Paroxysmal autonomic instability with dystonia after severe traumatic brain injury – a case report

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Abstract

Paroxysmal autonomic instability with dystonia (PAID) is a clinical syndrome characterized by episodes of systemic hypertension, tachycardia, tachypnea, hyperthermia, diaphoresis, intermitent agitation and certain forms of dystonia (decerebrate or decorticate posturing, rigidity and spasticity). It is a relatively uncommon complication of distinct cerebral conditions: traumatic brain injury, hydrocephalus, spontaneous subarachnoid or intracerebral hemorrhage, non traumatic brain anoxia. Lack of recognising and undertreatment of this syndrome can increase the risk of secondary injury to the brain. The incidence of complete syndrome of PAID is low; we present a case of posttraumatic PAID displaying the full clinical picture, aggravated by the occurence of sepsis.

Keywords: paroxysmal autonomic instability, severe traumatic brain injury, sepsis.

Introduction

Paroxysmal autonomic instability with dystonia (PAID) – formerly known as autonomic dysfunction syndrome (ADS) - is a clinical syndrome that occurs as an uncommon complication of distinct cerebral conditions: traumatic brain injury, hydrocephalus, spontaneous subarachnoid or intracerebral hemorrhage, non traumatic brain anoxia and suprasellar cysts (13). It consists in episodes of tachycardia, systemic hypertension, tachypnea, hyperthermia, diaphoresis, intermitent agitation and certain types of dystonia (decerebrate or decorticate posturing, rigidity and spasticity). Early diagnosis and the appropriate treatment of this complication during the clinical course of patients with severe traumatic brain injury (STBI) - can improve their neurological outcome (7); unfortunately, the absence of standardized diagnostic criteria and a confusing nomenclature of this clinical entity still make the systematic clinical research difficult.

Case report

A 16 years old young woman sustained a severe isolated traumatic brain injury after a road accident (pedestrian hit by a car). At the scene her initial Glasgow Coma Scale (GCS) score was 3 and the left pupil was fixed and dilated. An initial computed tomography scan showed:

- Diffuse cerebral edema with no midline shift
- Spots of subarachnoid hemorrhage spread over the supratentorial area
- Multiple microhemorrhages

disseminated within corpus callosum, thalamus, midbrain, corona radiata and a small amount of blood inside the occipital horns of lateral ventricles (Figure 1) - suggestive for difuse axonal injury (DAI).

