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CASE REPORT

Fatal Pulmonary Fibrosis due to Hermanski-Pudlak Syndrome: A Rare Case Report with Open Lung Biopsy Findings

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ABSTRACT

Introduction: Hermanski-Pudlak Syndrome is an extremely rare autosomal recessive disorder. Albinism, bleeding diathesis and other associated complications are the main manifestations of Hermanski-Pudlak Syndrome. **Case Presentation:** Here we report a 56-year-old woman who was referred with gradually increasing dyspnea. She had a past history of coughing, epistaxis, gums bleeding, easy bruising and severe sunburn in normal sun exposure. Her blood oxygen saturation was 87% in room air. Physical examination revealed oculocutaneous albinism, strabismus, horizontal nystagmus and fine inspiratory crackle. There was a reticulonodular pattern in chest radiography. Open lung biopsy confirmed the diagnosis of pulmonary fibrosis. Although the patient had been treated with Pirfenidone, she died because of respiratory failure.
Conclusion: Although Hermanski-Pudlak Syndrome is a rare syndrome, finding more about the pathophysiology of Hermanski-Pudlak Syndrome and also developing new methods of treatment is indisputable.

INTRODUCTION

Hermanski-Pudlak Syndrome (HPS) is a rare fatal genetic disorder that occurs in 1-2 per 1000000 person (1). Although HPS has been reported from different countries, about half of all cases were reported from Puerto Rico (2). However, updated epidemiological information is not available (3).

HPS is known to be an inherited autosomal recessive disorder which is divided into 10 subtypes based on genetic mutations which are HPS1, Adaptor Related Protein Complex 3 (AP3) Subunit Beta 1, AP3 Subunit Delta 1, HPS3, HPS4, HPS5, HPS6, Dystrobrevin Binding Protein 1 (DTNBP1), Biogenesis of Lysosomal Organelles Complex 1 Subunit 6 (BLOC1S3), and BLOC1S6. These mutations result in altered biogenesis of lysosomes and lysosome-related organelles and also intracellular protein trafficking defects that finally cause specific signs and symptoms in each type. However, the precise mechanism which leads to manifestations of HPS is not clear (1, 2). The common manifestations of HPS are oculocutaneous albinism and bleeding diathesis due to platelet storage defect. Serious associated complications are caused by accumulation of ceroid lipofuscin in different organs such as colon (granulomatous colitis) and lungs (life-threatening fibrotic restrictive lung disease). Other probable associated complications are renal failure and cardiomyopathy (3, 4). Here we report a case of HPS patient from Rasht (a city in north of Iran). To our best knowledge, this is the first reported case from north of our country.

CASE PRESENTATION

A 56-year-old female was admitted to our hospital complaining of gradually increasing dyspnea during the last 18 months which had been worsen since the last three weeks following an upper respiratory infection. The patient also had a history of coughing induced epistaxis, gums bleeding, easy bruising and also severe sunburn after normal sun exposure. The patient was otherwise asymptomatic. She was not taking any medications. She denied any occupational exposure to hazardous agents or smoking. Her parents were relatives. None of other family members were affected. Vital signs were within normal range but pulse oximetry showed that blood oxygen saturation was 87% in room air. On physical examination, the patient had white skin, hair, scalp, eyelashes and eyebrows together with gray eyes which indicate oculocutaneous albinism. She also had numerous ecchymoses on the skin of her body. Further examination revealed strabismus and horizontal nystagmus

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in her eyes. Examination of the respiratory system revealed fine bibasilar inspiratory crackles. Digital clubbing on extremities were also noticed. Laboratory tests didn't revealed a significant abnormality in complete blood count (CBC) and serum biochemistry. Partial thromboplastin time (PTT) was prolonged. However, Prothrombin time (PT) and international normalized ratio (INR) were within normal range. Partial pressure of CO2 (PCO2) was 47 mmHg in arterial blood gas (ABG) analysis. PH and HCO3 were 7.33 and 27 respectively in ABG. In chest radiography (Figure 1), there was a diffuse reticular pattern with no evidence of any other abnormality. Spirometry showed a restrictive pattern (forced vital capacity: 47% predicted). Diagnosis of Pulmonary Fibrosis (PF) was confirmed by open lung biopsy of left lower lobe (Figure 2). As it is shown, architectural derangement of lung tissue, remodeling and moderate anthracnosis was observed. In addition, alveolar septal widening along with collagen deposition and some degree of disseminated interstitial fibrosis were seen in the lung tissue. There were remarkable infiltration of chronic inflammatory cells as well as cystic space formation and hemorrhage.

