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Albinism with pulmonary fibrosis: Hermansky-Pudlak syndrome

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A 60-year-old, non-smoking, obese woman with asthma, arterial hypertension, and non-insulin-dependent diabetes, was admitted to the hospital because of a chronic, dry cough and exertional dyspnea. She had cutaneous albinism with colored eyes (Figure 1A) and horizontal nystagmus. The patient had a tendency to bruise and prolonged bleeding since childhood. On the basis of decreased platelet aggregation with epinephrine (6%; predicted 69-88%), and ADP (52%; predicted 69-88%) with normal blood cell counts, the bleeding and prothrombin times, concentrations of fibrinogen and factor IX and XI, coagulopathy was diagnosed many years before. In admission, high-resolution computed tomography revealed a reduced lung volume, a subpleural and peripheral reticular pattern, traction bronchiectasis and small areas of honeycombing (Figure 1B-D). Spirometry values were within normal limits (force vital capacity 91% of predicted), the diffusion capacity was moderately decreased (69% of predicted). The patient walked a normal distance in the 6-min walk test with significant desaturation (from 97% to 84%). Slight pulmonary hypertension (PH) was found in an echocardiogram (TVPG-33mmHg). All these symptoms were very suggestive for the Hermansky-Pudlak syndrome (HPS), and it was a stimulus for genetic examination, which confirmed heterozygotic conjugated mutations in both alleles of the HPS1 gene [c.355delC(p.His119fs) and c.1513C>T9p.Gln505*). The diagnosis of HPS with pulmonary fibrosis (PF) and PH was established. The patient's parents, a daughter and two sisters are healthy, but she has a brother with albinism.

HPS is a rare autosomal recessive disorder with an incidence of 1-2/1 000 000. There are ten subtypes, marked as HPS-1– HPS-10. Mutations in HPS-related genes result in anomalous development of lysosome-related organelles in specialized cells such as melanocytes or platelets [1,2]. Oculocutaneous albinism and bleeding diathesis occur in all subtypes, but PF is only found in types 1,2, and 4 [3]. Albinism is characterized by hypopigmentation of the skin and hair, with variable pigmentation of the iris. Radiologic and histologic features of PF

in HPS have a pattern of usual interstitial pneumonia, but this disorder frequently occurs in younger patients (age 20–40 years) [2,3]. It is often accompanied by PH. Rarer manifestations of HPS include granulomatous colitis, immunodeficiency, renal failure and cardiomyopathy. The wide spectrum of clinical presentation of the disease is due to different mutations in specific genetic loci of HPS. Diagnosis of HPS is established usually during childhood, by typical clinical findings, the absence of delta granules (dense bodies) in platelets upon whole-mount electron microscopy, and genetic analysis of the HPS genes [1,2]. Diagnosis at an older age, as in the presented case, is extremely rare. The delay in diagnosis in our patient was due to limited knowledge of this rare syndrome and mild symptoms of bleeding diathesis. The PF noticed in this patient was not severe, but reduced exercise tolerance was mainly due to PH. An antifibrotic treatment with pirfenidone was introduced for HPS patients with PF, but it is still not approved [4]. According to our best knowledge it is the first case of HPS presented in polish literature.