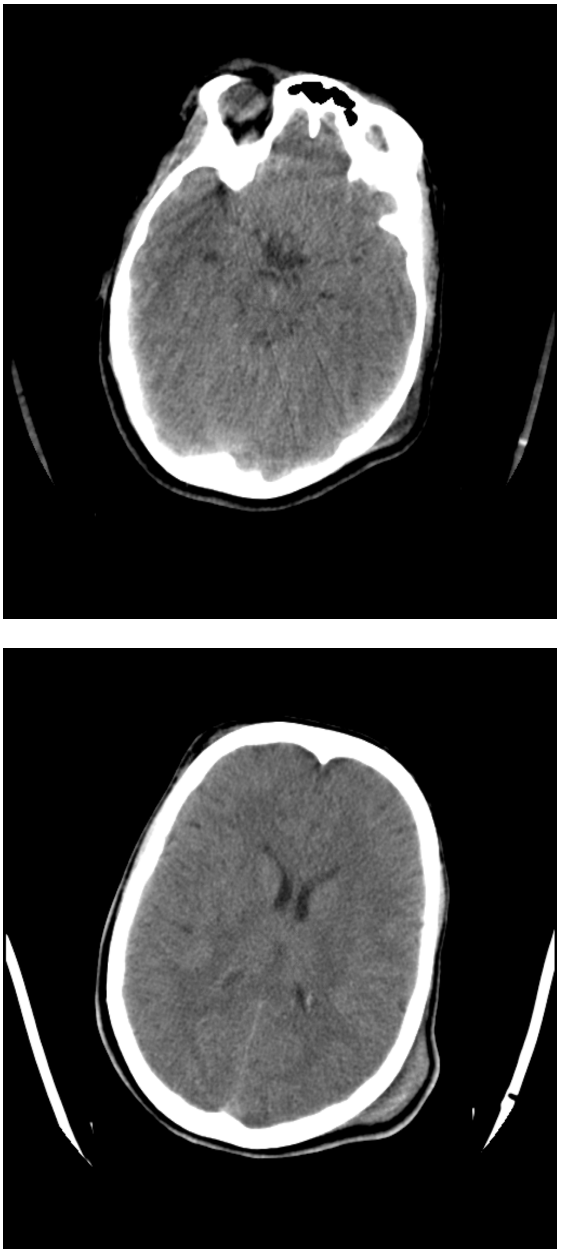


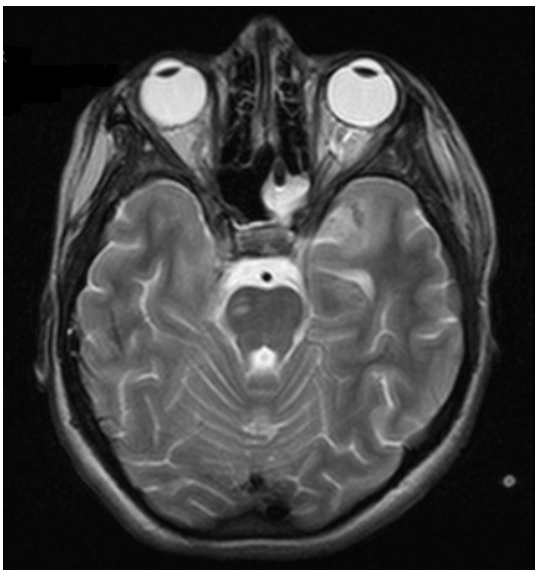
Figure 1 Initial CT - millimetric lessions in the antero-lateral mezencefalic region, right temporal lobe and in the left occipital horn

At the arrival to our Department she was intubated and sedated with fentanyl and midazolam; the continous sedation was briefly stopped in order to perform an accurate neurological examination: there was no eye opening to verbal or painful stimuli, the left pupil was fixed and dilated and the right pupil - intermediate and reactive to light. She was decerebrating on both sides to painful stimuli and spontaneously. The patient was admitted to the Neurosurgical Intensive Care Unit for conservative treatment; we decided to induce a barbiturate coma (thiopental 4 mg /kg/h) together with administration of mannitol, furosemide and normocapnic mechanical ventilation. After 24 hours, the neurological condition was slightly improved: decerebrate posturing on the left side and decorticate posturing on the rigt side to pain, unchanged pupillary reaction. A second CT scan performed on the same day revealed a smaller size of the subarachnoid hemorrhage spots, no midline shift and stable intraparenchymal microhemorrhages. The intravenous thiopental was then stopped and a continuous sedation with fentanyl 50 micrograms/ h and midazolam 3 mg/ h was started in order to facilitate ventilatory support, concurrent with anticonvulsant medication (carbamazepine 400mg/ 24 h, enterally).

The subsequent clinical evolution was uneventfull; on the fourth posttraumatic day we decided to stop the sedation. After 12 hours the patient developed episodes of synus tachycardia 130-140/min, hypertension SAP 160-170 mmhg, fever 38,5 - 39 °C, profuse sweating associated with flexor rigidity of upper limbs and extensor rigidity of the legs. The episodes were occuring spontaneously, lasting 45

minutes on average and were triggered by tracheal suction, current nursing procedures, physical therapy. They abated after repetead boluses of propofol, diazepam and fentanyl. Between paroxystic episodes all the vital parameters were comming back to the normal ranges. Initially the spells were tought as being vegetative seizures and the daily dose of carbamazepine was increased to 600mg/ day and fenobarbital was also added to the therapeutic scheme (400 mg/24 h) - with no result. Serial bacteriological work-up was negative until the seventh day and a magnetic resonance imaging (MRI) of the brain confirmed the diagnosic of grade III DAI (Figure 2).

