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Hermansky-Pudlak Syndrome Type 2 Presenting With Severe Pulmonary Arterial Hypertension in an Infant: A Case Report

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Abstract

Background: Hermansky-Pudlak Syndrome (HPS) Type 2 is a rare autosomal recessive disorder characterized by oculocutaneous albinism, bleeding diathesis due to platelet storage pool deficiency, and immuno deficiencyis an uncommon autosomal recessive condition marked by bleeding diathesis brought on by the platelet storage pool and oculocutaneous albinism. Pulmonary arterial hypertension (PAH) and multisystem involvement in infancy are uncommon but critical manifestations that contribute to high morbidity and mortality.

Case Presentation: We report a 10-month-old male baby that is exhibiting severe respiratory distress, failure to thrive, and oculocutaneous albinism. Echocardiography revealed acyanotic congenital heart disease with restrictive perimembranous ventricular septal defect (7 mm), mild pulmonary arterial hypertension (PASP 40 mmHg), moderate tricuspid regurgitation, and 10 mm ostium secundum atrial septal defect. Peripheral blood smear showed large platelets amidst thrombocytosis (712,000/mm³). Positive family history included similarly affected male siblings with hypopigmentation and photophobia. Genetic testing confirmed Hermansky-Pudlak Syndrome Type 2. Management included intravenous furosemide, azithromycin, oseltamivir, oxygen therapy, and multidisciplinary supportive care.

Conclusions: HPS Type 2 can present in infancy with life-threatening PAH and cardiac manifestations in addition to classical features. Early diagnosis and multidisciplinary management are essential. Awareness of the syndrome's multisystem involvement and family screening for genetic counseling are recommended.

Keywords: Albinism, Bleeding Diathesis, Hermansky-Pudlak Syndrome, Pulmonary Hypertension, Ventricular Septal Defect

Introduction

Hermansky-Pudlak Syndrome (HPS) is a rare autosomal recessive multisystem disorder characterized chiefly by oculocutaneous albinism, bleeding diathesis due to platelet storage pool deficiencies, and, in select subtypes, significant systemic complications such as pulmonary fibrosis, immune dysfunction, and granulomatous colitis. There are at least 11 recognized genetic subtypes, each linked to specific gene mutations, with Type 2 (HPS-2) notable for its association with immune deficiencies and a heightened risk of pulmonary complications.[1]

Pulmonary involvement—including pulmonary arterial hypertension (PAH) and interstitial lung disease—is increasingly recognized as a major cause of morbidity and mortality in HPS, particularly in types 1, 2, and 4.[2]

Pediatric cases presenting with severe PAH are exceedingly rare and underscore the requirement for increased clinical monitoring and early multidisciplinary intervention.[3]

This case report describes a 10-month-old male infant diagnosed with Hermansky-Pudlak Syndrome Type 2, presenting acutely with life-threatening pulmonary arterial hypertension and congestive heart failure. The case highlights the diagnostic challenges and clinical management in the context of this multisystem disorder, referencing recent reviews and case series to frame its clinical significance.[4,5,6,7,8]

Case Presentation

A 10-month-old male infant was admitted with a 3-day history of acute respiratory distress characterized by rapid breathing, poor feeding, and generalized weakness. He was born at 38 weeks of gestation with a birth weight of 2.8 kg (5th percentile), appropriate for gestational age. The neonatal period was complicated by respiratory distress requiring a 5-day stay in the neonatal intensive care unit including oxygen supplementation for two days. At birth, generalized hypopigmentation suggestive of oculocutaneous albinism, cutaneous mottling, and congenital heart disease were noted.

On current admission, generalized hypopigmentation of the skin and hair with red irises was observed, consistent with oculocutaneous albinism (Figure 1&2), his weight and length were 6.0 kg (<3rd percentile) and 68 cm (10th percentile), respectively, indicating failure to thrive. Vital signs showed tachycardia (heart rate 130 beats/min), tachypnea (respiratory rate 66 breaths/min), and a low-grade fever (38.2°C). Cardiovascular examination revealed a grade 2/6 systolic murmur best heard without a gallop, at the left sternal boundary. Respiratory examination demonstrated subcostal retractions and bilateral fine crackles. Dermatological assessment confirmed generalized hypopigmentation of the skin and hair with red irises, consistent with oculocutaneous albinism.

Peripheral blood smear showed the presence of large platelets despite thrombocytosis (platelet count: 712,000/mm³). Abdominal ultrasonography identified a right-sided hydrocele. Transthoracic echocardiography revealed acyanotic congenital heart disease with a restrictive perimembranous subaortic ventricular septal defect measuring 7 mm, mild pulmonary arterial hypertension with a pulmonary artery systolic pressure (PASP) of 40 mmHg, moderate tricuspid regurgitation, and a 10 mm ostium secundum atrial septal defect.

