An emerging phenotype of pulmonary arterial hypertension patients carrying *SOX17* variants

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Shareable abstract (@ERSpublications)
PAH due to *SOX17* variants is a severe phenotype associated with CHD, haemoptysis and radiological anomalies. Histopathology shows severe pulmonary arterial remodelling and malformations affecting pulmonary vessels and systemic arteries. https://bit.ly/3yWSYUP

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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.

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.