After hading reviewed all the clinical - laboratory findings coroborated with the imaging studies - we reevaluated the etiology of paroxystic episodes and we regarded them as manifestatons of posttraumatic paroxysmal autonomic instability with dystonia.



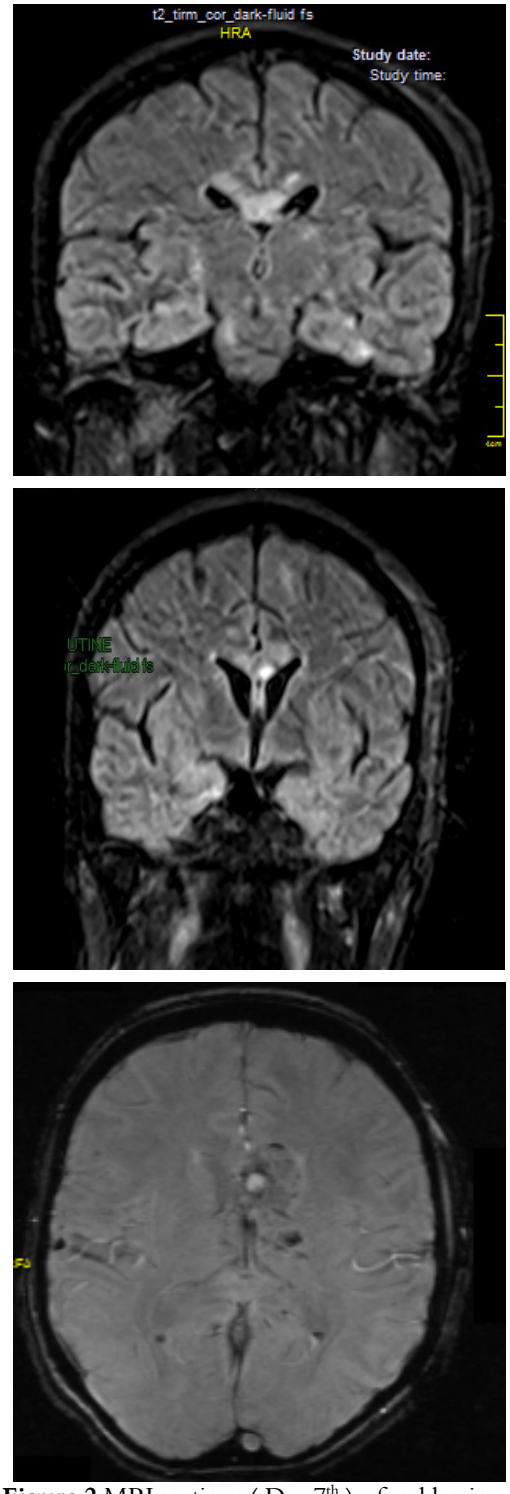


Figure 2 MRI sections (Day 7th) - focal lessions within the corpus callosum and the antero-lateral mezencefalic region

The differential diagnosis was made for:

- malign neuroleptic syndrome (the absence of specific medication)
- serotonine syndrome (no serotonine agonists or MAO inhibitors were previously given and addiction to recreational drugs was not confirmed)
- delirium tremens (no alcohol addiction)
- autonomic dysreflexia (lack of cervico-thoracic spinal cord injury)
- sepsis (excluded at the moment of first spells)
- diencephalic epilepsy (lack of response to anticonvulsant therapy)
- malignant hyperthermia (no exposure to trigger anesthetics)
- thyroid storm (no previous thyroid disease, absence of anterior cervical trauma).

