



Psychogenic non-epileptic seizures, anticipatory grief and limited access to medical care

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Abstract

Psychogenic non-epileptic seizures (PNES) in the context of meningoencephalitis can occur with sufficient stressors. Video-EEG is a critical diagnostic tool in such complex cases. Once the diagnosis of PNES is confirmed by video-EEG, psychiatric consultation with psychotherapeutic intervention to address underlying psychopathology and specific stressors that led to these conversion symptoms is required. Clinicians need to understand the importance of cultural themes, including the economics of healthcare, and anticipatory grief as causative stressors in pseudoseizures.

Key words: Enterovirus meningoencephalitis; psychogenic non-epileptic seizure; PNES; pseudoseizure; video-EEG; cultural themes; healthcare economics; anticipatory grief; psychiatric consultation; treatment; conversion disorders.

Introduction

Psychogenic non-epileptic seizures (PNES) are considered alternatively neuropsychiatric disorders combining both neurological signs and underlying psychological conflicts without associated epileptogenic pathology (electrographic correlation) and / or conversion disorders with neurological presentation precipitated by psychological stress / traumatic events, and descriptively have rapid changes in behavior resembling epileptic seizures without any organic etiology (American Psychiatric Association, 1994; Bowman & Markand, 1996; LaFrance *et al.*, 2006). Though literature focuses predominately on PNES as a conversion disorder (in some series 100% of patients with PNES), there is a minority sub-classification of non-conversion PNES (American Psychiatric Association, 1994; Alper *et al.*, 1995; Bowman & Markand, 1996; Wyllie *et al.*, 1999; Bhatia & Sapra, 2005; Mondon *et al.*, 2005). Differ-

entiation between true epileptic seizures and PNES requires video-EEG-telemetry (Iriarte *et al.*, 2003). Further, patients can present with both epilepsy and PNES. Such mixed presentations are found in 5-50% of patients with PNES (Russell, 2006).

Multiple bereavements have been associated with PNES and conversion disorders (Bowman & Markand, 1996; Kaufman *et al.*, 2007). In one case series of PNES, 44% of referred children had severe family stress (death of close family member, parental discord, or divorce) (Wyllie *et al.*, 1999). Conversion disorders have also been reported in cases of anticipated mourning (Kaufman *et al.*, 2007). Culture, politics, and socioeconomic may confound etiology, diagnosis, and treatment of PNES (Yeh, 1996; Bhatia *et al.*, 1997; Silva *et al.*, 2001; Agarwal, 2006). This is especially true in culture-bound syndromes, such as *ataque de nervios*, where PNES may present only as a syndrome symptom (Oquendo, 1995; Gates & Mercer, 1995; Guarnaccia & Rogler, 1999; Flaskerud, 2000).

In this complex case with mixed presentation, cultural issues led to limited access to medical care for the patient's mother, perception of mother's imminent death, and subsequent PNES.

Case report

This 20-year-old sub-Saharan African single female presented to the emergency room (ER) with progressive photophobia, headache, nuchal rigidity and positive Kernig's and Brudzinski's signs. ER CT scan of the head was negative for mass lesion, blood, or midline shift. ER lumbar puncture cerebrospinal

fluid (CSF) analysis revealed WBC 74 (lymphocytes 47), RBC 15, glucose 53, and protein 43. ER CBC with differential and comprehensive metabolic panel were within normal limits excluding mildly decreased K⁺ (3.3), CO₂ (23.6), and albumin (3.4). The patient was admitted with presumptive meningitis and initially treated with acyclovir, ceftriaxone, vancomycin, and azithromycin pending results of CSF sent for cultures and viral studies. RT-PCRs of CSF were positive only for the presence of enterovirus, a finding confirmed by repeat lumbar puncture with further CSF studies. Bacterial cultures of CSF, blood, and urine were all negative. Blood serologies were negative as well, except for IgG titers against CMV, EBV, and HSV, compatible with old prior exposure to these viruses. As infectious disease results became available, all antibiotics and antivirals were discontinued.

