An unprecedented intersection between Hermansky–Pudlak syndrome and rheumatic mitral stenosis

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A 57-year-old woman was referred to the 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 had 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 showed a soft first heart sound and a diastolic murmur over the mitral focus. Lung auscultation showed bilateral occasional coarse crackles in the lower zones. Electrocardiogram showed sinus rhythm. Posteroanterior X-ray showed left atrial enlargement, and bilateral reticular opacities in the mid and lower zones. Spirometry demonstrated findings consistent with restrictive lung disease. Thoracic computed tomography showed reticular lines in the middle and lower zones of both lungs, and focal hypodense areas compatible with subsegmental air trapping in the lower lobes of both lungs and ground glass opacities (Figure 1A–D). Bronchoalveolar lavage showed normal cytology.

The patient was born to third-degree consanguineous parents. She stated that she had prolonged bleeding episodes (>15 minutes) after tooth removal. Her sister had cutaneous albinism. Oculocutaneous albinism, interstitial lung disease, and bleeding diathesis raised the suspicion of 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 towards a 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 1–9 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 given a proband with oculocutaneous albinism and the absence of platelet delta granules on electron microscopy, or molecular diagnosis can be established given a proband with suggestive findings and biallelic pathogenic variants [1].

Successful lung transplantation was previously reported to be performed in

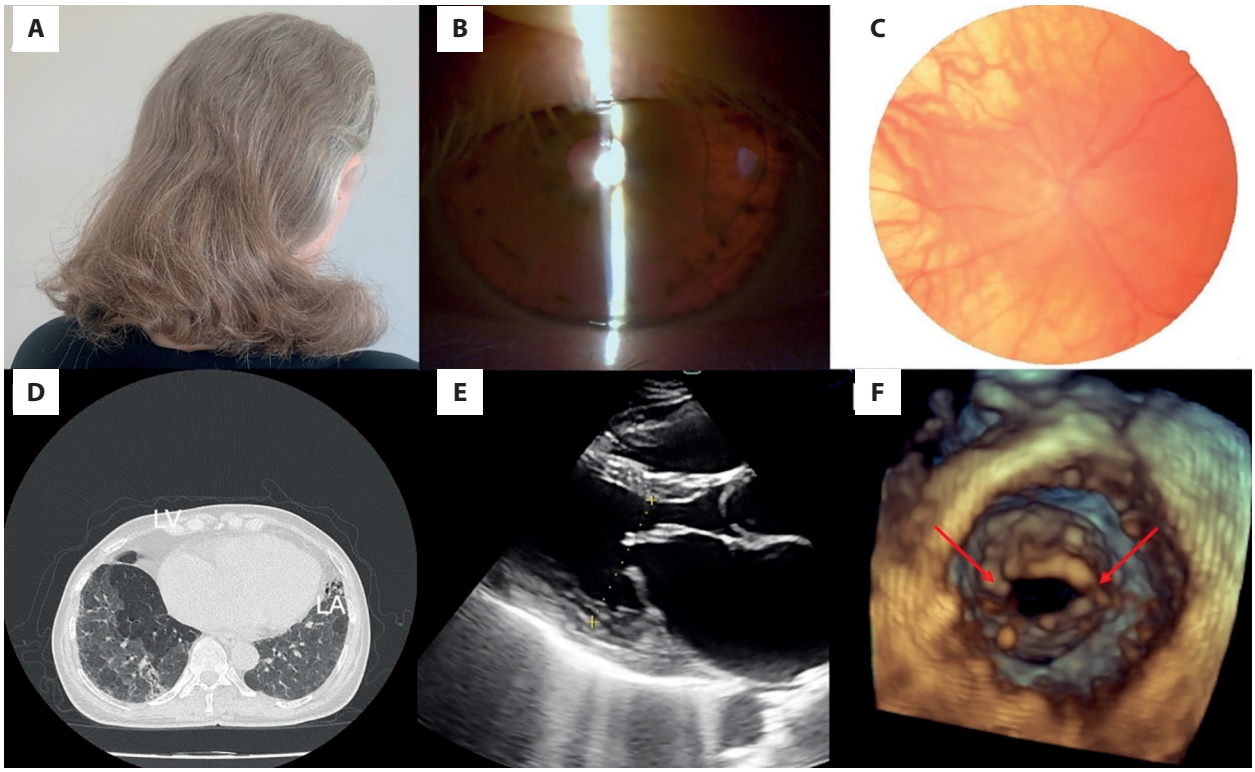

Figure 1. A. Patient's hair was white to brown in color. **B.** Slit-lamp exam showed absence of iris translucency on retro-illumination. **C.** Fundoscopic examination showed retinal hypopigmentation and prominent choroid vessels. **D.** Thoracic computed tomography showed ground glass opacities and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

Abbreviations: LA, left atrium; LV, left ventricle

HPS-1 despite bleeding diathesis [3]. Severe mitral stenosis due to rheumatic heart disease contributed to the functional limitation of our patient, and therefore we decided on 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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REFERENCES

1. National Library of Medicine. Hermansky-Pudlak Syndrome. https://www.ncbi.nlm.nih.gov/books/NBK1287 (accessed: 16.11.2023).
2. Torun A, Erdem A, Oguz M, et al. Successful treatment of pulmonary hypertension with macitentan in a patient with Hermansky-Pudlak syndrome. Kardiol Pol. 2023; 81(3): 300–301, doi: 10.33963/KP.a2023.0012, indexed in Pubmed: 36640015.
3. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2022; 43(7): 561–632, doi: 10.1093/eurheartj/ehab395, indexed in Pubmed: 34453165.
4. Lederer DJ, Kawut SM, Sonett JR, et al. Successful bilateral lung transplantation for pulmonary fibrosis associated with the Hermansky-Pudlak syndrome. J Heart Lung Transplant. 2005; 24(10): 1697–1699, doi: 10.1016/j.healun.2004.11.015, indexed in Pubmed: 16210149.
5. Turi ZG. The 40th anniversary of percutaneous balloon valvuloplasty for mitral stenosis: current status. Struct Heart. 2022; 6(5): 100087, doi: 10.1016/j.shj.2022.100087, indexed in Pubmed: 37288059.