Pulmonary arterial hypertension associated to toxic-oil syndrome. A long story short

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Introduction: Pulmonary arterial hypertension (PAH) is occasionally related to previous use of drugs or toxins. The toxic oil syndrome (TOS) is a model of drug-induced PAH caused by the prior use of denatured rapeseed oil. This rare condition caused an acute epidemic disease in Spain, including the development of pulmonary arterial hypertension, with a mortality rate of 82% from 1981 to 1987. Several cases have been discovered in the successive years until 2018. The clinical profile and outcome of those patients with PAH-TOS diagnosed since 1988 are unknown.

Methods: Historical cases of PAH-TOS since 1988 were collected. We analysed baseline characteristics, genetic testing, and the rates of lung transplantation or mortality in PAH-TOS, comparing these outcomes with incident idiopathic and heritable PAH cases (i/hPAH) from the Spanish Registry of Pulmonary Hypertension (REHAP).

Results: Thirty-nine patients with PAH-TOS between 1988 and 2018 were selected for this study. The median time between the toxic intake and the disease onset was 20.3 years (Interquartile range: 14.3 – 25.6). At least one patient per year was identified in that period, with a mean incidence of 1.63 cases/per year. Genetic testing was done in 21 patients, using a 37-gene Next Generation Sequencing panel, not finding any pathogenic or likely pathogenic variant. Importantly, in 3 out of 39 cases, the disease resolved (7.7%), while 4 cases needed lung transplantation. The 10-year mortality was 35.9%.

Cases of PAH-TOS were compared with 200 incident patients with i/hPAH collected from 2003 onwards. PAH-TOS patients were significantly younger when compared with i/hPAH patients (p<0.0035). At baseline, patients with PAH-TOS had higher haemodynamically severity when compared with i/hPAH (mean pulmonary artery pressure of 65.0 mmHg Vs 53.5 mmHg, and pulmonary vascular resistance of 15.1 Vs 12.1 Wood Units, respectively; p=0.003, and p=0.02). In PAH-TOS the 5- and 10-year survival free of lung transplantation was 81.3%, and 52.7%, similar to the rates in the i/hPAH group (76.6%, and 59.2%, respectively; Log-rank test p=0.881. Figure).

Conclusions: The toxic oil syndrome is a unique model of drug-induced PAH, with new cases diagnosed several years after the toxic exposure. We did not find genetic variants in PAH-SOT patients. As described in other drug-induced cases of PAH, some patients experience a resolution of the disease over time. The very long-term survival of these patients is similar to that of patients with idiopathic or heritable pulmonary arterial hypertension.