

Albinism and lung fibrosis in a young man – the first case of adult Hermansky-Pudlak Syndrome reported in Malaysia

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SUMMARY

A young gentleman of Indian descent with oculocutaneous albinism (OCA) was found to have severe pulmonary fibrosis at first presentation. Following investigations, he was diagnosed with Hermansky-Pudlak Syndrome (HPS). It is a genetic condition characterised by albinism, bleeding diathesis and multisystem disorder observed in individuals of particular descents. Although there is no curative treatment apart from lung transplantation, preventive measures to minimise pulmonary insult may change the natural history of the disease. Therefore HPS should be actively sought, monitored and risk factors addressed in individuals with OCA and bleeding diathesis particularly those of Indian descent as they may develop serious complications such as pulmonary fibrosis in the future.

KEY WORDS:

Albinism, lung fibrosis, Hermansky-Pudlak Syndrome

INTRODUCTION

Pulmonary fibrosis is uncommon in young adults¹ thus warranting further investigations as the management and prognosis vary amongst the different causes. Our case of a young gentleman with oculocutaneous albinism (OCA) diagnosed with severe pulmonary fibrosis exemplifies this issue.

CASE REPORT

A 36-year-old gentleman of Indian descent presented with a month history of progressively worsening dyspnoea on exertion and reduced exercise tolerance. This was associated with a non-productive cough and weight loss of six months duration. Further history revealed occasional epistaxis and gum bleeding. Apart from OCA, there was no other past medical history nor relevant family history. He was a smoker of 12 pack-years but there was no history of illicit drug use. He held an array of jobs, mostly as a trade vendor.

On examination, he had a divergent strabismus and nystagmus with hypopigmented skin and hair owing to the OCA. There was digital clubbing. Auscultation of the chest revealed fine end-inspiratory crepitations bilaterally from the bases up to the midzones. Other examinations were unremarkable.

The baseline blood investigations showed hypoalbuminaemia and type one respiratory failure. Initial sputum analyses for cytology and microbiology were

negative. The chest radiography was abnormal with marked reticulonodular changes bilaterally. Subsequently, a high-resolution computed tomography (HRCT) of the thorax revealed multiple subpleural bullae especially at the apices, extensive honeycombing and traction bronchiectasis indicative of severe lung fibrosis and multiple enlarged hilar and mediastinal lymphadenopathy. See figure 1.

In view of the rarity of severe pulmonary fibrosis in this age group, a literature search was performed which uncovered an uncommon condition of pulmonary fibrosis in individuals with OCA called Hermansky-Pudlak syndrome (HPS). The diagnosis was confirmed by platelet electron microscopy which demonstrated a reduction in platelet dense bodies which is consistent with the diagnosis of HPS. See figure 2.

The course of admission was complicated by episodes of self-limiting epistaxis and hospital-acquired pneumonia with *Klebsiella* and *Enterobacter* requiring courses of antibiotics including cephalosporins and carbapenems. Despite the resolution of infection, the dyspnoea worsened requiring continuous oxygen therapy. Therefore, he was trialed on a course of oral corticosteroids at a dose of 1mg/kg/d. However, there was no symptomatic improvements thus the corticosteroids were tapered down and stopped.

Unfortunately, he developed a right-sided tension pneumothorax, successfully relieved by an emergency intercostal chest tube. He then developed bilateral pneumothoraces requiring further intercostal chest tubes however he deteriorated and passed away soon after.

DISCUSSION

Hermansky-Pudlak syndrome (HPS) is an uncommon autosomal recessive disorder with a prevalence of 1:500000 to 1:1000000 worldwide². In individuals with OCA of Puerto Rican descent, the prevalence is 1:1800 but HPS is now increasingly recognised in individuals of Indian descent³.

The cardinal features of HPS are OCA and bleeding diathesis² with a variety of associated clinical features and severity in the eight different subtypes (HPS-1 to HPS-8). The diagnosis is confirmed by demonstrating the reduction or absence of platelet dense bodies on electron microscopy, prolonged bleeding time despite normal coagulation profile and platelet counts and molecular genetic testing².

HPS is a multisystem disorder, affecting primarily the lungs, kidneys and gastrointestinal tract manifesting as pulmonary

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Fig. 1: Axial HRCT image showing severe fibrosis and subpleural honeycombing bilaterally.

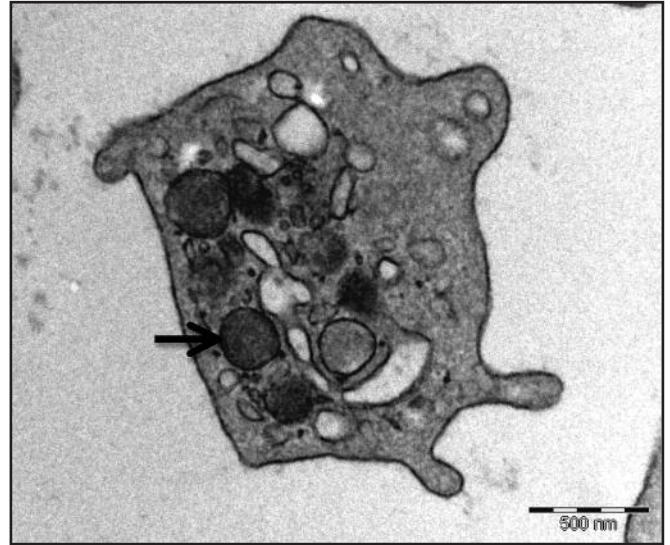


Fig. 2: Transmission electron microscopy of platelets showing a reduction in dense granules. The opaque circular organelles marked with an arrow are alpha granules. Dense bodies appear like a target lesion with a central density.

fibrosis, renal impairment and colitis. Clinical features result from an accumulation of ceroid lipofuscin in lysosomes leading to dysfunction of lysosome-related organelles². As in this patient, affected melanocytes, platelets and alveolar cells result in albinism, bleeding diathesis and pulmonary fibrosis respectively.

Pulmonary fibrosis, described in HPS-1 and HPS-4 subtypes, is the most serious complication accounting for most mortality. It usually presents in the thirties with most succumbing a decade later².

There is no known curative treatment for pulmonary fibrosis in HPS apart from lung transplantation. Corticosteroids have not been shown to be effective. Therefore, prevention of complications is vital. This includes avoidance of cigarette smoking, early treatment of lower respiratory tract infections and immunizations with pneumococcal and influenza vaccines. Currently pirfenidone is under testing².

CONCLUSION

HPS should be actively sought, monitored and risk factors for complications addressed in individuals with OCA and bleeding diathesis particularly those of Indian descent as they may develop serious complications such as pulmonary fibrosis in the future depending on the different subtypes of HPS. Although, there is no curative treatment apart from lung transplantation, preventive measures to minimise pulmonary insult may change the natural history of the disease although evidence for this is currently lacking.

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