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A

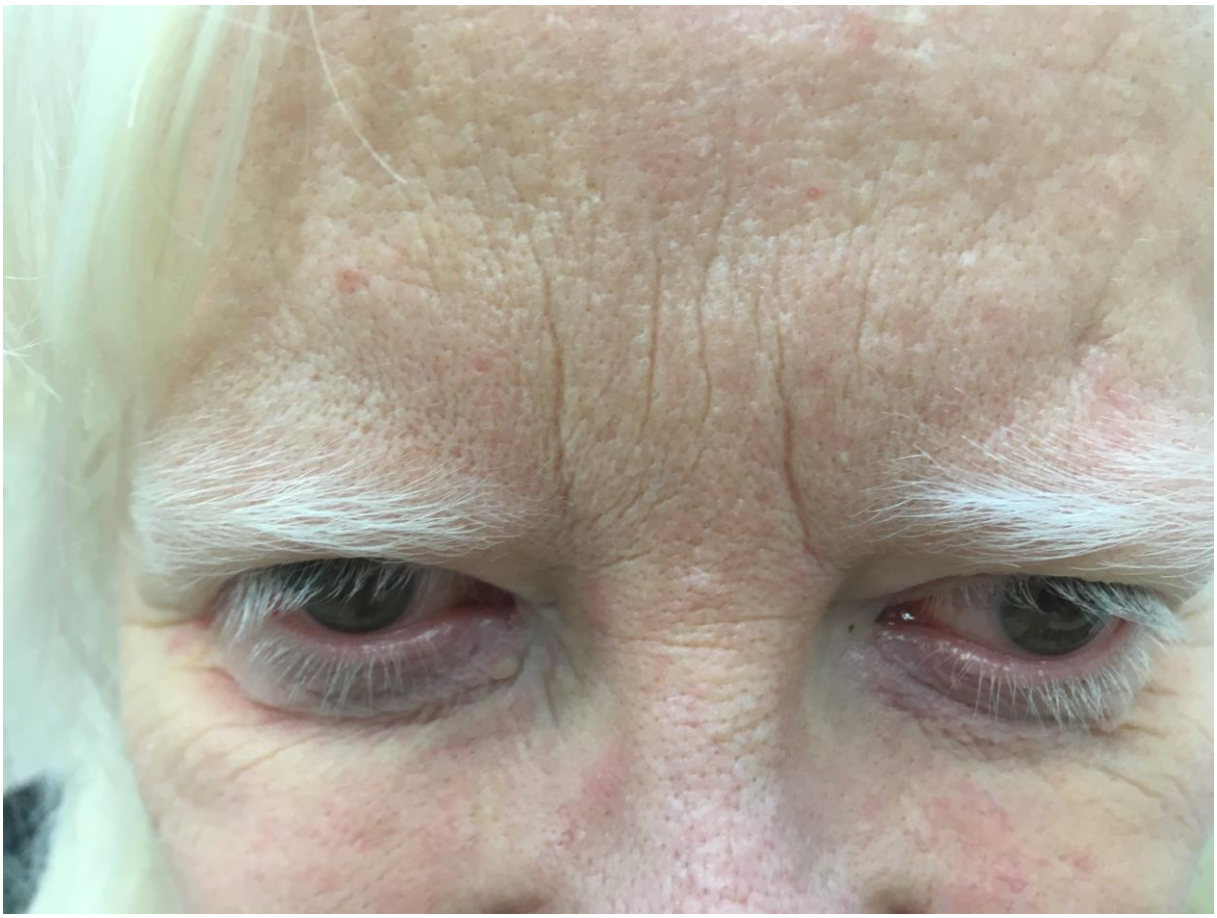
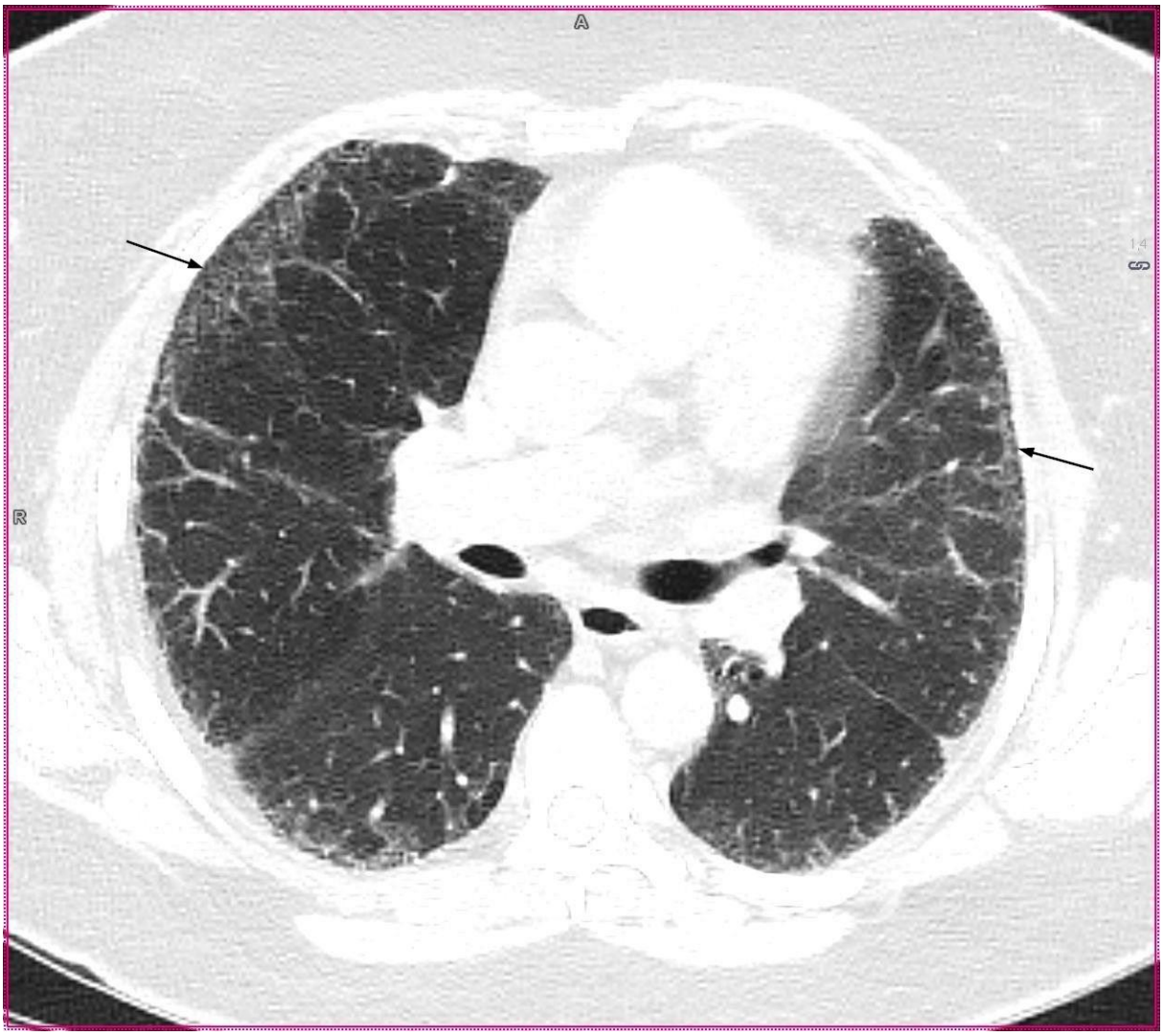