Shortly after admission to the adolescent unit the patient's hospital course was complicated by an episode during which she abruptly stopped speaking, lost muscle tone, and appeared apneic. After a second similar episode of apparent apnea with seizure-like activity, the patient was treated with IV lorazepam, intubated, and transferred to the pediatric ICU with evaluations by intensivist, pediatric infectious disease, and pediatric neurology. Fosphenytoin was initiated. The patient remained intubated for 48 hours; thereafter, the patient's oral anticonvulsant regimen was phenytoin 200 mg qhs and levetiracetam 1000 mg bid. The patient was diagnosed with enteroviral meningoencephalitis.

Brain MRI with and without contrast revealed multiple right parietal white matter abnormalities (largest focus 7 mm) consistent with demyelination, inflammation, or vasculitis. Repeat MRI, days later, revealed similar findings, but reduction in size of foci (largest parietal focus 5 mm). Two doses of intravenous immune globulin were given empirically following the second MRI for potential acute disseminated encephalomyelitis (ADEM) (Sahlas *et al.*, 2000). MRA and MRV were negative. Bedside EEG was interpreted as normal showing appropriate background for a predominantly sedated patient, normal arousal response to external stimuli, and no epileptiform or focal activity.

In spite of the ongoing anticonvulsant regimen, further seizure-like activities occurred multiple times over the ensuing 10 days lasting from 1-2 minutes to intermittently over two hours. These seizure-like activities were characterized by varying combinations of apparent apnea, hyperventilation, unresponsiveness, bilateral lower extremity shaking, writhing, thrashing, tonic-clonic movements, posturing, and even head/eye deviation to the left both with and

without post-ictal confusion. Prolonged (48-hour) video-EEG did not show any epileptiform activity and there were no electrographic correlates between these seizure-like activities and the EEG; neurology diagnosed PNES in this complex patient and psychiatric consultation was requested to elucidate the basis for these PNES.

During this psychiatric consultation, the patient denied any historical or current affective, psychotic, obsessive-compulsive, phobic, panic disorder, eating disorder, abuse, drug, alcohol, or nicotine features. However, the patient described the following significant personal and family stress consistent with the development of a conversion disorder by DSM IV criteria (American Psychiatric Association, 1994; Bowman & Markand, 1996; Wyllie *et al.*, 1999; Albrecht & Naugle, 2002; Kaufman *et al.*, 2007):

- Recent death of father two years before the patient's hospitalization. Her father developed diabetes type II in his late 20's and remained stable for nearly twenty years. In the year prior to his death, he rapidly deteriorated with first cardiac events, then blindness (6 months before his death) and finally renal failure with dialysis (4 months before his death) before dying from heart failure. Father had medical insurance.
- Mother has diabetes type II, became blind secondary to diabetic retinopathy one month prior to the patient's hospitalization, and also has end stage renal disease from diabetic nephropathy requiring dialysis in a country with limited access to hemodialysis. Mother does not have medical insurance. Patient had flashbacks to father's illness course and death in learning of mother's blindness.
- As her mother's presentation mirrors that of her deceased father, the patient believes that her mother's illness to be terminal if dialysis is not initiated. Patient acknowledges having anticipatory mourning for her mother.
- Patient has guilt over not being with mother at this time to both care for her and to initiate termination and closure, yet realizes that the moneys she earns in the US are needed for mother's medical care.
- Patient is angry with her older sibling, who though financially stable with ability to assist in mother's medical care has refused to do so.

After the initial psychiatric consultation, the patient had two further extended psychotherapeutic interventions addressing her specific stress, bases of conversion disorders, PNES, and means to cope with stress. She exhibited a gratifying response to these sessions with resultant resolution of seizure-like activities such that her last PNES occurred the morning prior to the consultation.

