained sub-par, and abstraction and frontal executive functioning also remained impaired. Repeat FAB and MoCA scores were 12 (reaching cut-off) and 22 (still below cut-off) respectively.

At discharge, there was no major behavioural problem. Mood was euthymic, and very occasionally irritable in response to stress. The frontal disinhibitory symptoms such as demanding and novelty-seeking behavior, inappropriate sexual overtures, physical aggression were not observed. Attention could be sustained better,

and he was less forgetful, and was doing ADL without any supervision, but with help of memory aids. He could sustain a short conversation with a few repetitions and occasionally would forget certain words, that had to be re-learned or recalled with cues. His reading comprehension was much improved. There was occasional craving for tobacco. Despite thorough psychoeducation, he could not unfortunately fully grasp the extent of his issues and his family members were requested to carry out stringent 24-hours supervision post-discharge. He was discharged on oral tablets risperidone 3mg, trihexyphenidyl 2mg and carbamazepine 300mg HS. The neurological treatment of oral donepezil 10mg and piracetam 800mg was continued. Neurocognitive rehabilitation sessions were continued as well. He was reevaluated monthly by both psychiatrist and neurologist. He is maintaining his improvement (on the same treatment that was advised at discharge) and there has been no deterioration in his condition as evidenced in his latest follow-up, which was six months after discharge [no deterioration on FAB [12] and marginal improvement on MoCA [23].

DISCUSSION

The most apparent point of interest in this case is the young age of onset of dementia post head injury. In literature, the most often period of onset of dementia is given as 50-55years, about a decade earlier than in those with no history of head injury [1, 5]. In contrast, here, the onset of symptoms were about 6 months after the RTA, and there has been previous research indicating that indeed within 6 months of the causative event of cerebral injury, there are highest chances of onset of dementia even in young patients, and if so happens then prognosis is graver over long term than those patients with longer gap between TBI and onset of clinically detectable cognitive impairment [6].

The surprising rapidity with which symptoms developed, especially after initial apparent phase of recovery begs the question whether in such cases, along with the commonly known processes that follow brain trauma i.e. diffuse axonal and free radical injury, microglial activation, apoptosis of damaged neuronal cells followed by modulation of micro- and macrovascular flow and activation of mechanisms promoting neuroplasticity which leads to minimization of loss of structural and functional elements and help the brain compensate [7].

Sometimes, there are additional underlying mechanisms triggered which hinder recovery and expedite the pathological process, thus shortening time to the initiation of clinical symptoms. Previous studies find that apolipoprotein E*e4 allele overexpression can be triggered by traumatic brain injury, in turn increasing migration of beta-amyloid type 4 peptides into the brain cells, thus speeding up an Alzheimer-like scenario over variable amount of time [7]. Alongside this, severe injury can induce proteinopathies – most notably, massive extent of dissociation of tau proteins – causing hyperphosphorylation, increased aggregation of microtubules and thus accelerate formation of neurofibrillary tangles; with this noxious phenomenon in ongoing in the backdrop, quick and uncontrolled tau breakdown also specifically gives rise to a highly neurotoxic variant called cis-P-tau which leads to much increased and sustained neurotoxicity and continues to trigger apoptosis of healthy neurons, thus perpetuating a vicious cycle of accelerated neurodegeneration [8]. TDP-43, another protein, plays some role, especially in tau-negative cerebropathies. Sometimes more severe brain injuries, which increases cleavage and ubiquitination of TDP-43 to give rise to highly neurotoxic fragment causing widespread neuronal damage, but this is less frequently found than the tauopathies. Sometimes, both these cascades can co-exist and are triggered simultaneously post severe TBI, causing accelerated onset of dementia. In such patients, biomarkers of tau, TDP-43 et al can be found elevated in cerebrospinal fluid i.e. CSF, and sometimes blood; significant levels denote tauopathy/ proteinopathy presence and likely severity [9]. This patient could not be tested such due to lack of access to any such testing facilities.

Another postulated theory is that disruption of glymphatic pathways, i.e. paravascular transport pathway in the cerebral tissue that exchanges interstitial solutes with CSF, can increase tau deposits significantly in areas of vascular disruption. These pathways are bound by end feet of perivascular astrocytes. Any disruption in vasculature will lead to a wide perimeter astrogliosis and hypertrophic astrocytes with impaired glymphatic flow; in this area, a dense concentration of CSF solutes that flow in through the disrupted barrier and fails to get cleared due to the impaired glymphatic clearance, then settle and are taken up by local cellular mechanism and later found as inclusion bodies. Post-TBI, this inflowing CSF solute is often rich in freshly

cleaved toxic tau variants, which then deposit locally as well as have facilitated spread through the interstitium to rest of the cerebrospinal system, and start their own chain of noxious neuronal events.[10] This also may account for the widespread cortico-cerebral atrophy present in this case.

