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CLINICAL QUIZ

Pulmonary hypertension in an adolescent with end-stage-renal disease—a diagnostic challenge: Answers

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Answers

What is the cause of the pulmonary hypertension in this patient?

The initial hypothesis was that the heart failure was related to left ventricular (LV) diastolic dysfunction secondary to systemic thrombotic microangiopathy (TMA) and end-stage renal disease (ESRD). This is consistent with the echocardiographic findings showing dilated LV with a normal systolic function. Although LV diastolic dysfunction is associated with elevated pulmonary pressure, the results of the catheterization showed that, in our patient, pulmonary hypertension (PH) was related to a pulmonary overflow due to a massive arteriovenous left-to-right shunt at the femoral level as demonstrated by the abnormally high oxygen saturation found in the inferior vena cava. Of note, the last Doppler assessing the fistula blood flow performed in 2008 was already showing high blood flow of 2 L/min.

How should the pulmonary hypertension in this patient be treated?

The femoral arteriovenous (A-V) fistula was closed surgically. Subsequent echocardiography showed normalization of the pulmonary pressure (32/10 mean 20 mmHg) and of the cardiac index (4 L/min/m^2). Renal function also improved [estimated gloomerular filtration rate (eGFR) increased from 27 to 38 ml/min/m^2] by relief of the steal phenomenon through the fistulae. Of note, our patient did not present signs of steal phenomenon in the lower limbs.

Discussion

Patients with ESRD require regular cardiac follow-up since cardiovascular disease is the leading cause of death. Recent studies demonstrate that up to 92% of children with ESRD have cardiovascular risk factors and that their cardiac follow-up is underprovided [1]. Moreover, patients with ESRD have an increased prevalence of PH [2] that may be caused by various mechanisms (Group 5 of the Dana Point classification) [3].

The present case report illustrates the multifactorial aspects of PH in ESRD. Indeed, elevation of pulmonary pressure could have been related to left-heart diastolic dysfunction, to ESRD itself, or to pulmonary overflow. Fortunately, PH was fully reversible after closure of the shunt, as suggested by the right heart catheterization that showed pulmonary vascular resistance (PVRi) within the reversible range in patients with cardiac shunts [4]. To date, no case of PH caused by an A-V access has been described in children, but several cases have been reported in adult patients [5, 6]. Invasive hemodynamic testing was reassuring in our patient, but did not exclude pulmonary vascular disease. It is indeed still debated whether or not increased pulmonary blood flow secondary to an A-V access can lead to pulmonary vascular disease in patients undergoing hemodialysis. Several conditions inducing an increase in neonatal and fetal pulmonary blood flow are known to produce pulmonary vessel remodeling [7–11] and PH. Our case stresses the difference between the terms "pulmonary vascular disease" and "pulmonary arterial hypertension"—they are not interchangeable. In

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congenital cardiac left-to-right shunts, patients with moderate to large defects can have pulmonary arterial hypertension, but not necessarily an irreversible pulmonary vascular disease (i.e., a permanently and extensively remodeled pulmonary vascular bed). In cases where pulmonary artery pressure and blood flow are high, but PVRi is within normal limits or slightly elevated, the patient can be considered a suitable candidate for closure of the shunt. In this scenario, pulmonary vascular lesions are likely not to be extensive. Our patient remains at risk for unfavorable pulmonary vessel remodeling because of the other risk factors associated with ESRD [12]. Indeed, alteration of pulmonary vessel endothelial function, with an increase of serum Endothelin-1 levels and a decrease of NO levels, has been found in patients with ESRD and PH when compared to patients with ESRD but without PH [6]. It has also been suggested that the pathophysiology of the pulmonary vascular disease in ESRD involves a variety of factors besides arteriovenous (A-V) access, such as uremia or elevated parathyroid hormone [13].

PH can also be post-capillary in patients with ERSD as LV diastolic dysfunction is a common finding in patients undergoing chronic hemodialysis [14], regardless of the etiology of ESRD. The TMA that our patient developed after his first renal transplant may have caused direct myocardial damage as seen in hemolytic uremic syndrome [15–17], and this might have contributed to the post-capillary component of his PH.

Conclusion

This report emphasizes the need to regularly check the A-V fistula blood flow in children as recommended in adult guidelines (e.g., NF-K/DOQI) in order to diagnose excessive shunting. We also confirmed the complexity and the multifactorial etiologies of PH in children with ESRD. We suggest that, as in cardiac left-to-right shunts, right heart catheterization should be performed when an arteriovenous shunt is suspected as a possible contributor to increased pulmonary pressure in patients with ESRD.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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