

CASE REPORT

Hermanski-Pudlak Syndrome with Cystic Fibrosis: A Case Report

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Introduction

Hermanski-Pudlak Syndrome (HPS) is a rare autosomal recessive disorder characterized by a triad of oculocutaneous albinism, bleeding diathesis and pulmonary fibrosis (PF). It was described by Hermansky and Pudlak in 1959, who reported diffuse PF in one of their patients.¹

HPS is known to affect roughly 1 in 500,000 to 1000,000 individuals worldwide with an increased incidence in those of Puerto-Rican heritage.² The rare incidence in non Puerto Rican regions has limited our experience on the HPS.¹

There are nine different types of Hermansky-Pudlak syndrome, which can be distinguished by their signs and symptoms and underlying genetic cause. Types 1 and 4 are the most severe forms, while types 1,2 and 4 are the only types associated with pulmonary fibrosis.³ However, the ambiguity of the disease along with the molecular heterogeneity of the different sub-variants makes diagnosis and potential management difficult.

Case Report

A 7-year old girl, 1st issue of her consanguineous parents presented with generalized hypopigmentation, whitish yellow hair and bilateral horizontal nystagmus since birth, cough with scanty expectorant since early childhood, gradually increasing breathlessness for last 6 months and fever for 7 days. She had repeated respiratory tract infection since her early infancy and was diagnosed as a case of cystic fibrosis 6 months back which was



Fig 1 Yellowish white hair and digital clubbing

confirmed with two positive sweat chloride tests on separate days. There was a history of sib death who had similar physical features, as generalized hypopigmentation, whitish yellow hair and horizontal nystagmus. The sib died at her 5 month of age due to respiratory tract infection. The patient was easy bruised to any minor trauma and gum bleeding during brushing teeth.

On examination, she had oculocutaneous albinism, yellowish white hair, elongated face, bilateral horizontal nystagmus and digital clubbing. She was

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febrile, tachycardic and tachypnoeic with oxygen saturation was 88% at room air. She had dyspnoea at rest. Breath sound was diminished with crepitations in both lung fields.

Investigation reports showed,

- CBC : Hb%: 9 gm/dl, TLC: 900/mm³
N: 25%, L: 70%, Platelet: 2 lacs/ mm³
- Chest X-ray showed hyperinflation of lungs, nodular densities, patchy opacities and prominent hilar lymphnodes.
- Posterior pharyngeal swab culture showed pseudomonas growth which was resistant to all antibiotics.
- CRP: 270mg/ L
- Blood culture: No growth

She was treated supportively and as per protocol of cystic fibrosis. Unfortunately, the child died due to febrile neutropenia with septic shock.

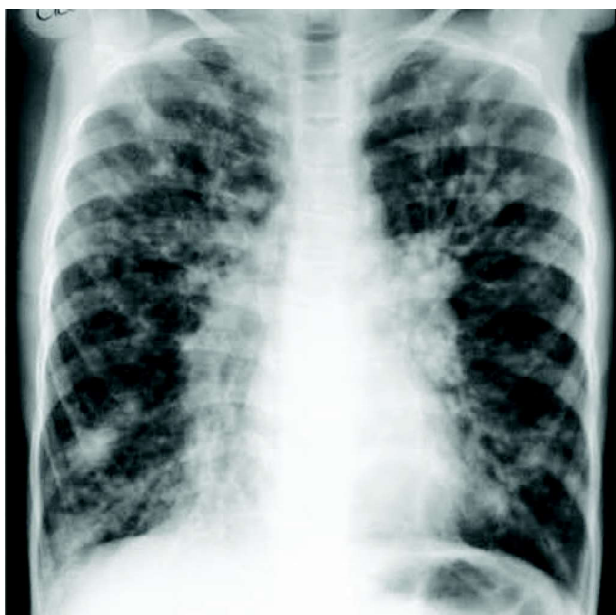


Fig 2 CXR showed hyperinflated lungs with nodular densities and patchy opacities.

Discussion

Hermansky-Pudlak syndrome (HPS) is a multi-system disorder characterized by oculocutaneous albinism and platelet storage deficiency, which can also lead to prolonged bleeding, pulmonary fibrosis, and granulomatous colitis.²

The HPS genes are involved in the formation and trafficking of lysosome-related organelles (LROs), which have been identified in melanocytes, platelets and alveolar type II epithelial cells.² These lysosome related organelles required for breakdown of liposomes and results accumulation of ceroid lipofuscin that leads to PF and colitis.¹

The diagnosis is typically made by the presence of skin and hair hypo-pigmentation, characteristic ocular abnormalities, and the absence of dense bodies in platelets on microscopic evaluation.⁴ Dense granules contain factors such as serotonin, calcium, and adenine nucleotides, which are necessary for platelet aggregation, and play a significant role in hemostasis.²

Patients with type 1 Hermansky-Pudlak syndrome due to a mutation in the HPS1 gene are more likely to develop pulmonary fibrosis and typically have lung disease of a greater severity than patient without this mutation. The prognosis is poor, and patients usually die from pulmonary fibrosis in the fourth to fifth decades of life.⁴

Previous chest radiographs and spirometry will be helpful in assessment of pulmonary status. High resolution computerized tomography of lung reveals abnormalities in 82% of patients. Reticular opacities involving the entire lung with lower zone predominance, subpleural honey combing, and traction bronchiectasis is typical of the PF.¹

Patients are typically treated with oxygen in an attempt to alleviate dyspnoea. An antibiotic, pirfenidone, may slow the progression of pulmonary fibrosis but is effective only in patients with significant residual lung function. The only definitive treatment for pulmonary fibrosis related to Hermansky-Pudlak syndrome is lung transplantation.⁴

Conclusion

This is a case of Hermansky-Pudlak syndrome presented as a case of cystic fibrosis in a 7 year old girl. Presentation of pulmonary fibrosis was early in this case. However, establishing definitive diagnosis of HPS by genetic testing could not be done due to unavailability of the test. Although managing with the multidisciplinary care, we fail to save the patient due to associated sepsis.

References

1. Vani R, Keertivasan S, Anbananthan K. Hermansky-Pudlak syndrome: A case report. *The Journal of Association of Chest Physicians* 2014;**2**:78-80.
2. Alcid J, Kim J, Bruni D, Lawrence I. A Rare Case of Hermansky-Pudlak Syndrome Type 3. *J Hematol* 2018;**7**:76-78.
3. Gahl WA, Huizing M. Hermansky-Pudlak Syndrome. *Gene Reviews* 2014;**53**:2629-34.
4. Carter BW. Hermansky-Pudlak syndrome complicated by pulmonary fibrosis. *Bayl Univ Med Cent* 2012;**25**:76-77.
5. Bagheri A, Abdollahi A. Hermansky-Pudlak Syndrome; a Case Report. *J Ophthalmic Vis Res* 2010;**5**:269-72.
6. Hengst M, Mahavadi P, Naehrlich L. Early pulmonary phenotype in Hermansky-Pudlak syndrome: Analysis of the child-EU registry. *European Respiratory Journal* 2016.
7. Yusuf L, Dukka S, Ciantar E. Hermansky-Pudlak syndrome in pregnancy: A case report. *Obstetric Medicine* 2016;**9**:171-73.