A differential diagnosis of acute traumatic encephalopathy was washed out as the cognitive symptoms very clearly came as part of a secondary process, and were not present from the time of the primary TBI. Chronic traumatic encephalopathy (CTE) was also considered and discarded, as our case did not meet the requisite of repetitive brain traumas, even if the clinical picture and progress of symptoms were very similar. This is perhaps so because both this case and CTE has very similar underlying pathophysiology. [11]

The interlude of seeming recovery, in this case, could be due to reduction of gross initial neurological symptomatology due to resolution of the traumatic injuries and before the secondary wave of above-described noxious molecular level changes had escalated enough to cause clinical symptoms as described in the case above.

Treatment in such cases engender a multimodal approach with close liaison of Neurology and Psychiatry. Regular and aggressive neurocognitive rehabilitation, occupational therapy, physiotherapy and supportive psychotherapy with insight building with ample psychopharmacological and neuropharmacological support should be instituted in the initial phases. In maintenance phase, management plan should be customized to the patient's remaining deficits - with graded withdrawal of services if patient is recovering, or regular follow-ups to keep pace with the changing therapeutic needs of the patient. Patient and family should be counselled regarding the potential lifelong requirement of therapeutic support and lifestyle management.[12]

Our patient's persisting cognitive and executive function deficits correspond to the extensive frontal gliotic patches and the secondary global mild cerebro-cortical degeneration (moderate over temporal lobes). More sophisticated neuroimaging like magnetic resonance spectroscopy (shows pathophysiology correlating to metabolite levels), or positron emission tomography (measures tau deposition patterns in brain), or susceptibility weighed imaging (detects microhaemorrhages, very small blood-brain-barrier disruptions and tau deposition, especially in young patients) are being found to be specifically useful in cases of post-TBI dementia and CTEs. If available timely and affordable to patient, perhaps such imaging studies would have helped to understand the extent of neuronal damage, its permanence and helped to ascertain a more specific prognosis.[13]

Likely prognosis here is guarded due to extent of initial injury, its sequelae and most importantly, the vehemence with which onset and progress of the secondary lasting and pathological development of neurobehavioral changes akin to dementia came on - that traditionally occurs insidiously over years, in old age and without TBI. Previous studies suggest such changes are never truly compensated, even with pharmacological agents to help neuroplasticity and extensive neurocognitive and behavioural remediation. There are often lasting deficits in working memory, critical thinking and emotional continence, causing easier decompensation into neuro-psychiatric illnesses in face of stress. Also, cognitive symptomatology worsens much faster than in those without TBI, especially if there is lack of proper medical and social support. Such persons tend to have some preserved quality of life and can work, function and occasionally even thrive in facilitated settings, only if they lead very disciplined lifestyles with adequate and ongoing social (including legal, government concessions if available etc.), neurocognitive, psychiatric monitoring and support lifelong [12].

Being aware of the cascade of proteinopathies that may permanently damage the neurocognitive potential of a TBI patient is crucial for practitioners of neuropsychiatry, in order to modify their management plans, which will have to be, for now, at least in the ordinary Indian clinical scenario, targeting symptom management and prevention of further deterioration. Specific imaging and biomarker testing, as mentioned above, are neither commonly available nor easily affordable. Speaking of definitive treatment – preventive or treatment mitigating extensive neuronal damage by tau immunotherapy, or developing molecules targeting inhibition of pertinent stages in post-translational modifications of tau or ubiquitination of TDP-43, and so on, are all still largely in research and developmental phases and show promise in small experimental formats, but are not yet cleared for widespread use in regular clinical set-ups [14].

It would be educational to keep monitoring this case (and also endeavour to find, document and monitor similar cases) longitudinally, in effort to understand the course of neurodegenerative changes and timeline. Also, if mitigative treatment becomes available in the near future, it will be crucial to note whether it makes

a significant prognostic difference in terms of long-term preservation of quality of life and autonomous functioning. If and when preventive treatment becomes available, if its impact is found significant, such data can have incredible potential to change existing protocols of both TBI and CTE - be it instituted as a norm or only in specific circumstances.

[NOTE: Written consent has been taken from patient and family for publication of this case report on condition that no identifying information will be disclosed. The scales FAB and MoCA are freely available online in public domain and do not require permission.]

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