Pulmonary capillary hemangiomatosis or hepatopulmonary syndrome in a patient with calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia syndrome?

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To the Editor: We were interested in the article, which reported a woman with calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia (CREST) syndrome who developed progressive dyspnea on exertion and was later diagnosed with pulmonary capillary hemangiomatosis (PCH) that was confirmed by an open lung biopsy.[1] We would like to remark that the diagnosis of PCH is inconclusive from just history, treatment, and histological changes. This case also does not specify a clear connection between PCH and CREST syndrome; therefore, we believe we need to explore another possible disease association.

PCH is an extremely rare form of pulmonary artery hypertension (PAH) and has a poor prognosis. Also, pulmonary hypertension is one of the manifestations of CREST syndrome, despite that in this case, right heart catheterization which is considered the gold standard was not done to determine pulmonary hypertension. Right heart catheterization is a definitive diagnostic technique characterized by the presence of pre-capillary pulmonary hypertension including pulmonary artery wedge pressure $\leq$15 mmHg in addition to a mean pulmonary artery pressure $\geq$25 mmHg at rest and a pulmonary vascular resistance >3 Wood units. There is also no evidence of bronchoalveolar lavage stained positive for iron using Perl which suggests iron deposition in the lung. The ground glass appearance in computed tomography (CT) scan is ambiguous and cannot be taken as conclusive evidence of PAH. Instead, the high-resolution CT scan showing diffuse centrilobular ground-glass opacities is more consistent with PCH.[2] Furthermore, the use of drug ambrisentan and consecutive improvement also suggest no association of PCH with PAH as there is evidence which suggests the application of ambrisentan alone is linked with disease progression and hospitalization for worsening PAH.[3] This leads us to regard the patient does not suffer from PCH.

Furthermore, in our clinical setting, we encountered a 10-year-old boy who presented with telangiectasis, hypoxia, and similar CT scan and histological manifestation. It was later determined that the patient is suffering from hepatopulmonary syndrome which is a rare complication of liver cirrhosis and/or portal hypertension. The unique pathologic feature of hepatopulmonary syndrome is dilatation of the pulmonary pre-capillary and capillary vessels [Figure 1]. Similarly, in this case, the lung biopsy is inconsistent with findings of PCH; instead of alveolar thickening with intense capillary proliferation, there is vasodilation. Additionally, a CT angiography demonstrates marked dilatation of pulmonary artery >3 cm in PAH, but the case study failed to report this evidence.[1] Likewise, we made our diagnosis based on a contrast-enhanced CT scan, right heart catheterization, and lung biopsy. There is evidence insinuating a link between primary biliary cirrhosis and CREST syndrome.[4] Primary biliary cirrhosis may finally result in cirrhosis, and the introduction of liver toxin, mainly nitric oxide into the lung may lead to pulmonary vessel dilation. Therefore, it is likely that the patient is suffering from hepatopulmonary syndrome.[5] In conclusion, we suggest more evidence is needed for a definitive diagnosis of PCH and to consider hepatopulmonary syndrome as a differential diagnosis in this stage may help to get a more clear clinical picture which will help in suitable treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's guardians have given their consent for his images and other clinical

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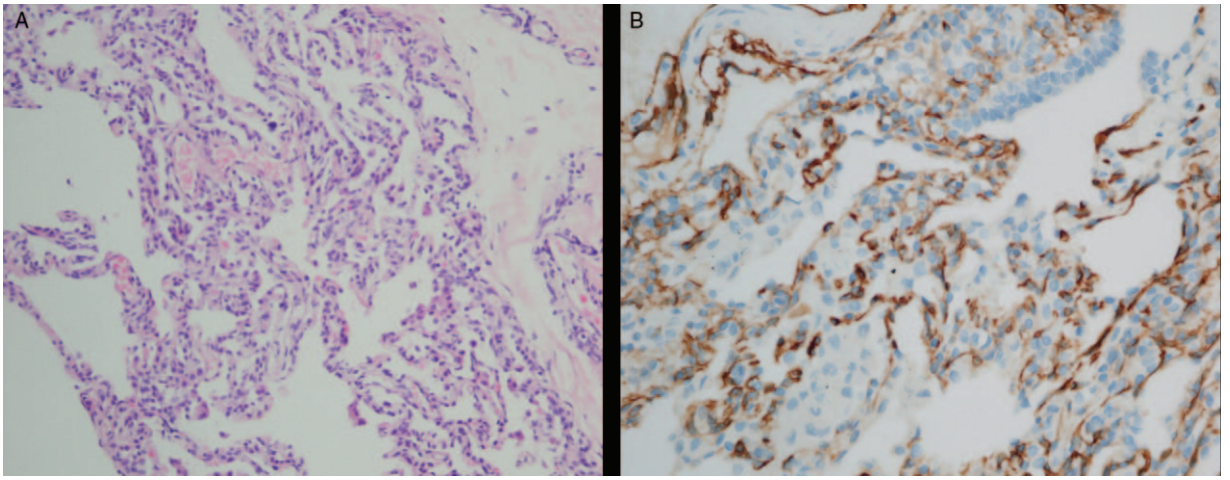

Figure 1: Lung tissue biopsy shows pre-capillary and capillary vessels dilation between inter-alveolar space in a 10-year-old boy with hepatopulmonary syndrome (A: Hematoxylin-eosin staining; B: CD31 immunohistochemistry, Original magnification ×200.)

information to be reported in the article. The patient's guardians understand that his names and initials will not be published and due efforts will be made to conceal the identity of the patient, although anonymity cannot be guaranteed.

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