SUDDEN ONSET OF PARKINSON'S DISEASE AFTER TRAUMATIC BRAIN INJURY – AN UNUSUAL CAUSE OF DIFFICULT WEANING

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CASE REPORT

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Abstract

History of trauma brain injury (TBI) is associated with an increased risk of developing Parkinson's disease (PD), considering that dopaminergic neuronal system is especially vulnerable to injury due to its localization. The onset of PD is considered to be rather late in patients with severe TBI and related to the development of chronic neuroinflammation. Relatively few data are available regarding sudden PD diagnosis after severe TBI. We present the case of a 76-year-old male patient admitted to our unit with multiple trauma after a car accident. He was found with a Glasgow Coma Scale of 7 and required intubation at the scene of the accident. The patient had previously no history of neurological disease. On admission he was continuously sedated, mechanically ventilated, and hemodynamic unstable. Supportive therapy was initiated, and 72 hours later neurologic evaluation revealed bilateral resistance to passive movement and intermittent tremor involving both upper and lower limbs. Neurological examination confirmed specific symptomatology for Parkinson's and levodopa administration was initiated three times daily. After 24 hours, neurologic symptoms faded and the patient was successfully extubated. Neurologic re-evaluation after ICU discharge confirmed PD diagnostic. From our knowledge this is one of a few reports available about sudden PD onset after severe TBI. Although the history of the patient revealed no signs of any neurological deficit therapeutic test with levodopa facilitated a secure extubation.

Keywords: traumatic brain injury, Parkinson's disease, weaning criteria, intensive care, levo-dopa

Introduction

Multiple trauma continues to be one of the leading cause of morbidity and mortality worldwide, with an incidence characterized by three age-related peaks: first in the early childhood, second during young adulthood and last after the age of 75[1]–[3]. Traumatic brain injury (TBI) associated with other extra-cranial lesions was reported to be the main

cause for long-term morbidity and disability[3]–[5]. Data revealed that patients with history of TBI have an increased risk for developing neuropsychiatric disorders and cognitive decline, compared to the general population[6]. Association between TBI and haemorrhagic extra-cranial lesions with traumatic shock is considered an everyday challenge for every trauma team, taking into account that promoting "permissive arterial hypotension" in order to decrease blood loss, may aggravate brain lesions[4]. The combination between TBI and severe haemorrhages is even more problematic, considering that after the primary brain injury caused by the direct effect of the external forces, secondary brain injuries caused by blood-brain barrier disruption and cerebral circulation derangements may occur[4], [7], [8].

Patients with TBI often require airway protection and respiratory support in order to prevent hypoxemia, hypercapnia and aspiration pneumonia[9], [10]. Data regarding weaning from mechanical ventilation in patients with TBI are limited and most of the practical used protocols derive from patients without neurological dysfunction[10], [11]. Taking into account that neurological status is often compromised, a number of criteria from the weaning trial protocols cannot be applied in patients with TBI[10], [11]. Moreover, statistical data revealed that one out of five patients with neurological dysfunction may experience a failed extubation[10].

Parkinson's disease (PD) or ''shaking palsy'', is the second most com¬mon neurodegenerative disorder after Alzheimer's disease, affecting as much as 3% of patients older than 65 years old, especially males[12]. Aetiology of PD remains unknown, with supposition that this is the result of genetic and environmental (trauma, toxics) conjunction[13]–[15]. The most common features of PD are motor symptoms like bradykinesia, rigidity, tremor and postural instability, but the diagnosis is often preceded by early nonmotor features, such as disorders of rapid eye movement sleep (REM) behav¬iour, depression, cognitive and olfactory impairment, and constipation[13], [16], [17].

The two pathological mechanisms found to be responsible for the age-related late onset of the disease are the progressive loss of dopaminergic neurons, especially in the pars compacta of the substantia nigra, with the subsequent disruption of neurotransmission and the accumulation of the alpha-synuclein inclusions, or Lewy bodies in the remaining neurons[17]. Considering the neurodegenerative character of PD, the onset is gradual with mild symptoms[17].

In the late 20th century, the link between neurodegenerative diseases and repeated mild traumatic brain injuries caused by contact sports such as boxing or football, has been brought into attention as a public health problem[17], [18]. Still, only recently a single TBI event was reported to have long-term neurological repercussions, such as a neurodegenerative disease[19]. Taking into account that from the first reports PD development was mainly associated with different types of TBI (from mild to severe), intense research was dedicated in this direction in the early 80s[16], [19]. TBI is now considered the determinant non-genetic risk factor for PD occurrence[17].

The most frequent causes of admission in the intensive care unit (ICU) for PD patients are usually related to complications like trauma, infections, or acute cardiovascular events and not with the primary disease[20], [21]. The majority of patients with PD admitted to the ICU have already an established neurological diagnosis and a proper treatment prior to the admission [12]. Since ICU patients are often in need of sedatives, mechanical ventilation and advanced monitoring systems, a proper neurological assessment may be highly challenging[12].

We report the case of a 76-year-old male, admitted to the ICU with multiple trauma, after a car accident, who developed specific symptomatology for PD, complicating the weaning from mechanical ventilation and prolonging the ICU stay.

Case report

A 76-year-old male patient was admitted into the emergency department (ED) after a car accident while driving home from work. Although his past medical history included ischemic heart disease, atrial fibrillation, hypertension, moderate mitral valve regurgitation, lumbar arthrodesis on L3-L4 level, his family informed that he was an active person without any neurological or psychiatric conditions.

