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Paroxysmal Autonomic Instability with Dystonia (PAID) Syndrome: A Rare Occurrence

Distoni ile Paroksismal Otonomik İnstabilite (PAİD) Sendromu: Nadir Bir Olgu

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ABSTRACT

Paroxysmal autonomic instability with dystonia (PAID) is still under-recognized in clinical settings due to its rarity. This syndrome may mimic certain life-threatening conditions. We present a rare case of PAID syndrome. A 45-year-old female was brought to the hospital with an altered level of consciousness. An urgent computed tomography of the brain was performed, and a diagnosis of obstructive hydrocephalus secondary to cerebellar hemorrhage was made. Her family refused major surgery but consented to cerebrospinal fluid diversion. However, after several days in the ward, she developed ventriculitis. She was successfully treated with intravenous ceftriaxone. After several weeks at home, she developed episodic attacks of hypertension, tachycardia, and diaphoresis with hyperthermia and diaphoresis. She also had episodes of restlessness and generalized dystonic movements. She was diagnosed with PAID syndrome, and treatment was initiated. Her symptoms were successfully treated after three days.

Keywords: Paroxysmal autonomic instability with dystonia (PAID), dystonia, ventriculitis

ÖZ

Distoni ile paroksismal otonomik instabilite (PAİD), nadir görülmesi nedeniyle klinik ortamlarda hala yeterince tanınmamaktadır. Bu sendrom, belirli yaşamı tehdit eden durumları taklit edebilir. PAID sendromunun nadir görülen bir vakasını sunuyoruz. Kırk beş yaşında bir kadın, bilinç düzeyinde değişiklikle hastaneye getirildi. Acil beyin bilgisayarlı tomografisi çekildi ve serebellar hemorajiye bağlı obstrüktif hidrosefali tanısı konuldu. Ailesi büyük bir ameliyatı reddetti ancak beyin omurilik sıvısı yönlendirmesine razı oldu. Ancak koğuşta birkaç gün geçirdikten sonra ventrikülit geliştirdi. İntravenöz seftriakson ile başarılı bir şekilde tedavi edildi. Evde birkaç hafta geçirdikten sonra, hipertermi ve diyaforez ile birlikte hipertansiyon, taşikardi ve diyaforez atakları geliştirdi. Ayrıca huzursuzluk ve yaygın distonik hareketler atakları da yaşadı. PAID sendromu tanısı kondu ve tedaviye başlandı. Semptomları üç gün sonra başarıyla tedavi edildi.

Anahtar Sözcükler: Paroksismal otonomik dengesizlik ve distoni (PAID), distoni, ventrikülit

INTRODUCTION

The Autonomic Nervous System (ANS) is divided into two components, the parasympathetic and sympathetic nervous systems (1). The balance in this system fine-tunes the numerous voluntary and involuntary bodily processes in our body (2). However, there are some medical conditions that cause an imbalance in these systems, which include malignant hyperthermia, neuroleptic malignant syndrome, autonomic dysregulation and traumatic brain injury (3). Autonomic dysregulation (dysautonomia) can cause a complex physiological

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picture, leading to imbalances in enteric, cardiac, motor, and respiratory systems. Paroxysmal autonomic instability with dystonia (PAID) is a subset of dysautonomia, which can mimic certain life-threatening conditions (4). PAID is a complex syndrome which is still under-recognised in clinical settings due to its rarity. We would like to present a case of PAID syndrome, information that could be very valuable for doctors around the world.

CASE REPORT

A 45-year-old female was brought to the hospital with altered level of consciousness. Before being brought in, she was complaining of severe headache and nausea. Her Glasgow Coma Scale was 7/15. An urgent computed tomography (CT) of the brain was done, and a diagnosis of obstructive hydrocephalus secondary to cerebellar hemorrhage was made. She was intubated and was on mechanical ventilation. Her family refused major surgery but consented for cerebrospinal fluid diversion. Her condition stabilized, but her recovery of consciousness with poor recovery in consciousness. Tracheostomy was done, and the patient was weaned off the ventilator.

However, after several days in the ward, she developed ventriculitis. The white cell count was raised (26,000 per microliter). Her blood culture and sensitivity revealed *Klebsiella pneumoniae*. Other blood parameters were normal. She was treated with intravenous ceftriaxone for one week. Her family was informed regarding the poor prognosis of the patient, and understood. She was referred to the rehabilitation unit before being discharged home.

However, after several weeks at home, she developed episodic attacks of hypertension, tachycardia, and diaphoresis with hyperthermia. She also had episodes of restlessness. According to her husband, the patient had generalized dystonic movements that resolved spontaneously after several minutes. These dystonic movements were increasing in frequency daily, with at least one attack.

Her blood investigations were normal, with no signs of infection. A repeat brain CT scan had no changes. After admission to the Neurosurgical Unit, the symptomatic management was commenced. She was given propranolol 10 mg three times a day via her nasogastric tube. She was also started on paracetamol, which helped her with the fever. Oral lorazepam was started to reduce her restlessness and dystonic movements. The patient responded well after two days into the treatment. She was discharged home after a week in the hospital.

DISCUSSION

PAID is sometimes seen among patients undergoing neuro-rehabilitation. This syndrome is often overlooked and misdiagnosed. Manifestations include arrhythmias, electrocardiographic alterations, hypohidrosis, increased intracranial pressure, neurogenic lung disease, and subnormal temperature in flaccid limbs. These are accompanied by dystonia of either rigidity, or decerebrate posturing during at least one episode per day for three consecutive days (2).