Figure 1A.

Picture of the patient: hypopigmentation of the skin and hair, iris are pigmented (patient consent obtained).

B



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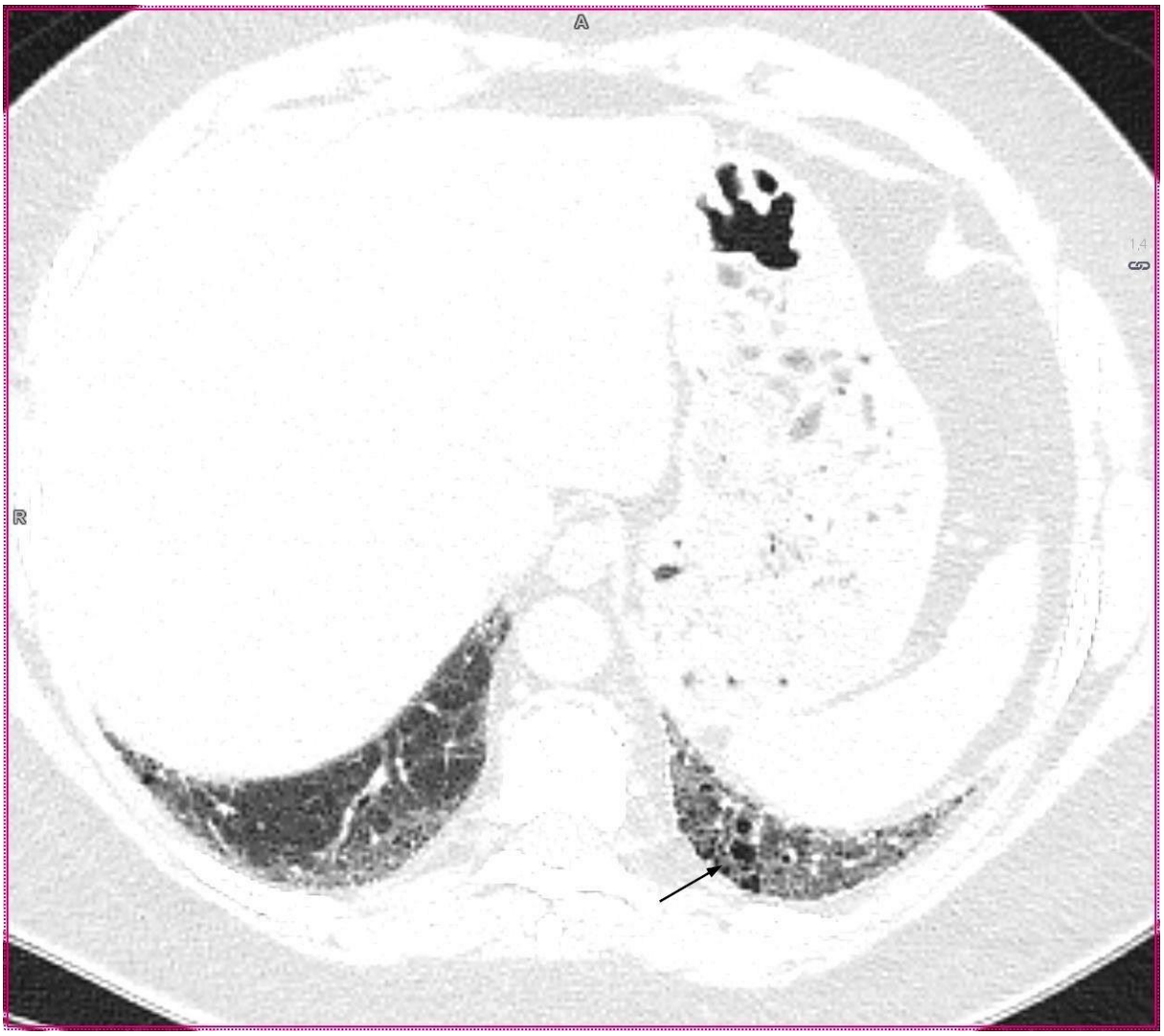

Figure 1 B, C.