Although PNES was determined to be the basis of the seizure-like activity at the end of the hospitalization, in light of initial clinical epileptic seizures, the patient was discharged four days after the psychiatric consultation on phenytoin 200 mg qhs and levetiracetam 1000 mg bid pending outpatient neurological assessments. When seen in outpatient neurology follow-up two weeks after discharge, the patient continued to be free from any seizure-like activities. Four weeks after discharge, an outpatient routine EEG was normal after which all anticonvulsants were discontinued. Six months after discharge, the patient remained without any further seizure-like activities.

Discussion

This unusual case addresses multiple themes – a) appropriate diagnosis and treatment for suspected meningitis / meningoencephalitis (neuroimaging, lumbar puncture for CSF studies, broad spectrum antibiotics and antivirals pending results of cultures, serologies, and PCRs) with consultations by intensivist, infectious disease, and pediatric neurology based upon disease severity; b) video-EEG for evaluation of PNES when the patient developed seizure-like activity that was not felt to be consistent with true epileptic seizures; c) after PNES confirmed by the video-EEG, psychiatric consultation with psychotherapeutic intervention to address underlying psychopathology and specific stresses that led to these conversion symptoms; d) influence of multiple bereavements and anticipated bereavement on the development of PNES; e) realization of the influence of cultural and socioeconomic conflicts as key factors.

Since meningitis and meningoencephalitis may have significant morbidity and mortality, empiric treatments are indicated until comprehensive study results are available (Debiasi & Tyler, 2006). The severity of illness is impacted by patient's age and immune status (Chadwick, 2006; Debiased & Tyler, 2006). This patient was a young adult, not immune compromised and HIV negative. While adult enteroviral meningitis is most often benign without seizures, the presence of seizures and changes in mental status in this case was more consistent with meningoencephalitis (Debiased & Tyler, 2006). MRI with contrast is indicated to rule out specific causes of encephalopathy such as ADEM, a post-infection or post-vaccination immune mediated demyelinating disease. Though normally no active infection is found, ADEM has been reported with CSF positive enterovirus by PCR (Saitoh *et al.*, 2004). In this case, limited white matter signal abnormalities were al-

ready decreasing in size when empiric intravenous immune globulin was given pending the results of the second MRI (Sahlas *et al.*, 2000). This raises the issue of rapidity of tests, test results, and impact on treatment, length of hospitalization, and costs. With current infectious disease technologies, especially PCR analyses, rapid diagnosis and specificity of treatment for meningitis has improved while minimizing unnecessary utilization of antibiotics and antiviral agents, decreasing length of hospitalization, and decreasing health costs (Rammers *et al.*, 2000; Chadwick, 2006).

The initial apneic episode with loss of muscle tone and subsequent seizure-like activity was presumed to be a clinical seizure; however the bedside EEG was normal without epileptiform or focal activity. Were the initial ictal events true epileptic seizures or not? Epilepsy and seizures are clinical diagnoses (Pohlmann-Eden *et al.*, 2006; Duncan *et al.*, 2006). In one series of idiopathic generalized epilepsy, 45% of patients had initial normal EEGs (Betting *et al.*, 2006). Although seizures are not considered common complications of enteroviral meningitis, these may occur with meningoencephalitis and require appropriate intervention while being further diagnosed (Modlin *et al.*, 1991; Chadwick, 2006; Debiased & Tyler, 2006). As such, though it could not be determined if the first ictal events were true epileptic seizures, anticonvulsant therapy was initiated in this case. Further seizure-like activities had varying presentations including bilateral non-synchronous motor behaviors (thrashing and writhing) without post-ictal confusion that strongly suggested non-epileptic seizures (Gates *et al.*, 1985). The gold standard for diagnosing PNES is video-EEG telemetry; this patient underwent a 48-hour video-EEG that confirmed PNES (Iriarte *et al.*, 2003; Cuthill & Espie, 2005).

