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CASE REPORT

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Pulmonary hypertension secondary to veno-occlusive disease in a 15-years old boy: a case report.

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ABSTRACT

Pulmonary hypertension (PH) is a pathology characterized by a mean arterial pressure of the pulmonary artery greater than 20 mmHg and with a classification system based on its etiologies. Among the etiologies of pulmonary hypertension, there is the veno-occlusive disease, a rare pathology characterized by a continuous process of occlusion of pulmonary venules and veins leading to a progressive increase in pulmonary vascular resistance, whose pharmacological treatment results with traditionally used drugs for HP is still undetermined while pulmonary transplantation shows as the only definitive treatment. We report the case of a young patient complaining of dyspnea on exertion with rapid evolution to an acute case of hydropneumothorax, whose diagnosis of veno-occlusive disease was established after imaging studies associated with pulmonary catheterization. Combined treatment with vasodilator drugs of different classes was initiated, and the patient presented sustained remission of symptoms and improved quality of life for five years, while his medium expectative of life was 3 years long after the diagnosis.

KEY WORDS: Pulmonary hypertension; pulmonary veno-occlusive disease; cardiac insufficiency; pneumology.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is characterized by a mean arterial pressure of the pulmonary artery greater than 20 mmHg and by a pulmonary artery occlusion pressure less than or equal to 15 mmHg measured by right heart catheterization [1]. Its pathophysiology is variable and still uncertain, but it is known to involve remodeling of the arterial layers, with changes in pulmonary vascular resistance, and endothelial dysfunction, with excessive vasoconstriction [2-3]. Accordingly, PAH is classified as type 1 by the WHO among the various forms of pulmonary hypertension (PH), subdivided into seven subtypes [2]. Group 1 pulmonary hypertension, in this context, is characterized as a rare and severe form of precapillary PAH not associated with pulmonary or left heart chamber pathologies and resulting from a primary vasculopathy of the pulmonary circulation [4]. In Brazil, among PAH, it is estimated that only 1.1% of patients have veno-occlusive disease as an etiology, this being the rarest subtype of pulmonary arterial hypertension, while idiopathic PAH is the most prevalent [5].

Among the child population, pulmonary hypertension has an even more dismal and reserved prognosis, with an estimated life expectancy of 10 months after diagnosis, in contrast to the estimated 2.8 years among the adult population [6]. Furthermore, in this age group the prevalence of PH is even rarer, constituting only 0.48 people per million in the UK, mostly associated with congenital cardiovascular and/or pulmonary defects and therefore diagnosed at birth [6]. Pulmonary venous occlusive disease results from a progressive pathological process of pulmonary vein occlusion of unknown etiology, despite the identification of genetic and environmental factors that may influence its onset [6]. Its clinical presentation is variable and ranges from progressive dyspnea, palpitations, edema and cyanosis to pleural effusion, hypotension and digital clubbing, varying according to the severity of pulmonary arterial hypertension [7-8].

Thus, the gold standard for the diagnosis of veno-occlusive disease is histopathological examination of lung biopsy with evidence of remodeling of veins and venules resulting in occlusion of their lumen [9]. However, due to the difficulty of access to the method, high resolution chest CT scan showing thickened septa, ground-glass opacities, small ill-defined bilateral diffuse nodules, pulmonary artery enlargement and mosaic pattern with predominance at the bases combined with a detailed clinical examination are used in daily practice [10]. The management of PAH of veno-occlusive etiology remains a challenge, since the definitive treatment of veno-occlusive disease is bilateral lung transplantation and the use of vasodilators conventionally prescribed in pulmonary hypertension may precipitate the occurrence of severe acute pulmonary edema and death among these patients [7]. In this context, we report the case of a patient diagnosed with pulmonary arterial hypertension of veno-occlusive etiology and treated with oral vasodilators.

CASE REPORT

PATIENT INFORMATION: The patient is a 15-year-old student, coming from a family with no reported comorbidities, living in a rural community in northeastern brazil

CLINICAL FINDINGS: A 15 year old student started experiencing dyspnea on exertion, with progressive evolution and associated with episodes of central cyanosis, which led him to seek primary health care, where laboratory tests and chest X-rays were ordered, the results of which showed no alterations, and physical exercise was prescribed to improve respiratory capacity. On the first day of strength training, the patient developed episodes of emetic symptoms, headache, and worsening dyspnea, which was already characterized as dyspnea on minimal effort, tachycardia, and tenesmus. Physical examination revealed a reduced vesicular murmur in the right hemithorax, oxygen saturation of 50%, and heart rate of 150 beats per minute.

