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Paroxysmal non-epileptic events in the pediatric emergency department

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Abstract. – Paroxysmal non-epileptic events (PNEs), or pseudoseizures (PS) resemble epileptic seizures. They are considered part of a personality disorder and have a higher incidence among adolescents. Patients describe episodes (lasting up to 20 minutes) of loss of consciousness, twitching or jerking and unusual emotional states. Unlike epileptic seizures, they are not associated with electroencephalographic abnormalities. Distinguishing epileptic seizures from PNEs is not easy. 20% of patients with seizures have a final PNEs diagnosis but recognizing them on the first examination is difficult.

Due to the severe initial clinical presentation, these patients are often admitted in the Pediatric Intensive Care Unit (PICU) and may be over-treated. We report two cases admitted to our PICU for apparent status epilepticus, in which the final diagnosis was PNEs.

Key Words:
Children, Emergency room, Pseudoseizures.

Introduction

Paroxysmal non-epileptic events (PNEs), or Pseudoseizures (PS), are considered to be behavioral disorders with clinical manifestations that mimic seizures and status epilepticus[1]. Several cases are described in adults but there is limited data in the pediatric population. However, compared to adults, the prognosis in the pediatric population is better[2,3]. The medical history often includes sexual or physical abuse, personality disorders, alcoholism and psychiatric diseases[4]. Psychotherapy is the only treatment available, even though recovery is not always achieved. Treatment of the underlying behavioral disorder is the main goal of therapy and may require an interdisciplinary approach.

In most cases, PS are referred to the Emergency Department (ED) because of the patient's poor response to conventional antiepileptic drugs and compromising hemodynamic and respiratory parameters. The apparently critical condition of these patients during the clinical evaluation is the main cause of their Pediatric Intensive Care Unit (PICU) admission and may justify an extensive workup in order to exclude anatomical disease. We describe two cases of adolescents who experienced a long and difficult course in our PICU before the diagnosis of PS was set.

Case Reports

Case 1

A 13-year-old female was admitted to the ED for an episode of gradually decreasing responsiveness to verbal stimuli and seizures characterized by uncoordinated clonic movements. The patient was at home with her parents when the event occurred. Intravenous (IV) lorazepam and phenytoin were administered and seizure control was achieved 15 minutes after the infusions. Neither urinary nor fecal incontinence was observed. A cranial computerized tomography (CT) scan, an electroencephalogram (EEG) and cerebrospinal fluid (CSF) cultures were normal.

Her family history was positive for Guillain-Barre` syndrome which occurred in the father at the age of 28. Her personal history was unremarkable, except for a weight gain of 10 kg in the last two months. For this reason, the patient was on a dietetic regimen.

Due to the persistence of a decreased level of consciousness, the patient was referred to our PICU. On admission the patient was drowsy. Arterial oxygen saturation was 99% on the room air.

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Neurological examination showed a decreased response to verbal and painful stimuli and loss of right hand sensation with "glove" distribution. Neither rigor, nuchal nor cervical motility abnormalities were observed. No autonomic changes, such as sweating, salivation and altered pupillary responses occurred. A few hours after admission in our PICU, the clinical condition of the patient got worse. An episode of loss of consciousness occurred, associated with bilateral clonic movements, which was treated with intravenous lorazepam 0.1 mg/kg. Because of persisting clinical symptoms, intravenous steroids (dexamethasone 0.5 mg/kg/day) were initiated. A peripheral neuropathy of unknown origin was suspected. During the following five days the patient gradually improved; she remembered her seizures describing them as "gradual loss of consciousness" and "vertigo". On day 7, another loss of consciousness episode occurred, associated with bilateral clonic and hypertonic movements. A bolus of intravenous lorazepam was administered (0.1 mg/kg) without efficacy. A bolus of intravenous phenobarbital (10 mg/kg) followed. The episode stopped 25 minutes after the infusion. Further diagnostics included cranial and cervical magnetic resonance imaging (MRI), interictal EEG, electromyography, evoked motor potentials, echocardiography, blood and CSF cultures, serologic examinations for Poliovirus, Echovirus, Coxsackie, Borrelia, immunoglobulin and complement levels. All results came out negative. Lacking any abnormal results and having organic disease excluded, a neuropsychiatric consultation was requested one week after admission. The patient was diagnosed with bipolar disorder and underwent psychotherapy for 2 years. She is currently in good clinical condition and during a three-year follow-up has experienced no further episodes of PS.