PAID is a complex syndrome and is difficult to diagnose. Understanding the pathophysiology is of utmost importance to diagnose and subsequently treat the syndrome. PAID is believed to be caused by altered actions of the hypothalamus, which interacts with the brainstem through a series of feedback loops and midbrain lesions. This may lead to dystonia by interfering with normal inhibitory mechanisms, making patients tonically active and finally resulting in a hyperexcitable spinal reflex (2).

PAID syndrome appears to be a unique condition which usually follows brain injury. This syndrome may echo many life-threatening conditions. This would mean early recognition and management are very important. There may be a delay in initiation of subsequent management, which may cause an increase in morbidity among the affected patients. The differential diagnosis of PAID syndrome includes other clinical entities such as delirium tremens, sepsis, meningitis, dystonia, neuroleptic malignant syndrome, thyroid storm, and malignant hyperthermia. While most of these conditions can mimic PAID syndrome, the paroxysmal nature of symptoms such as autonomic activation, and generalised dystonia confirms the diagnosis of PAID (5).

The occurrence of episodes is always cyclical, with at least one episode per day. Due to the episodic nature of these manifestations, electroencephalography during an episodic attack will be difficult to obtain. The onset of these typical clinical signs generally occurs in the first week after brain injury and may persist for weeks or months, particularly in patients with a history of hypoxic brain injuries. Data have shown that 15% to 33% of patients develop PAID syndrome in the acute period after an insult to the brain (6). PAID syndrome complicates rehabilitation since it prolongs hospital stay. Morbidity is also increased, and an generally unfavourable functional outcome is expected (7).

The pathophysiology is still uncertain. It is speculated that PAID syndrome may be the result of the disinhibition or activation of central sympathetic excitatory regions located in the brain. These parts of the brain include the lateral periaqueductal grey substance, paraventricular hypothalamic nucleus, lateral parabrachial nucleus, and rostral ventricular medulla (8).

PAID is diagnosed based on specific criteria, which are shown in Table 1. PAID syndrome patients are usually free of symptoms or signs between the paroxysms. Malignant hyperthermia may also mimic PAID syndrome due to the hypermetabolic state, which happens after the patients have been given drugs such as non-depolarising agents and inhalational volatile agents (4).

Various medications have been used to manage PAID syndrome. However, there is no clear evidence that suggests that one medication regimen is better than another. After treating the underlying cause, adrenergic disinhibition has been successfully controlled with opiates such as morphine and dopamine agonists like bromocriptine. Additionally, benzodiazepines and baclofen

Table 1. Clinical criteria of PAID syndrome (5)

Criteria of PAID syndrome
• Temperature of more than 38.5 ^{o}C
• Hypertension
• Tachycardia of more than 130 beats per minute
• Respiratory rate of more than 40 breaths per minute
• Intermittent agitation (Rancho Los Amigos level ≤4)
• Diaphoresis
• Dystonia (rigidity or decerebrate posturing)

PAID: Paroxysmal autonomic instability with dystonia

have been used. The use of clonidine may also help to reduce blood pressure. Benzodiazepines, such as lorazepam, have sedating effects and muscle relaxant properties, which may help the patients during their uncontrolled symptoms (9).

It is important to know that withdrawal from opiate therapy may also provoke signs that falsely suggest PAID. The use of bromocriptine is effective in neuroleptic malignant syndrome, in which the clinical features suggest PAID. Dantrolene, on the other hand, has direct muscle relaxant properties and may reduce fever caused by prolonged muscle contraction, and also reduce the somato-sympathetic spinal reflexes that contribute to sympathetic excitation (5). Table 2 lists a review of commonly used medications and their uses in PAID syndrome.

The PAID manifestations observed in our patient only developed after the patient developed ventriculitis secondary to hydrocephalus. Ventriculitis may have caused the involvement of the midbrain structures. To the best of our knowledge, this is the first case report of PAID syndrome in association with Central Nervous System infection. PAID syndrome should be included as one of the differential diagnoses when a patient with similar signs and symptoms presents to the hospital. An early diagnosis and appropriate treatment can be established as soon as possible, thus reducing patient morbidity.

CONCLUSION

PAID can mimic a life-threatening condition. It is necessary to distinguish PAID syndrome from other conditions that can mimic it, such as sepsis, dystonia, delirium tremens, neuroleptic malignant syndrome, meningitis, and thyroid storm. Early diagnosis and treatment can lead to rapid recovery.

Table 2. Treatment guide for PAID syndrome

Symptoms	Medication
General symptoms	Morphine, labetalol/ Propanolol and gabapentin
Agitation	Lorazepam
Resistant hypertension & hyperthermia	Clonidine
Persistent dystonia or posturing	Dantrolene

PAID: Paroxysmal autonomic instability with dystonia

Ethics

Informed Consent: Permission as written consent obtained for publication. No patient identification or details are revealed.

Footnotes

Authorship Contributions

Surgical and Medical Practices: V.V.P., P.S., Concept: V.V.P., S.R., Data Collection or Processing: V.V.P., Analysis or Interpretation: R.K.M., Literature Search: V.V.P., R.K.M., Writing: V.V.P., S.R., P.S.

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