After stabilization, the patient was tested for the H1N1 virus, which was negative, and a CT scan of the chest without contrast revealed multiple small pulmonary nodules with ground-glass attenuation, sparse and with a lobular center pattern, and hypertensive hydropneumothorax in the right lung. Subsequently, with persistent low saturation, the patient underwent orotracheal intubation. After intubation, he improved his general condition and was extubated after four days, and was discharged 15 days after hospital admission with instructions to return to the pulmonology outpatient clinic.

TIMELINE: The patient noticed progressive dyspnea associated with central cyanosis and sought medical attention in May 2017. In the same month, one week after the onset of symptoms, he was admitted to a health care facility with hydropneumothorax, which led him to be intubated. After fifteen days, in the middle of June 2017, he was discharged from the hospital with clinical improvement. One week later, he returned to the outpatient clinic with the results of exams performed, and therapy with oral vasodilators was instituted. Five years after the beginning of his management, he is asymptomatic and with a good quality of life measured in consultations held every six months since then, the last meeting being in May 2022.

DIAGNOSTIC ASSESSMENT: At the outpatient clinic, supplemental oxygen therapy was instituted, and an echocardiogram, plethysmography, and lung scintigraphy were requested. The echocardiogram showed moderate pulmonary arterial hypertension associated with mild tricuspid insufficiency and mild right chamber dilatation with preserved right ventricular systolic function, while the pulmonary scintigraphy showed multiple subsegmental areas of hypoperfusion diffusely distributed in both lungs and more evident in the upper lobes. Plethysmography, in turn, suggested nonspecific ventilatory disorder with markedly reduced diffusion.

THERAPEUTIC INTERVENTION: These exams led to the institution of therapy with sildenafil 60mg/day and rivaroxaban 15 mg/day and to the request of a pulmonary catheterization, whose result showed a pulmonary artery pressure of 80x45 mmHg, confirming the diagnosis of pulmonary hypertension.Later, with the progressive clinical improvement presented by the patient, a therapeutic scheme with sildenafil 60mg/day and ambrisentan 10mg/day was instituted, with the suspension of home oxygen therapy. This intervention differed from the conventional treatment of pulmonary hypertension of veno-occlusive etiology, which is based on early lung transplantation

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FOLLOW UP AND OUTCOMES: In this context, the patient experienced remission of the main symptoms, with evident objective and subjective improvement 5 years after the beginning of treatment measured in consultations held every six months since then, the last meeting being in May 2022. During the 5 years, the patient had no significant clinical occurrences.

