An emerging phenotype of pulmonary arterial hypertension patients carrying SOX17 variants

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Abstract

Background The phenotype of pulmonary arterial hypertension (PAH) patients carrying SOX17 pathogenic variants remains mostly unknown.

Methods We report the genetic analysis findings, characteristics and outcomes of patients with heritable PAH carrying SOX17 variants from the French Pulmonary Hypertension Network.

Results 20 patients and eight unaffected relatives were identified. The median (range) age at diagnosis was 17 (2–53) years, with a female:male ratio of 1.5. At diagnosis, most of the patients (74%) were in New York Heart Association Functional Class III or IV with severe haemodynamic compromise, including a median pulmonary vascular resistance of 14.0 (4.2–31.5) WU. An associated congenital heart disease (CHD) was found in seven PAH patients (35%). Patients with CHD-associated PAH were significantly younger at diagnosis than PAH patients without CHD. Four patients (20%) suffered from recurrent haemoptysis requiring repeated arterial embolisations. 13 out of 16 patients (81%) for whom imaging was available displayed chest computed tomography abnormalities, including dilated, tortuous pulmonary vessels, ground-glass opacities as well as anomalies of the bronchial and nonbronchial arteries. After a median (range) follow-up of 47 (1–591) months, 10 patients underwent lung transplantation and one patient benefited from a heart–lung transplantation due to associated CHD. Histopathological analysis of lung explants showed a congested lung architecture with severe pulmonary arterial remodelling, subpleural vessel dilation and numerous haemorrhagic foci.


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Conclusions PAH due to SOX17 pathogenic variants is a severe phenotype, frequently associated with CHD, haemoptysis and radiological abnormalities. Pathological assessment reveals severe pulmonary arterial remodelling and malformations affecting pulmonary vessels and thoracic systemic arteries.