Seizures in Idiopathic Pulmonary Arterial Hypertension

Jamir Pitton Rissardo[1] Ana Letícia Fornari Caprara[1]

[1]Department of Medicine, Federal University of Santa Maria, Santa Maria, Rio Grande do Sul, Brazil

Address for correspondence Jamir Pitton Rissardo, Department of Medicine, Federal University of Santa Maria, Rua Roraima, Santa Maria, Rio Grande do Sul 97105-900, Brasil (e-mail: jamirrissardo@gmail.com).

Int J Epilepsy 2018;5:107–109

Abstract

Pulmonary arterial hypertension (PAH) is a progressive pulmonary vasculopathy. A 29-year-old female patient presenting with dyspnea and syncope within 6 hours of onset was admitted to our hospital. The patient stated that she looked for a neurologist months ago because she experienced abrupt shaking limbs occurring during physical activity. She was diagnosed with focal seizure, and carbamazepine (CBZ) was started. On admission, she reported that the dyspnea had started in the last week and recurrent episodes of syncope in the last few hours. A right heart catheterization was diagnostic of PAH. She was started on spironolactone, furosemide, sildenafil, warfarin, and supplemental oxygen. On 10th admission day, the patient was seizure free and the dose of CBZ was tapered. In the follow-up, the patient remained seizure free. An investigation to search for a chronic lung disease or hypoxemia, systemic disorder, hematological disorder, and metabolic disorder was negative.

Keywords
- seizure
- syncope
- pulmonary hypertension

Introduction

Idiopathic pulmonary arterial hypertension (IPAH) is a progressive pulmonary vasculopathy that, if left untreated, may lead to an increase in pulmonary vascular resistance with ensuing heart failure. In this context, the inability to adequately increase the cardiac output, mainly during exercise, results in the clinical manifestations of IPAH, such as dyspnea, lethargy, and fatigue.[1] However, to the authors' knowledge, IPAH presenting with focal seizure has not been reported until the present moment. Here, we report a case of a young adult female patient who presented with shaking limbs elicited by physical activity. After 3 months of the motor symptoms onset, she developed dyspnea and was diagnosed with IPAH.

Case History

A 29-year-old female patient presented to our hospital with dyspnea and syncope with approximately 6 hours of onset. The patient stated that she looked for a neurologist 3 months ago because she experienced shaking limbs. Her symptoms began with abrupt shaking of left limbs and ipsilateral head-turning followed by bilateral limbs shaking and impairment of consciousness, lasting an average of 2 minutes, and with no memory of the episode. These episodes occurred during physical activities, such as climbing two flights of stairs. The neurological examination was normal. She was previously healthy and her family history was unremarkable. Laboratorial tests were within normal limits. A brain magnetic resonance imaging (MRI) was normal. Electroencephalography (EEG) on voluntary hyperventilation showed some spikes with sharply contoured activity in the right hemisphere. Diagnosis of focal seizure was made and carbamazepine (CBZ) 100 mg once daily was started. Subsequently, the dose was gradually increased until the achievement of drug therapeutic levels.

On admission, she reported that the dyspnea had started in the last week and the recurrent episodes of syncope, in the last few hours. Upon further questioning, she still had seizures and was in use of 1,000 mg CBZ. The physical examination was normal. Laboratory tests were within normal limits. A cranial computed tomography (CT) and an electrocardiogram were normal. An echocardiogram was suggestive of pulmonary hypertension. A right heart catheterization revealed high mean pulmonary arterial pressure (70 mm Hg), high pulmonary vascular resistance (38 Wood units), normal mean capillary wedge pressure (12 mm Hg), and negative

Dr. Jamir Pitton Rissardo's ORCID is 0000-0001-6179-2177.

received
January 13, 2019
accepted after revision
March 16, 2019
published online
May 16, 2019

DOI https://doi.org/10.1055/s-0039-1688528
ISSN 2213-6320.

vasoreactivity test. A CT pulmonary angiography and lung scintigraphy were negative to pulmonary thromboembolism. She was started on spironolactone 25 mg/day, furosemide 80 mg/day, sildenafil 60 mg/day, warfarin 5 mg/day, and supplemental oxygen. On 10th admission day, the patient was seizure free and the dose of CBZ was tapered.

Two years later, the patient remained seizure-free. An investigation to search for a chronic lung disease or hypoxemia, systemic disorder, hematological disorder, and metabolic disorder was negative.

Discussion

Pulmonary hypertension is characterized by elevated pulmonary arterial pressure. The World Health Organization (WHO) classifies pulmonary hypertension into five groups based on etiology. In this way, pulmonary arterial hypertension, which is the term used to describe group 1 from WHO classification, is rare and is caused by a proliferative vasculopathy of small pulmonary arteries.[2] In addition, this could occur due to a genetic predisposition (heritable pulmonary arterial hypertension) or due to an unknown mechanism (idiopathic pulmonary arterial hypertension).[1]

The clinical manifestations of IPAH are nonspecific. Thereby, they are often mistakenly attributed to an alternate medical condition, delaying the diagnosis until symptoms become severe. In a French national registry study, a total of 674 adult patients with pulmonary arterial hypertension were analyzed. The time between the onset of symptoms and diagnosis was 27 months; at the diagnosis, approximately