Consequently we added metoprolol – starting with 25mg daily and increasing the dose up to 100 mg/ 24 h with a modest cardiohemodynamic response. Adding clonidine (0,45 mg/24 h) led to a notable improvement of blood pressure control. The evolution was aggravated by the occurence of both pulmonary (ventilator associated pneumonia VAP on the 7th day) and urinary (day 10th) infectious complications, with positive blood cultures for Staphylococcus aureus MRSA. The daily febrile spikes (39,7 -40,5°C) worsened the clinical manifestations of PAID: increased spasticity and joint stifness, rabdomyolysis (creatine kinase levels up to 1600 IU/L; normal range: 96 – 140 units/L), tachypnea 45-50 breaths/ min – compelling us to induce deep sedation and paralysis during severe episodes. Enteral baclofen (100 mg/24 h) and clonazepam 3 mg / 24 h were added – with slight improvement of dystonia. The evolution of sepsis was favourable under antibiotic therapy; the normal renal function was preserved and no need for vassopressors was noted. On the 20 th day- a tracheostomy was performed and the full ventilator weanning was possible on day 35, by T tube.

On the 36th posttraumatic day the patient was able to open the eyes spontaneously, to follow simple commands on the right side (ie. grasp the hand); she was exhibiting increased flexor tone in her upper extremity and increased extensor tone in her lower extremity. Concomitant with the resolution of the infectious complications the frequence of dystonic episodes diminished; the area of diaphoresis was gradually confined to the chest and cephalic zone, muscle dystonia became asymetrical and maximal values of blood presure and pulse during “crises” decreased. Thirthy days later (day 70) the patient was awake, with white blood cells and procalcitonine levels within normal ranges, fed by mouth and decanulated. She was space orientated, with short term memory severely affected, lacunar amnesia, able to speak, with slow ideation; there were also major joint deformity and stifness (ankle, wrist) (Figure 3). The PAID episodes continued according to a stable pattern (2-3 per day), of reduced intensity, mainly trigerred by emotional stimuli. The young patient was discharged to a rehabilitation facility with a Glasgow Outcome Score of 3p (conscious but requiring others for daily support due to severe disability) under current therapy with metoprolol, clonidine, baclofen, carbamazepine and clonazepam.