Psychiatric comorbidity with conversion disorder PNES has been estimated to be 70%, most frequently as mood and anxiety disorders (Wyllie *et al.*, 1999; Bhatia & Sapra, 2005; Mondon *et al.*, 2005). This case was significant for the lack of underlying psychopathology but the presence of significant stresses with psychic pain consistent with the development of a conversion disorder (American Psychiatric Association, 1994; Bowman & Markand, 1996; Wyllie *et al.*, 1999; Albrecht & Naugle, 2002; Kaufman *et al.*, 2007). In treating patients with PNES, video-EEG confirmation of the diagnosis, accurate presentation of this diagnosis to the patient, and psychiatric consultation are but the first steps; successful treatment requires psychotherapy with psychotropics for psychopathology, understanding the origin of the PNES in the context of underlying stresses, and then

creating effective coping mechanisms (Kroenke & Swindle, 2000; Iriarte *et al.*, 2003; Kaufman *et al.*, 2004; LaFrance & Barry, 2005; Russell, 2006). Key stresses in this case concerned loss, anticipated loss, limited access to healthcare, and cultural and socioeconomic conflicts.

Family stress, especially bereavement of a family member, has been associated with conversion disorders and specifically with PNES (Buchsenschutz *et al.*, 1975; Maloney, 1980; Lancman *et al.*, 1994; Bowman & Markand, 1996; Griffith *et al.*, 1998; Wyllie *et al.*, 1999; Krawetz *et al.*, 2001; Kaufman *et al.*, 2007). Multiple losses can cause compounded psychological effects (Kaufman & Kaufman, 2005; Kaufman & Kaufman, 2006; Kaufman *et al.*, 2007). When the father died, the patient underwent therapeutic grief within a cohesive and supportive family. His medical insurance permitted maximal available medical care. After his death, the family's socioeconomic status decreased until ultimately the mother was no longer medically insured. The patient emphasized sending significant funds earned in the US to her homeland to assist in her mother's healthcare. With progressive decline in her mother's health status mirroring her father's course prior to his death, the patient developed anticipatory grief with flashbacks to her father's death. To have healthy uncomplicated grief, "meaning-making" is often required – but in the present situation, the patient did not find "meaning," but rather socioeconomic and cultural conflicts (Niemeyer, 2000; Niemeyer *et al.*, 2002; Niemeyer, 2006; Niemeyer *et al.*, 2006). The patient acknowledged inability to cope with the imminent loss of her mother and felt victimized by a) multiple losses, b) cultural disparities in healthcare, c) responsibility to provide funding preventing her presence with mother, and d) lack of family cohesion in this perceived crisis. These factors were the basis for the patient's PNES.

Would this patient have developed PNES had she never lived in the United States or a westernized country with excellent access to medical care? The patient acknowledged that were she not in the United States, but in sub-Saharan Africa, she would have expected her mother to die from her end-stage renal disease without receiving dialysis. Further, she commented that though distressed and coping with anticipatory grief, she would not have been as conflicted over her mother's imminent death. The patient understood the limited resources that exist for medical care in her homeland and the lack of dialysis. Specifically, her homeland has only one dialysis center and an estimated 4.3 patients treated by renal replacement therapy (any form of dialysis) per million population (p.m.p.) in comparison to

4871 dialysis centers and 1030 p.m.p. in the United States (Moeller *et al.*, 2002; Naicker, 2003; Global Dialysis 2007a; Global Dialysis, 2007b). Global healthcare is influenced by social and economic constraints with marked disparities, especially regarding dialysis, noted between richer and poorer nations such that the 2001 survey of 120 nations showed a parallel between gross domestic product and dialysis prevalence – Japan 1730, North America 980, European Union 580, and Africa 50 p.m.p. respectively (Moeller *et al.*, 2002; Friedman, 2003). By being in the United States, she was forced to appreciate the stark socioeconomic and healthcare comparisons – significant funds spent on healthcare, ready access to all forms of healthcare including dialysis, multiple private and government sponsored insurance policies in addition to charity care for those with no insurance (including visitors and illegal immigrants).

Conclusion

PNES in the context of meningoencephalitis can occur with sufficient stressors. Video-EEG is a critical diagnostic tool in such complex cases. Clinicians need to understand the importance of cultural themes, including the economics of healthcare, and anticipatory grief as causative stressors in PNES.

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