Table 1 Case reports of subjects with IPAH presenting with seizure

References			Izzo et al[3]	Present case
Age (y)/sex			4/F	29/F
Presenting symptoms			Nocturnal events of arousal, unresponsiveness, up-rolling of eyes, lasting a few minutes	Limbs shaking after exercise
Comorbidities			NR	None
Seizure		Type	Nocturnal frontal lobe	Focal to bilateral tonic–clonic
		EEG	Sharply contoured activity	Voluntary hyperventilation showed some spikes with sharply contoured activity in the right hemisphere. The other parameters were normal.
		Treatment	Levetiracetam	Carbamazepine
		Resolution	Refractory	Refractory
Neuroimaging		Cranial CT scan	NR	Normal
		Brain MRI	Normal	Normal
IPAH characteristics	Suggest	Clinical manifestations that suggest an investigation	Two daytime syncopal episodes	Dyspnea and syncopal episodes within 6 hours of onset
		Echocardiogram	NR	Suggestive of IPAH
	RHC	MPAP (mm Hg)	73	70
		PVR (Wood unit)	40	38
		MCWP (mm Hg)	NR	12
		Vasoreactivity test	NR	Negative
	Exclude remain groups	CT pulmonary angiography	NR	Only signs of pulmonary hypertension
		Lung scintigraphy	NR	Only signs of pulmonary hypertension
		Investigation of other disorders	NR	Chronic lung disease or hypoxemia, systemic disorder, hematological disorder, and metabolic disorder
	Time from the seizure onset until the diagnosis of IPAH		Several months	3 months
	Management		Intravenous treprostinil, tadalafil, warfarin, and nocturnal supplemental oxygen. Addition of nifedipine after another syncopal episode. Levetiracetam was discontinued	Spironolactone 25 mg/d, furosemide 80 mg/d, sildenafil 60 mg/d, warfarin 5 mg/d, and supplemental oxygen. Carbamazepine was discontinued

Abbreviations: CT, computed tomography; EEG, electroencephalography; F, female; IPAH, idiopathic pulmonary arterial hypertension; MCWP, mean capillary wedge pressure; MPAP, mean pulmonary arterial pressure; MRI, magnetic resonance imaging; NR, not reported; PVR, pulmonary vascular resistance; RHC, right heart catheterization.

75% of patients belonged to the New York Heart Association functional class III or IV.[1]

IPAH presenting with seizure has been rarely reported in the literature. We identified one pediatric case report in the literature and we compared it with the present adult case (►**Table 1**).[3] A literature search was performed in Embase, Google Scholar, Lilacs, Medline, SciELO, and Science Direct, on a set of terms that included seizure, pulmonary arterial hypertension, and syncope.

In the cases of ►**Table 1**, both subjects received a prompt cardiac evaluation after the syncopal episode. Also, both failed treatment with anticonvulsants but responded well to pulmonary vasodilator therapy.[3]

The initial clinical presentation, in this case, could be seizure or syncope. The symptoms, including head-turning, jerking limbs, confusion, and no memory of the episode, seem to favor a seizure. Moreover, the absence of sweat and lightheadedness before the spells contribute to this diagnosis.[4,5] However, another possible explanation could be an anoxic–epileptic seizure, which is a biphasic sequence of syncope followed by a true convulsive epileptic seizure characterized by tonic–clonic phases lasting more than 30 seconds. It has been reported in children with cardiac problems but rarely in adults.[6]

The mechanism of IPAH presenting with seizure is probably based on pulmonary vasoreactivity. This hypothesis is supported by the fact that during strenuous physical activity, when the pulmonary artery pressure increases, there is an inability to adequately increase the cardiac output.[7] Thus, hypoxic manifestations such as exertional dyspnea, lethargy, and fatigue may occur. In this way, an intense pulmonary vasoreactivity could result in cerebral hypoxia facilitating the occurrence of proepileptogenic foci, which could lead to seizure activity.[2,3] Furthermore, EEG findings in the cases described in ►**Table 1** can be explained by hypoxia, since hypoxia may cause generalized or focal EEG discharges in adults, as already described in experiments with nitrogen inhalation.[8]

It is noteworthy that pediatric patients, when compared with adults, present higher percentages of acute pulmonary hypertensive crises, which could partially be explained by the greater pulmonary vasoreactivity in those as already stated by Barst et al.[2]

Conflict of Interest

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Authors' contribution

J.P.R.: Study design, data collection, and drafting and revising the manuscript.

A.L.F.C.: Study design, drafting, and revising the manuscript.

References

1 Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France: results from a national registry. Am J Respir Crit Care Med 2006;173(9):1023–1030

2 Barst RJ, Ertel SI, Beghetti M, Ivy DD. Pulmonary arterial hypertension: a comparison between children and adults. Eur Respir J 2011;37(3):665–677

3 Izzo A, McSweeney J, Kulik T, Khatwa U, Kothare SV. "Nocturnal seizures" in idiopathic pulmonary arterial hypertension. J Clin Sleep Med 2013;9(10):1091–1092

4 Reuber M, Chen M, Jamnadas-Khoda J, et al. Value of patient-reported symptoms in the diagnosis of transient loss of consciousness. Neurology 2016;87(6):625–633

5 Henderson MC, Tierney LM, Smetana GW. The Patient History: Evidence-Based Approach. China: McGraw Hill Professional; 2012:281–292

6 Battaglia A, Guerrini R, Gastaut H. Epileptic seizures induced by syncopal attacks. J Epilepsy 1989;2(3):137–145

7 Runo JR, Loyd JE. Primary pulmonary hypertension. Lancet 2003;361(9368):1533–1544

8 Gastaut, H, Bostem F, Naquet R, Guardiola A. Hypoxic activation of the EEG by inhalation of nitrogen. I. First results obtained in generalized epilepsies. Revue Neurologique 1959;100:501–510