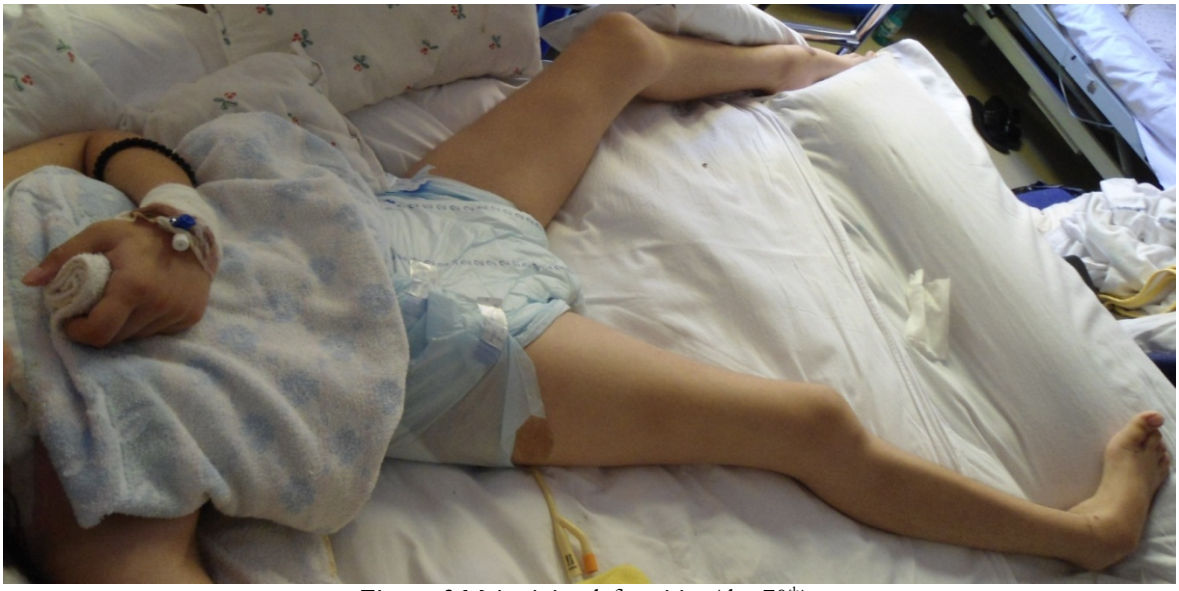


Figure 3 Major joint deformities (day 70th)

Discussion

Paroxysmal autonomic instability with dystonia (PAID) is a clinical syndrome characterized by episodes of systemic hypertension, tachycardia ≥ 130/min, tachypnea ≥ 30/min, hyperthermia ≥ 38,5 °C, diaphoresis, intermitent agitation and certain forms of dystonia (decerebrate or decorticate posturing, rigidity and spasticity) - that occur at least once per day for at least three days consecutively in a patient with severe traumatic brain injury. (GCS ≤ 8) (9). Despite their well defined clinical manifestations, PAID episodes are still underdiagnosed. This is the result of a non- unitar nomenclature and a persisting confusion between terms like: autonomic dysfunction, central fever, vegetative storm, acute mesencephalic syndrome, hyperpyrexia with muscle contracture (9). Some authors still consider that it is not clear if it is a distinct disorder from diencephalic seizures (13); although the mecanism of PAID remains unclear, it is unlikely to have true epileptic basis as seizures have never been confirmed by EEG (10). The pathogeny of PAID is partially explained by the "disconnection" theory; according to an excitator/ inhibitor model, following the disconection between cortical and subcortical centers from mesencephalo- diencephalic structures, the mesencephalic lesions play a central role in generating paroxysms (5).

PAID has an estimated incidence of 8-15% (3) in TBI, more frequent in young people (12) with DAI (12).

The syndrome has a three stage evolution(8):

I – immediately posttraumatic (nonspecific)

II – starts after cessation of current sedation in the Intensive Care Unit and the symptoms occur at maximum intensity, triggered by external stimuli or spontaneously

III – characterized by attenuation of the typical paroxysms - it usually overlaps the neurological improvement; the joint stifness with severe motion limitation is

frequent and isolated PAID episodes are still possible up to 14 months after initial trauma. (7).

PAID is a diagnostic of exclusion, based essentially on clinical findings (1,6). The differential diagnosis work-up is made for: malignant hyperthermia, neuroleptic malignant syndrome, serotonine syndrome, thyroid storm (11), sepsis, delirium tremens, autonomic disreflexy, diencephalic epilepsy. The treatment is directed to:

- blood pressure and heart rate control – by central α agonists (clonidine, dexmedetomidine) and beta blockers (metoprolol, labetalol)
- fever decrease (antipyretics, external cooling methods)
- sedation (benzodiazepines: midazolam, clonazepam)
- reducing contracture and spasticity to prevent permanent joint deformities and rabdomyolysis (baclofen oral or intratechal, dantrolen, orthopedic devices)
- analgesia (morphine, fentanyl).

The use of anticonvulsant is controversial; Baguley and all. demonstrated the efficiency of gabapentine in controling PAID paroxysms, possibly due to a modulation of spinal transmision of trigger stimuli. (5).Bromcriptine (a central dopaminergic agonist) was succesfully used in several case series (2).

The case we presented is particular by the presence of all clinical, epidemiological (11) and evolutive features of PAID. Despite the relative frequent occurence of signs of PAID in patients afflicted with severe TBI, the incidence of full syndrome is much lower and the number cases communicated in the literature is scarce. (9). Moreover, it suggests that sepsis – a current element of differential diagnosis – can be an aggravating factor for PAID evolution.

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