From the emergency report we mention that he was found unconscious (Glasgow coma scale = 7 points) with blood pressure 84/48 mmHg, pulse 128 beats/min and with a respiratory rate of 30 breaths per minute (Revised Trauma Score = 4.9438/12). After endotracheal intubation and mechanical ventilation support initiation, he was transported to our trauma centre. Immediately after his presentation in the ED a whole-body contrast-enhanced computed tomography (CT) scan was performed, revealing bilateral frontoparietal cortico-subcortical haemorrhagic suffusions, anterior midbrain haemorrhagic suffusion, multiple bilateral ribs fractures, left shoulder blade fracture, bilateral pulmonary contusions, and right femoral shaft fracture (ISS (Injury severity score) = 41 points/75).

The patient was admitted to the ICU from the operating room after femoral external fixation under general anaesthesia. On admission he was sedated, mechanically ventilated with hyperdynamic hemodynamic status with vasopressor support (Noradrenaline = 0.8 micrograms/kg/min). APACHE II (Acute Physiology and Chronic Health Evaluation II) score 15 points, SOFA (Sequential Organ Failure Assessment) score of 8 points. After 48 hours hemodynamic dysfunction was restored, being guided with echocardiography hemodynamic monitoring and vasopressor support was ceased.

A second cerebral CT scan was order by the neurosurgeons in order to evaluate TBI progress, however no additional lesion was discovered.

On the fourth day after the initial admission sedation was progressively lowered and ceased, thus the ventilatory indices used to predict successful weaning (RSB Index, CORE index, Integrative Weaning Index, CROP index, Airway Care Index) argued in favour of extubation. Neurological status was quantified using the FOUR Score (11/16 points) and the VISAGE Score (3/4 points) also indicating a successful extubation. However, bilateral tremor and muscle rigidity were identified, deciding to declare a failed weaning trial. After re-evaluating the therapeutic management, a drug-induced Parkinsonism was excluded. On the next day, after achieving a light sedation the previous bilateral tremor and muscle rigidity reoccurred, rising the suspicion of a Parkinsonism or Parkinson's disease, therefore a neurology examination was ordered. After confirming the characteristic clinical features, a therapeutic probe with levodopa was prescribed. After 24 hours neurologic symptoms have faded and a safe extubation was performed. After a week the patient was transferred to the orthopaedics ward in ordered to continue specific treatment. Neurologic re-evaluation after ICU discharge confirmed Parkinson's disease with sudden precipitation after severe TBI.

Discussions

TBI is one of the leading cause of morbidity and mortality, affecting people from all age groups, considering that the causes of injury are very heterogenous[1], [3]. We presented a case of a 76-year-old male patient

with multiple trauma secondary to a car accident. He was admitted to the ICU with traumatic shock and neurologic dysfunction secondary to severe TBI. Besides a complex cardiovascular history, no neurological disorder or deficit was identified during family interview. After managing the cardiovascular dysfunction, neurological assessment and a weaning trial were performed. However, surprisingly he developed muscle rigidity and asymmetrical tremor raising suspicion of PD onset or parkinsonism. It was already stated that TBI and PD are related through various pathological mechanisms[19].

The neurological deficit secondary to TBI is related to the direct cerebral tissue destruction, as well as to neuroinflammation and to excitotoxicity emerged immediately after the initial hit[5], [7]. Dopamine system proved to be particularly susceptible to the lesions produced by the primary and secondary injuries associated with TBI[22]. Since dopaminergic neurons are localised in the midbrain (ventral tegmental area and substantia nigra), they are particularly exposed to TBI[23]. In addition to it, dopamine system is a frequent target to the mechanical forces applied to the skull, considering the long axonal projections in the nigrostriatal and mesolimbic pathways which are particularly exposed to shearing forces[22], [23]. TBI is associated with exacerbated glutamate release, causing neuron overstimulation, increased intracellular Ca2+release and finally cellular damage and apoptosis[5]. Increased intracellular Ca2+ is correlated as well with mitochondrial dysfunction and excessive oxidative stress[24]. Nevertheless, neuroinflammation precipitated by the initial injury, characterised by increased release of pro-inflammatory cytokines, microglial activation and inflammatory cells infiltration, enhance local neuronal injury[5], [19], [24]. Taking into consideration that the patient had no previous clinical sign of PD, the traumatic dopaminergic neuron destruction was considered to be significant. However, according to the published data, PD onset after a traumatic event has variable delay of months or years[17], [19]. Since our patient developed a clearly sudden onset of PD, we suppose that he was already in a prodromal phase of PD.

PD diagnosis is currently based mostly on specific clinical features and neurological examination, using available criteria[13]. Considering that our patient was treated in the ICU after the multiple trauma event, diagnosis was initially based on very few clinical data and on response to levodopa administration. Although several studies in the literature may recommend different imaging techniques in order to confirm diagnostic, these are not easily available[13].

Weaning from mechanical ventilation is considered a daily challenge for TBI patients, because of their decreased level of consciousness and associated respiratory distress[11]. If prolonged sedation and mechanical ventilation are associated with increased rate of ventilator associated-pneumonia, raised costs and a higher mortality, extubation failure is related as well with prolonged ICU stay, poorer outcome and increased mortality[25]. Even if the initial weaning trial from mechanical ventilation was almost positive, the abnormally onset of asymmetrical tremor and muscle rigidity made us delay extubation in order to ensure patient safety.

Conclusions

The present case report supports the previously published hypothesis that a single TBI can lead to PD with the particularity of a sudden onset of symptoms, during the ICU stay. To our knowledge this is one of a few reports available about sudden Parkinson disease onset after severe TBI. Another particular feature presented is the PD diagnosis challenges in a critically ill patient. Nevertheless, assuring the best safety for a patient with TBI during weaning and liberation from mechanical ventilation should always be

one of the main objectives for every intensivist.

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