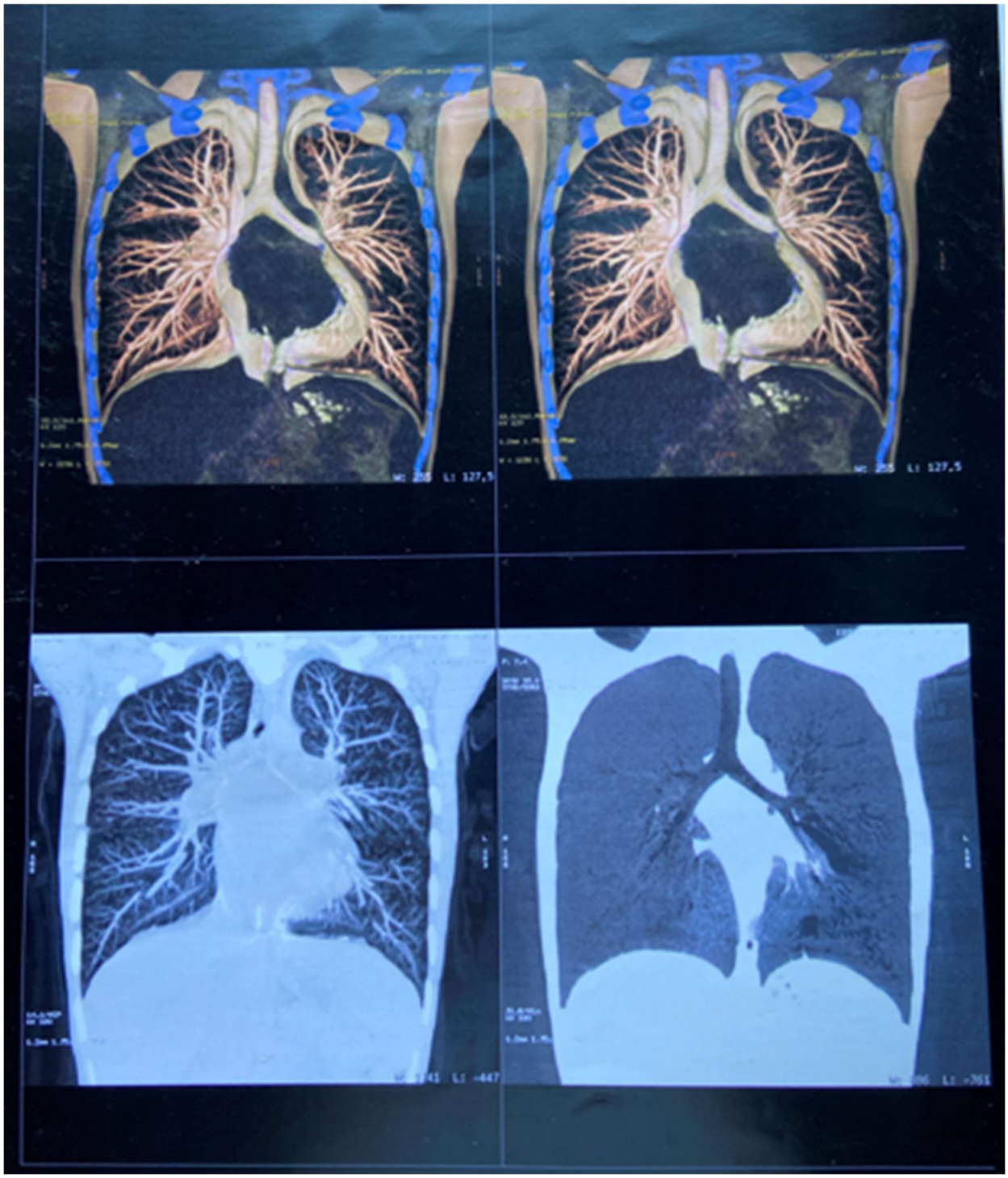

Figure 1. Lung scintigraphy showing multiple subsegmental areas of hypoperfusion diffusely distributed in both lungs and more evident in the upper lobes.

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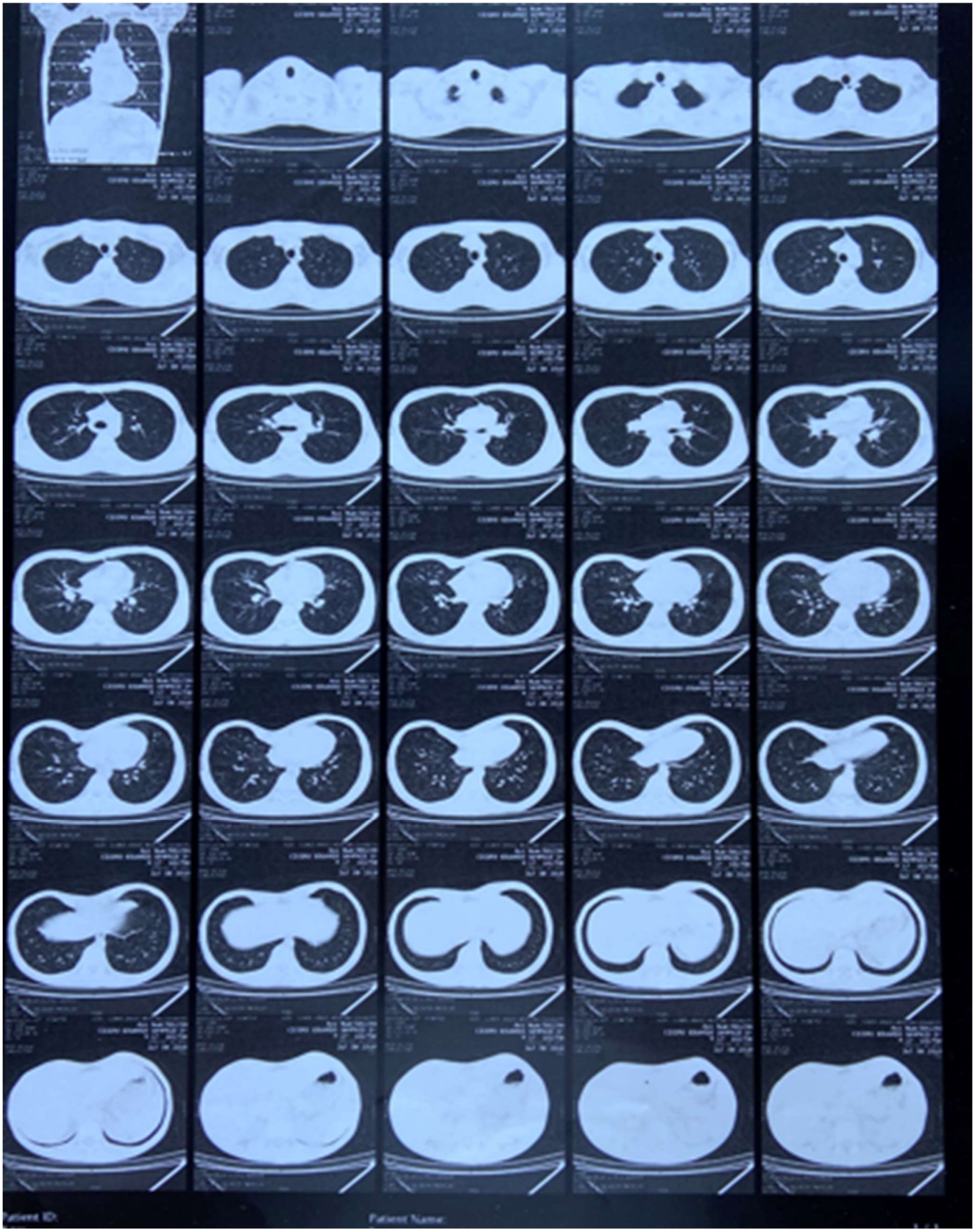