Despite using supplemental oxygen by nasal cannula, the oxygen saturation did not reach the normal level. So, the oxygen was given by a face mask. She was advised to avoid cigarette smoke and other dangerous respirable agents. We also asked the patient to protect her eyes and skin against sun light exposure. Influenza and pneumococcal vaccinations were done. The patient was under treatment of Pirfenidone (200mg, orally, three times a day). However, the patient died five days after admission due to refractory respiratory failure.

CONCLUSION

The presented case of HPS syndrome revealed that there is a lack of precise information about different aspects of this syndrome such as the epidemiology and pathophysiology. In addition, new methods of treatment and management of HPS with especial emphasis on PF are necessary to provide a better quality of life and reduce the mortality and morbidity rate.

DISCUSSION

Hermanski-Pudlak syndrome is characterized by the triad of hypopigmentation (4), bleeding diathesis and other systemic complications resulted from ceroid deposition in lungs and other organs (5). HPS can be clinically suspected by appearance and physical examination of patients and is confirmed by molecular genetic analysis (4). In our case, the patient had the above mentioned triad. In addition, PF was confirmed by lung open biopsy. However, no genetic analysis was done since the related laboratory test is not available in our region.

Ceroid deposition in lungs of these patients often leads to PF (type1, 2 and 4 of HSP) (6, 7). PF is an important fibrotic restrictive lung disease which can lead to high mortality and morbidity in patients with HPS. Death caused by PF often occurs between 40 and 50 years of age (4, 6). PF can initially present with symptoms such as dyspnea, but finally it will develop hypoxia at rest and even death as it happened to our patient (4). Although the exact mechanism of PF in HPS is still in dark, it is believed that accumulation of ceroid lipofuscins and also peptides that modulate mesenchymal cells function lead to dysfunction of type II alveolar cells which finally result in tissue remodeling and fibrosis (6, 8). The radiological manifestations of PF is interstitial patterns and infiltration in both lungs as it was seen in our case.

The best option for treatment of patients with advanced PF , as a potentially fatal condition, is lung transplantation (9). The other choice is Pirfenidone which is a small molecule capable of inhibiting Transforming growth factor beta (TGF-β) molecules with anti-inflammatory and anti-fibrotic activities. This drug is not curative but it affects lung fibrosis without impairing the fibroblasts (9). Animal and human studies have demonstrated that administration of oral Pirfenidone can reduce the fibrosis (8). On the other hand, a clinical trial performed by Gahl et al to investigate the efficacy of Pirfenidone revealed that there is no significant difference between the Pirfenidone (800mg, TID) and placebo groups (10). Other important parts of recommended treatment are infection prophylaxis by vaccinations (such as influenza and pneumococcal), supplemental oxygen, chest physiotherapy, nutritional supports and also treatment of related psychiatric disorders (6). Although our patient was on progress in treatment with Pirfenidone, she died at the fifth day of hospitalization because of refractory respiratory failure due to PF.

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AUTHOR CONTRIBUTIONS

All authors contribute in present study.

CONFLICT OF INTEREST

None declared.

ETHICAL STANDARDS

Written informed consent was obtained from the patient's husband.

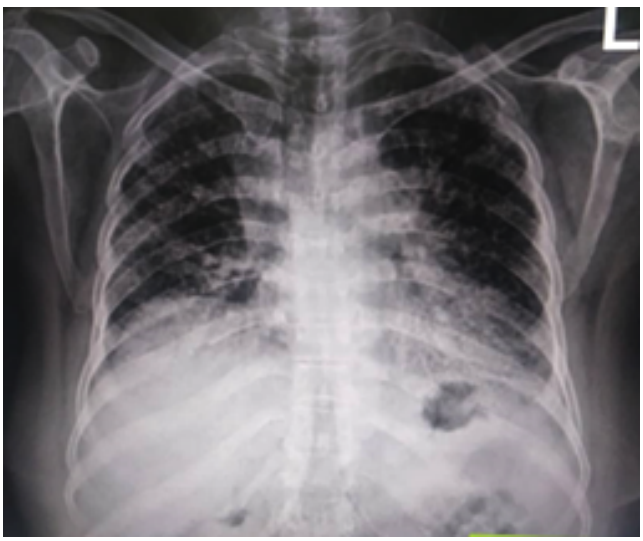

Figure 1. Chest X-ray radiography showing bilateral reticular infiltration with middle and lower zones predominance.

