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The unprecedented intersection: Hermansky–Pudlak Syndrome and rheumatic mitral stenosis

Short title: Hermansky–Pudlak syndrome and rheumatic mitral stenosis

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A 57-year-old woman was referred to cardiology outpatient clinic for chronic exertional dyspnea. Her medical history included hospitalization for acute rheumatic fever at the age of 21. She was treated with parenteral penicillin and acetylsalicylic acid, but neglected her annual cardiac check-up.

Her fingertip oxygen saturation was 95%. Her hair and eyebrows were white to brown. Horizontal nystagmus was present. Cardiovascular examination revealed a soft first heart sound and a diastolic murmur over the mitral focus. Her lung auscultation revealed bilateral occasional coarse crackles in the lower zones. Electrocardiogram showed sinus rhythm. Posteroanterior X-ray showed left atrial enlargement, bilateral reticular opacities in the mid and lower zones. Spirometry demonstrated findings consistent with restrictive lung disease. Her thoracic computed tomography showed reticular lines in the middle and lower zones of both lungs, focal hypodense areas compatible with subsegmental air trapping in the lower lobes

of both lung and ground glass opacities (Figure 1A–D). Bronchoalveolar lavage showed normal cytology.

The patient was born to third-degree consanguineous parents. She added that she had prolonged bleeding episodes (>15 minutes) after tooth removal. Her sister had cutaneous albinism. Oculocutaneous albinism, interstitial lung disease and bleeding diathesis were suspicious for Hermansky–Pudlak syndrome (HPS). High-throughput sequencing was performed, and a homozygous p.Met325Trpfs*6 (c.972del) was found in the *HPS1* gene.

Transthoracic echocardiogram showed normal left ventricular systolic function, left atrial enlargement and rheumatic mitral stenosis (severe, mitral valve area = 1.4 cm^2, measured *via* planimetry). Transesophageal echocardiogram demonstrated commissural fusion of the mitral leaflets, trace mitral regurgitation and no left atrial thrombus (Figure 1E–F). In accordance with European Society of Cardiology guidelines [2], we performed percutaneous balloon mitral angioplasty. Mitral valve area increased to 1.8 cm^2, and mean gradient fell from 10 mm Hg to 3 mm Hg. There were no perioperative bleeding complications. After several weeks, her functional capacity improved to class II.

This case illustrates the path to the diagnosis of HPS and the incidental discovery of rheumatic mitral stenosis in a patient with oculoalbinism and dyspnea. HPS is a very rare disorder with an estimated worldwide prevalence of one to nine in 1 000 000 individuals [3]. HPS is caused by genetic mutations resulting in defective lysosome-related organelles, which synthesize and store melanin, and platelet dense granules, which store small signaling molecules involved in platelet aggregation [1]. The disease can also cause interstitial lung disease, which could eventually lead to pulmonary hypertension [2].

The diagnosis of HPS can be established in a proband with oculocutaneous albinism and absence of platelet delta granules on electron microscopy, or molecular diagnosis can be established in a proband with suggestive findings and biallelic pathogenic variants [1].

Successful lung transplant was previously reported to be performed in HPS-1 despite bleeding diathesis [3]. Severe mitral stenosis due to rheumatic heart disease contributed to the functional limitation of our patient, therefore we decided on the percutaneous balloon mitral angioplasty despite the risks of tamponade [4]. With proper transesophageal echocardiogram guidance, we performed interatrial septal puncture and balloon dilatation of the mitral valve without complications in our patient with HPS.

Article information

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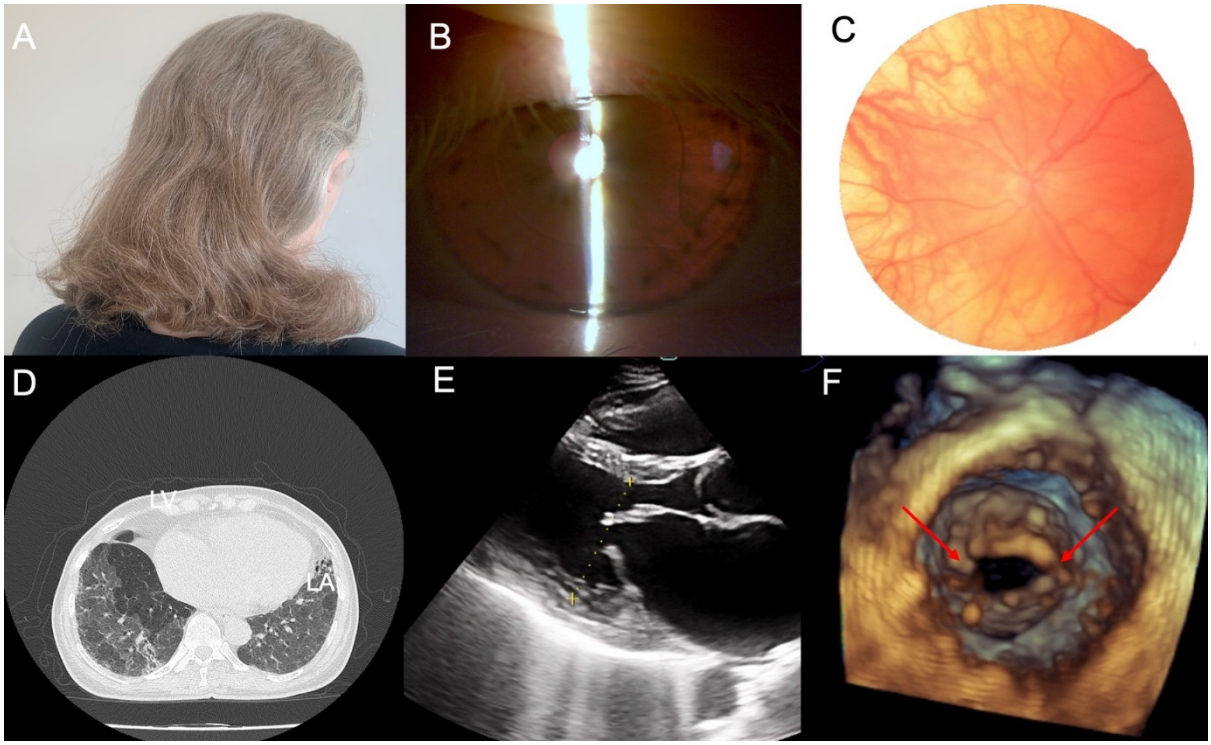

Figure 1. A. The patient's hair was white to brown in color. **B.** Slit-lamp exam showed the absence of iris translucency on retro-illumination. **C.** Fundoscopic examination revealed retinal hypopigmentation and prominent choroid vessels. **D.** Thoracic computed tomography showed ground glass opacities and reticular lines with focal hypodense areas compatible with subsegmental air trapping in the lower lobes of both lungs. **E.** Parasternal long axis view on transthoracic echocardiogram showed restricted mitral bileaflet motion, typical for rheumatic mitral stenosis. **F.** Three-dimensional transesophageal echocardiogram showed the orifice of the mitral valve, commissural fusion of the mitral leaflets (red arrows) — a finding indicating that the mitral valve is amenable to percutaneous balloon mitral valvuloplasty

Abbreviations: LA, left atrium; LV, left ventricle