NEW RESEARCH

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"Nocturnal Seizures" in Idiopathic Pulmonary Arterial Hypertension

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CASE REPORTS

The usual differential diagnoses of nocturnal events in children include parasomnias, nocturnal seizures, nocturnal reflux (Sandifer syndrome), hypnic jerks, periodic limb movements of sleep, and sleep disordered breathing. We report a previously healthy young girl who presented to the sleep clinic for evaluation of nocturnal events which were diagnosed as medically refractory nocturnal seizures. It was not until a syncopal event occurred in the daytime, which prompted referral for cardiac evaluation, the diagnosis of idiopathic pulmonary arterial hypertension (IPAH) was made. Sleep physicians should consider IPAH in the differential diagnosis of nocturnal events in children.

Keywords: Nocturnal events, syncope, children, pulmonary hypertension

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The evaluation of nocturnal spells in children presents a challenge to sleep physicians. The differential diagnosis includes a variety of epilepsy syndromes (including nocturnal frontal lobe epilepsy [NFLE] and benign rolandic epilepsy), nocturnal asthma, various parasomnias, gastroesophageal reflux, allergies, obstructive sleep apnea, periodic limb movements of sleep, and nocturnal panic attacks (**Table 1**).[1] Careful history, including review of systems, appropriate investigations including video-EEG monitoring, pH probe, brain MRI, and video-recording of the event by the parents to be reviewed by the physician may offer clues to the diagnosis in many cases. Differentiating parasomnias from NFLE in particular is challenging, given the bizarre behaviors and movements occurring in both these disorders.[4] We report a case of nocturnal events in a young girl which were precipitated by decreased cardiac output secondary to previously undiagnosed idiopathic pulmonary arterial hypertension (IPAH). This is a rare cause of nocturnal events, but warrants consideration as aggressive treatment can reduce the significant morbidity and mortality associated with it.

REPORT OF CASE

A 4-year-old girl started experiencing episodes out of sleep characterized by arousal, waxing and waning responsiveness, up-rolling of eyes, pallor, cyanosis, hypotonia, teeth grinding, and moaning lasting a few minutes to a maximum of 40 minutes, occurring around 03:00-04:00. An EEG showed nonspecific sharply contoured activity in the midline during sleep, without actually capturing the typical event; however, she was started on levetiracetam (LEV) with a presumed diagnosis of nocturnal seizure. The episodes continued to occur on a weekly basis, despite dose escalation of LEV. Brain MRI was normal. Several months later, she experienced two daytime syncopal episodes, prompting a cardiac evaluation. Cardiac catheterization confirmed the diagnosis of IPAH, revealing markedly elevated pulmonary artery pressure (PAP) of 99/53, m = 73 mm Hg, cardiac-index of 1.4 liters/minute/meter^2, and pulmonary vascular resistance of 40 indexed Woods units. These hemodynamics are consistent with the notion that this patient experienced syncopal episodes due to acutely reduced cardiac output.

She was started on continuous intravenous treprostinil, tadalafil, warfarin, and nocturnal supplemental oxygen. There were no further nocturnal events on this regimen, but she did suffer two brief episodes of daytime syncope 3 months after initiation of therapy, prompting the addition of nifedipine. She presented to our sleep center for a second opinion regarding these nocturnal spells. We did not feel that they were epileptic in nature. LEV was discontinued with no further events. Polysomnography showed normal sleep architecture, no sleep disordered breathing, and mild nighttime hypoxemia (11% of time spent between 92% and 96%). Repeat cardiac catheterization after 1 year of pulmonary vasodilator therapy demonstrated a dramatic improvement in hemodynamics with nearly normal PAP of 32/14, m = 23 mm Hg, cardiac-index of 4.3 liters/minute/meter^2, and pulmonary vascular resistance of 2.6 indexed Woods units.

DISCUSSION

IPAH is a rare disease, causing narrowing of the small pulmonary arteries, resulting in increased pulmonary artery pressures, right heart failure, and eventually death.[5] The causes of IPAH are largely unknown. In addition to IPAH, there are a number of conditions which are associated with pulmonary hypertension, including congenital heart disease, collagen

Table 1—Causes of nocturnal events in children[1]

Sleep Related Epilepsy
Nocturnal frontal lobe epilepsy
Benign epilepsy of childhood with centrotemporal spikes (formerly rolandic epilepsy)
Juvenile myoclonic epilepsy
Continuous spike waves during NREM sleep (formerly electrical status epilepticus of sleep)
Parasomnias
Confusional arousals
Sleepwalking
Sleep terrors
REM sleep behavior disorder
Nightmare disorder
Sleep related groaning (Catathrenia)
Exploding head syndrome
Sleep Related Movement Disorders
Restless legs syndrome
Periodic limb movement disorder
Sleep related leg cramps
Sleep related rhythmic movement disorder
Sleep related bruxism
Sleep Related Respiratory Disorders
Obstructive sleep apnea
Nocturnal asthma
Cardiac Disorders
Idiopathic pulmonary arterial hypertension
Other Medical and Psychiatric Causes
Nocturnal panic attacks
Posttraumatic stress disorder
Gastroesophageal reflux disease
Acute and chronic pain syndromes
Atopic dermatitis and other allergic disorders

vascular disease, hemoglobinopathy, thromboembolic disease, disorders of the respiratory system, sleep disordered breathing, and exposure to drugs/toxins.[6] Although many are uncommon in children, these conditions must each be ruled out before a diagnosis of IPAH is made.

While episodic reduction in cardiac output and the associated decrease of cerebral perfusion leading to syncope and/or seizures is well documented (usually occurring during the day and with exertion) in pulmonary hypertension patients, there are no cases in the literature describing these episodes presenting with bizarre, nocturnal, complex motor movements. Our patient failed treatment with anticonvulsants but responded well to pulmonary vasodilator therapy.[6]

This case adds to the differential diagnosis of complex nocturnal behaviors in children. It attempts to increase awareness among sleep specialists, who may be requested to evaluate these nocturnal events for atypical parasomnias, of this rare but treatable disease.

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