Figure 2. Lung scintigraphy showing multiple subsegmental areas of hypoperfusion diffusely distributed in both lungs and more evident in the upper lobes.

DISCUSSION

Current treatments for pulmonary hypertension aim to allow patients to achieve a low mortality risk status by controlling symptoms and stabilizing disease progression [11]. This requires that patient undergoes diagnostic screening for bronchopulmonary and cardiovascular abnormalities and risk stratification risk stratification based on ethnicity and treatment with commercially available vasodilator drugs from the classes of 5-phosphodiesterase inhibitors (PDE-5), soluble guanylate cyclase stimulators (sGCS), endothelin receptor antagonists (ERA), prostacyclin analogues, and prostacyclin receptor agonists [6,11,12].

Moreover, the therapeutic strategy used at the beginning of treatment has a great influence on the patient's prognosis, and the early use of combination therapies involving different classes of vasodilators is recommended in the management of patients with PAH, even among childs and in those classified as having a low risk of morbidity, given the understanding of the correlation of multiple abnormalities in the production of vasoactive substances in the pathophysiology of pulmonary hypertension [13]. In this context, combination therapy of 5-phosphodiesterase inhibitors with endothelin receptor antagonists has shown promise in halving hospitalizations for worsening PH compared to patients using a monotherapy regimen [14]. With regard to pulmonary hypertension due to veno-occlusive disease, the prognosis remains more dismal than that of pulmonary arterial hypertension due to other etiologies, with the need for further studies on the subject to clarify whether the advances experienced in the treatment of PAH are reproduced in patients with this condition [15]. Nevertheless, the symptomatic treatment employed in idiopathic PAH is also applicable in PAH of venous-occlusive etiology, with the possibility of using diuretics in case of congestive signs and oxygen therapy in order to correct hypoxemia, a condition that may aggravate pulmonary vasoconstriction [15].

In these patients, the use of combined therapy of vasodilators proved advantageous in those who did not have the genetic mutation characteristic of the disease, allowing longer and better survival free of lung transplantation [16]. Thus, the low survival of patients with pulmonary veno-occlusive disease can be circumvented by individualization of treatment and by the application of beneficial therapeutic schemes for other classes of PAH [16].

CONCLUSIONS

Pulmonary arterial hypertension secondary to veno-occlusive disease continues to represent a condition of high morbidity and mortality. However, the new therapeutic schemes used in the treatment of PAH due to other etiologies may be a promising alternative in the management of these patients and represent an alternative for the improvement of quality of life in relation to the symptomatic-only therapy prior to lung transplantation currently used.

SUPPLEMENTARY INFORMATION

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Informed Consent Statement: *Informed consent was obtained from all subjects involved in the study.*
Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*

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