Chest computed tomography, axial image. B: subpleural and peripheral reticular pattern (arrows). C: small area of honeycombing (arrow).

D

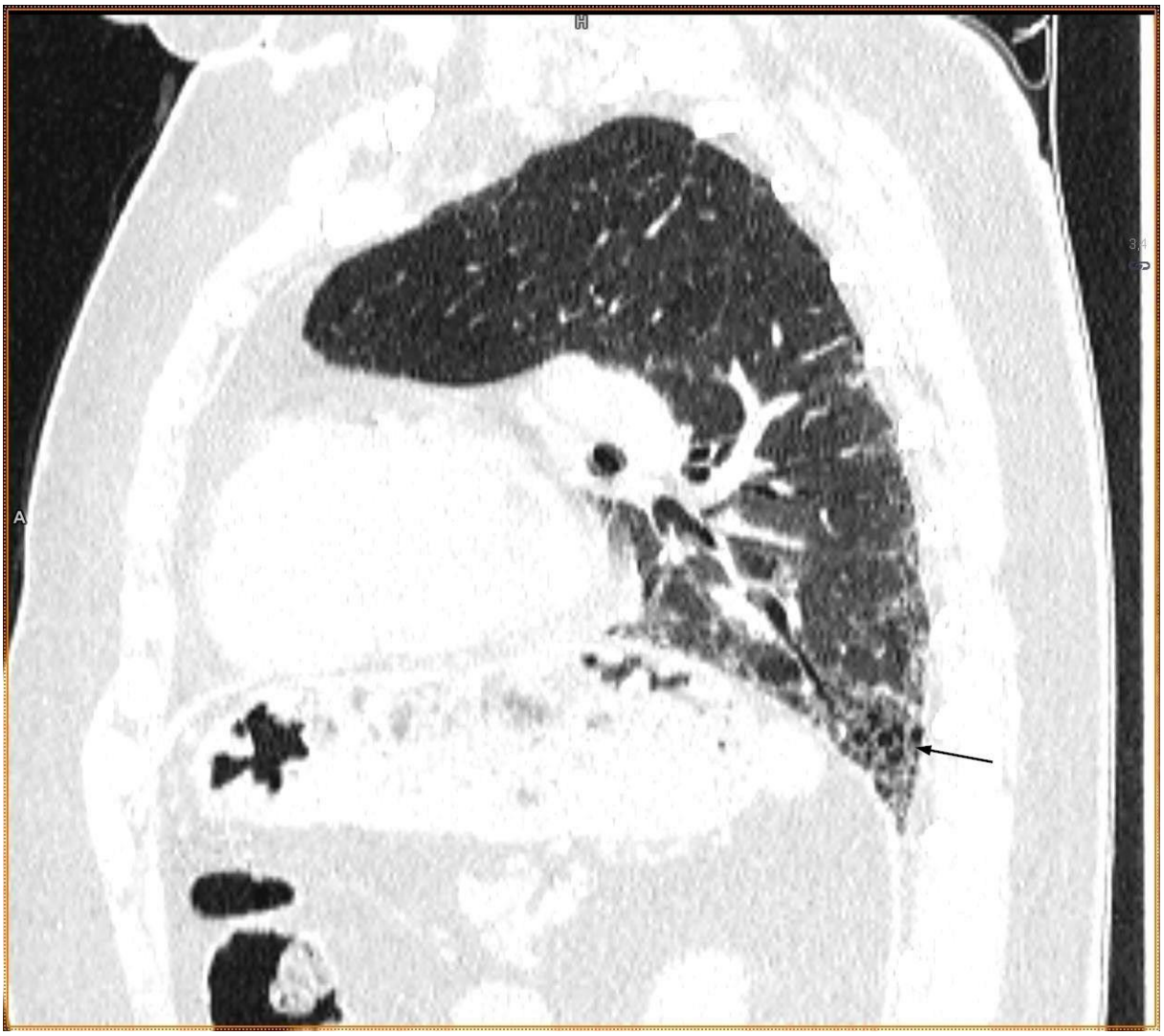

Figure 1 D.

Chest computed tomography, sagittal reconstruction: reduced lung volume. Subpleural reticular pattern and honeycombing (arrow).