To the Editor: A 65-year-old woman with calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome was admitted to hospital because of progressive dyspnea on exertion for about 1 year. In the past, she had been diagnosed as gastroesophageal reflux disease and scleroderma for 10 years. Physical examination showed masked face, Raynaud’s phenomenon, finger sclerodactyly, and skin telangiectasia on her neck and back [Figure 1a and 1b]. The titer of anticientromere antibody in serum increased to 1:1000. Analysis of arterial gas on room air revealed the partial pressure of arterial oxygen (PaO₂) was 54 mmHg (1 mmHg = 0.133 kPa) and carbon dioxide (PaCO₂) was 32 mmHg. Echocardiogram showed severe tricuspid regurgitation and elevated pulmonary arterial pressure of 78 mmHg. Chest high-resolution computer tomography demonstrated diffuse mild ground-glass opacities in both lung fields [Figure 1c] and dilated central pulmonary artery [Figure 1d]. Open lung biopsy demonstrated characteristic more than two layers of capillaries on alveolar walls [Figure 1e], which was confirmed by CD34 immunohistochemical staining [Figure 1f]. Therefore, the patient was diagnosed as pulmonary capillary hemangiomatosis (PCH) associated with CREST syndrome, and treated by prednisone and ambrisentan. One month later, her symptoms obviously improved and repeated echocardiogram report showed pulmonary systolic pressure decreased to 46 mmHg.

PCH is a rare cause of pulmonary arterial hypertension (PAH), which is characterized by an uncontrollable proliferation of pulmonary capillaries and difficult to be diagnosed ante mortem. Less than 100 cases of PCH have been described previously and only three cases in China. There was only a single case of PCH associated with CREST syndrome in the past literature. The patient presented with dyspnea on exertion, CREST syndrome, PAH, and bilaterally diffuse ground-glass opacities. Although isolated PAH without pulmonary fibrosis might occur in 10% of patients with scleroderma, which could not explain the presentations of this patient. Pulmonary veno-occlusive disease (PVOD) is similar to PCH, which has been reported a few cases associated with scleroderma previously. Images of PVOD include both diffuse ground-glass opacities and widespread thickened interlobular septa, but the later was absent in this patient, which indicated the diagnosis of PCH only. Then open lung biopsies of this patient showed proliferation of capillary channels within alveolar walls, which is the most distinctive histological feature of PCH.

The pathogenesis of PCH associated with CREST syndrome is unclear, and this patient’s skin telangiectasia perhaps related to her pulmonary capillary proliferation. Vascular endothelial cell injury is thought to play a key role in the fibroproliferative response of CREST syndrome. It is tempting to speculate that in susceptible individuals, the factors mediating endothelial cell injury in scleroderma induce uncontrolled capillary proliferation resulting in PCH.

PCH is important to be recognized because continuous intravenous prostacyclin and calcium channel blockers have been reported to cause sudden respiratory distress and death in these patients. Prognosis of this disease remains poor and most of them died in 2 years since diagnosis and the only definitive treatment is lung transplantation. Nevertheless, this patient was treated by glucocorticoid and ambrisentan, an oral endothelin-receptor antagonist, and then her symptoms improved obviously meanwhile pulmonary systolic pressure decreased, which indicated PCH associated with CREST syndrome might response to oral drug therapy and avoid lung transplantation.

In conclusion, PCH associated with CREST syndrome is rare and difficult to be diagnosed and treated, which is a challenge for physicians, radiologists, and pathologists.
Declaration of patient consents
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s)/patient’s guardians has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients/patient’s guardians understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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