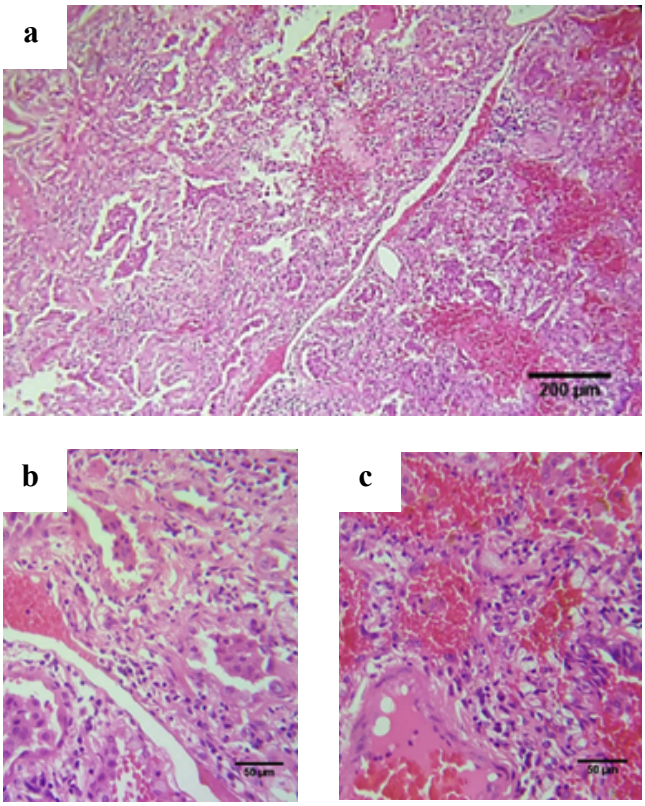

Figure 2. Microscopic examination of lung sections after open biopsy of left lower lobe revealed tissue remodeling, fibrosis, prominent mononuclear inflammatory cells infiltration, and focal hemorrhage, (H&E staining, (a)×100, (b) and (c) ×400).

REFERENCES

1. Stearman RS, Cornelius AR, Young LR, Conklin DS, Mickler EA, Lu X, et al. Familial Pulmonary Fibrosis and Hermansky-Pudlak Syndrome Rare Missense Mutations In Context. Am J Respir Crit Care Med. 2019;200(2).
2. Vicary GW, Vergne Y, Santiago-Cornier A, Young LR, Roman J. Pulmonary fibrosis in Hermansky–Pudlak syndrome. Ann Am Thorac Soc. 2016;13(10):1839-46.
3. Bastida JM, Morais S, Palma-Barqueros V, Benito R, Bermejo N, Karkucak M, et al. Identification of novel variants in ten patients with Hermansky-Pudlak syndrome by high-throughput sequencing. Ann Med. 2019:1-8.
4. Loredana Asztalos M, Schafernak KT, Gray J, Berry A, Paller AS, Mancini AJ. Hermansky-Pudlak syndrome: Report of two patients with updated genetic classification and management recommendations. Pediatr Dermatol. 2017;34(6):638-46.
5. Girot P, Le Berre C, De Maissin A, Freyssinet M, Trang-Poisson C, Bourreille A. Crohn's-like acute severe colitis associated with Hermansky-Pudlak syndrome: A case report. World J Gastroenterol. 2019;25(8):1031.
6. Gupta A, Utpat K, Desai U, Joshi JM. Hermansky–Pudlak syndrome with interstitial lung disease: A holistically worked up couplet. Lung India: Official Organ of Indian Chest Society. 2019;36(4):345.
7. Seward SL, Gahl WA. Hermansky-Pudlak syndrome: health care throughout life. Pediatrics. 2013;132(1):153-60.
8. O'Brien K, Troendle J, Gochuico BR, Markello TC, Salas J, Cardona H, et al. Pirfenidone for the treatment of Hermansky–Pudlak syndrome pulmonary fibrosis. Mol Genet Metab. 2011;103(2):128-34.
9. ÇİLEDAĞ A, KOÇER BC, KÖKTÜRK N, KAYA A, ÇELİK G, NUMANOĞLU N. A rare cause of interstitial lung disease: Hermansky-Pudlak syndrome. Tuberkuloz ve Toraks (Tuberc Thorax). 2011;59(1):85-8.
10. Gahl WA, Brantly M, Troendle J, Avila NA, Padua A, Montalvo C, et al. Effect of pirfenidone on the pulmonary fibrosis of Hermansky–Pudlak syndrome. Mol Genet Metab. 2002;76(3):234-42.