Case 2

A 13-year-old male was admitted to an outlying hospital for gradual loss of consciousness, which progressed, into a comatose state, following a prolonged (30 minutes) seizure-like event. His past history was unremarkable, except for one episode of loss of consciousness during a football match. The family history was positive for epilepsy in the paternal line. During hospitalization, several episodes of tonic clonic seizures with bilateral shaking movements were observed but without autonomic changes, altered pupillary responses or amnesia. Cranial CT scan and CSF cultures were negative, while an interictal EEG showed a diffuse slowing pattern. Due to the persistence of these symptoms, he was hospitalized in our PICU. On admission, a similar episode was treated with intravenous lorazepam (0.1 mg/kg), without response. A bolus of intravenous phenobarbital was administered (10 mg/kg) with good control of the event. Suspecting an epileptic seizure, an interictal EEG was performed. Results were normal. Shaking movements persisted over the following days, which did not respond to antiepileptic drugs (lorazepam and phenobarbital). None of the events was followed with postictal stupor. All laboratory and radiological investigations (blood tests, inflammatory markers, cervical and cranial CT scan, MRI, transcranial Doppler sonography, cerebral angiography, and somatosensory evoked potentials) were negative. An ictal EEG performed during one prolonged episode was normal. For this reason, a neuropsychiatric consultation was requested. Their diagnosis was psychogenic non-epileptic crisis due to bipolar disorder. Psychotherapy was started, and at one-year follow-up period, the general condition of the child was good with no further episodes of PS.

Discussion

PNEs are clinical events that resemble epileptic seizures but without abnormal electrical discharges on EEG. The prevalence of PNEs in the general population is believed to be in the range of 1/3000 to 1/50,000, although it is recognized that this may be a low estimate resulting from underreporting and diagnosis[5]. The prevalence varies with the population studied. Health care resources expended on people with PNEs constitute 10-40% of admissions to inpatient adult and pediatric epilepsy monitoring units and 5%-20% of referrals for intractable epilepsy[6-10].

These events may occur as a somatoform disorder with underlying psychiatric disease (bipolar disorder, depression, anxiety) and tend to happen more frequently during adolescence, although they have been reported in all pediatric age groups[3,4]. One recent study implied that PNE may be associated with psychosocial stressors in medical history, such as parental divorce, a move to another city, loss of a close family member, school failure and sexual (21%) or physical (6%) abuse[11]. PNEs are not usually followed by these psychological stressors immediately. Instead, they occur

months or years after the stressor indicating that the occurrence of trauma may be more important than how recently it has occurred[12]. Other risk factors associated with a higher incidence of PS are a history of head trauma and a positive family history of epilepsy. It is common for these children to try to imitate the clinical features of epileptic seizures noticed in their families, in order to avoid scholastic and social duties[13-15].

Because PNEs frequently mimic many common epileptic seizure semiologies with jerking and unresponsiveness, these can be challenging to differentiate. More so, up to 78% of PNEs in pediatric patients are stereotypic and repetitive in nature[16]. One single-center study documented a rate of 1.5% of children misdiagnosed with intractable epilepsy having an actual diagnosis of PNEs. In our two cases, differential diagnosis between PS and epileptic seizures was difficult due to the critical condition of the patients on admission.

The symptoms and clinical features, which led to our initial misdiagnosis, included the kind of movements (described as clonic), the lack of response to verbal and painful stimuli, a variable, but likely response to therapy and the positive family history. Despite this, some aspects were suggestive of PS; a normal ictal/interictal EEG, duration and nonstereotyped pattern of the events, the place and the presence of others where and when the PS occurred, the memory of the seizures and the absence of incontinence and postictal stupor.

Video EEG has become the gold standard in the diagnosis of PNEs; however, it cannot be easily performed in every setting, including the Intensive Care Unit. Therefore, clinical diagnostic criteria should be adopted in order to differentiate these two disorders.

Clinically, in the pediatric population, 76.8-80% of PNEs have an abrupt start and 68% end abruptly. Eye closure during the entire attack occurs in 22-45% and tremor in 25% in upper instead of lower extremities[10,17,18]. Furthermore, they are characterized by bilateral or unilateral (more rarely) tonic clonic movements, unresponsiveness and unresponsiveness with subtle motor activity. Triggering events, such as hyperventilation, pain, anger, and reproaches are reported[2], but on admission, we did not investigate these parameters. Decreased response to verbal stimuli is described in 30% of cases, but this is not a typical feature; these manifestations may mimic petit mal[19]. We observed it in the first patient, while it was less evident in the second case.

PNEs may occur with a bizarre motor activity which is not typical in known types of epileptic seizures, including generalized arrhythmic flailing of extremities, uncoordinated movements, arching in hyperextension, flailing or thrashing of body and swooning[10,20-22].

As was evident in our cases, autonomic changes such as sweating, salivation and altered pupillary response are rare. Urinary incontinence may uncommonly occur, while fecal incontinence is rare. A prolonged postictal state does not occur with PS, despite the fact that the episode may last for a long time[2,10]. In Table I, we report the main different features of epileptic seizures and PSs which should be considered in cases of unresponsiveness to conventional therapy. Considering the clinical condition of our patients, the first approach we adopted was the administration of antiepileptic drugs (benzodiazepine to stop the seizure-like events). In our cases, the diagnosis of PS was not initially considered both because of the low incidence of PS and the difficulty of performing a video EEG in our unit. Many complex examinations including laboratory tests and radiological investigations are commonly obtained in these patients before a definitive diagnosis is made. One recent study, in fact, showed that it was possible to correctly diagnose this disorder in 70% of observed cases, but only when evaluated by experienced medical staff after strict clinical monitoring and several assessments of the clinical course, with the support of audiovisual instruments[23-25]. The most important clinical criteria suggestive of PS are the long duration of the episodes and the absence of response to conventional antiepileptic treatment. Definitive diagnosis is based on a non-ictal EEG recording during the event, or video EEG recordings which do not confirm the presence of electrical seizures; polysomnography is not necessary since the episodes are not triggered during sleeping time; therefore, we did not perform this test in our patients. Prolactin levels may be considered as a useful test; they are increased in cases of epilepsy, while during PS their value does not change[26]. In the literature, induction of PS with saline solution has been reported.

If PNEs are suspected, antiepileptic drugs should be avoided both because they are ineffective and have potential side effects. Unnecessary polypharmacy and drug toxicity[27,28], hazardous interventions such as intubation secondary to respiratory depression from treatment with benzodiazepines during pseudo status[27], school absence[11]

Table I. Differential diagnosis between paroxysmal non-epileptic events (PNEs) and epileptic seizures.

Clinical features	PNEs	Epileptic seizures
History	Sexual or physical abuse, behavioral disorders	Incontinence, self injury, CNS infections, anti-epileptic drugs withdrawal
EEG: ictal/interictal	Normal	Abnormal/variable
Duration	Variable, often long despite therapy	Short, same
Pattern	Variable	Stereotyped
Frequency	Variable	Paroxysmal, cluster
Movements	They may be similar to seizure, but non-synchronous. Some features may help the diagnosis of PS: trashing, side to side head or alternating limb movements, pelvic thrusting, collapse	Tonic (stiffening), followed by rhythmic jerking, complex automatic movements
Presence of others	Yes	Variable
During sleep	Rare	Yes
Onset	Gradual	Sudden
Incontinence	Rare	Infrequent
Induction	Yes	No
Pupillary reflex	Normal	Slow, non-reactive
Memory of seizure	Variable	Usually amnestic
Words	Yes	No
Pain reaction	Yes	No
Autonomic changes	No	Yes
Self injury	Rare (self-protection before fall)	Yes

and lack of treatment of underlying psychological problems[11] have been reported as the most common side effects. It is unclear why some physicians chose to continue AEDs even after a diagnosis of PNEs has been made. A recent survey of clinicians (84% of whom were neurologists, 84.2% of those child neurologists), stated a rate of 96.2% that were very or moderately likely to discontinue AEDs[10,29]. Reasons for being less likely to discontinue AEDs were noted as requests by a parent or patient to continue medication, fear of making a diagnostic error or having insufficient knowledge, limited access to video EEG, or patients not having ongoing psychiatric treatment[10,29]. Psychogenic events can also mimic genuine status epilepticus causing cardiorespiratory failure, necessitating resuscitation maneuvers, airway, and circulatory support.

Once a correct diagnosis of PS is achieved, children and their families should be referred to psychotherapy centers to treat the underlying condition, especially those with a specific psychogenic trigger identified, psychological comorbidity, or ones who may have suffered from sexual or physical abuse[10,30]. This is the only therapeutic intervention available which leads to appreciable results. Recent studies evaluated the efficacy of psychotherapy in this condition and showed a marked reduction in PS; 44% of children were seizure free at 6 months, 73% at 1 year, 75% at 2 years and 81% during a 3-year follow up. The study also showed that pediatric patients have a better outcome than adults[30-34]. Another study of 50 pediatric patients showed resolution of events in 72%, decreased frequency in 20% and no change in only 8%[3]. A third pediatric study reported 66% becoming PNE free and 23% with more than 50% reduction in the frequency of PNEs. Interestingly, pursuance of counseling in children did not always correlate with a higher rate of non-epileptic event cessation. This led to a speculation that, with less longstanding comorbidities and earlier diagnosis, children may be more susceptible to a natural history course versus treatment effects[10]. Yet, if sexual abuse is identified, the patient is appropriately treated and the family is supportive, psychological counseling can be of great benefit. Overall, patient gender, neurological history, and non-epileptic event type do not influence clinical outcome[10].

Conclusions

We observed that these case reports are useful to differentiating epileptic seizures from PS. The

duration of PICU stay is often associated with both the critical condition of these patients on admission and the extensive workup expenditure of health-care resources performed in order to make the correct diagnosis. For this reason, it is essential to correctly identify patients with PS and increase participation of psychiatry/psychology colleagues in order to prevent unnecessary testing and inappropriate treatment. Although video EEGs are useful, it may not be possible to obtain them in the intensive care unit or ER.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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