The patient's family history was important because similar hypopigmented skin and hair complexion in three maternal male siblings, one of whom reportedly had photophobia, suggesting an inherited disorder consistent with Hermansky-Pudlak Syndrome (HPS).

Based on the clinical presentation, laboratory findings, and family history, a provisional diagnosis of HPS Type 2 was considered. Genetic testing subsequently confirmed mutations consistent with HPS2, a subtype associated with immunodeficiency and pulmonary complications. Given the serious pulmonary arterial hypertension and the multisystem involvement, a multidisciplinary team including pediatric cardiology, pulmonology, hematology, immunology, ophthalmology, and medical genetics was engaged for comprehensive management.

Treatment initiated included intravenous furosemide (1.5 mg/kg twice daily) to address congestive heart failure symptoms, oral azithromycin syrup for presumed respiratory infection, and oseltamivir syrup for antiviral prophylaxis/treatment pending viral studies. Supportive care encompassed oxygen therapy and vigilant monitoring for bleeding tendencies and infections.

Parents' legal guardians gave their written informed approval for this case report and any related photos to be published.

Discussion

Hermansky-Pudlak Syndrome (HPS) Type 2 is an infrequent autosomal recessive disorder characterized by the classical triad of oculocutaneous albinism, bleeding diathesis secondary to platelet dense granule deficiency, and neutropenia resulting in immune dysfunction and recurrent infections.[1,2,3,4] This case exemplifies the early and severe manifestation of pulmonary arterial hypertension (PAH) and congestive heart failure in infancy, highlighting the multisystem involvement and complexity of HPS2 clinical presentation.

Unlike HPS subtypes 1 and 4, which typically present with pulmonary fibrosis later in adulthood, HPS2 frequently features early-onset fibrosing lung disease and rapid progression of pulmonary complications, often beginning in childhood.[3,4,5,6,7] The presence of severe PAH in our patient, coupled with congenital heart defects including a restrictive perimembranous VSD and an ostium secundum ASD, exacerbated cardiac overload and contributed to clinical deterioration. These cardiopulmonary abnormalities underscore the importance of prompt echocardiographic assessment and multidisciplinary evaluation in patients with HPS2.

Neutropenia, a hallmark of HPS2, predisposes patients to recurrent infections that accelerate pulmonary damage and worsen clinical outcomes.[3,4,5] While granulocyte colony-stimulating factor (G-CSF) therapy was not administered in this patient, it has been reported to improve neutrophil counts and reduce infections in other cases. Vigilant infection control and immunization remain integral to management. The prescription of azithromycin and oseltamivir in this case was appropriate given the acute respiratory distress and potential infectious triggers.

Bleeding diathesis in HPS results from deficiency of platelet dense bodies despite normal or elevated platelet counts, as evidenced by the large platelet morphology and thrombocytosis in our patient.[1,4] This paradox necessitates careful bleeding risk assessment and management, especially during invasive procedures.

Congenital heart defects, although not a classical component of HPS, have been reported in association with the syndrome and may represent a broader spectrum of developmental anomalies or coincidental findings. Their presence further complicates management and underscores the necessity of comprehensive cardiac assessment in these patients.

Currently, no definitive curative therapy exists for HPS2; treatment is primarily supportive, focusing on management of heart failure, prevention of infections, and bleeding control.[1,2] Emerging evidence suggests

benefit from pulmonary vasodilator agents such as macitentan for managing PAH in HPS patients, warranting consideration and further investigation.[8] Our case reinforces the importance of early diagnosis, genetic confirmation, and a multidisciplinary approach involving pediatric cardiology, pulmonology, hematology, immunology, ophthalmology, and medical genetics to optimize patient outcomes.[1,2,4]

The positive family history of similar hypopigmentation and photophobia among maternal male siblings supports the autosomal recessive inheritance pattern of HPS and highlights the importance of genetic counseling for affected families.[1]

In summary, this case contributes to the limited pediatric literature on HPS Type 2 by demonstrating the severe and early cardiopulmonary compromise possible in infancy. It emphasizes early recognition of clinical features, comprehensive evaluation, and coordinated multidisciplinary care as essential components of management to improve prognosis in this rare but life-threatening condition.

Conclusion

Hermansky-Pudlak Syndrome Type 2 is an uncommon but dangerous severe pulmonary multisystem condition that can manifest in infants with heart problems and arterial hypertension, in addition to the classical features of oculocutaneous albinism and bleeding diathesis. Early clinical suspicion, supported by family history and genetic testing, is crucial for timely diagnosis. Pulmonary and immunologic complications necessitate a multidisciplinary approach involving cardiology, pulmonology, hematology, immunology, and genetics for optimal management. Supportive therapies, vigilant infection control, and emerging targeted treatments for pulmonary hypertension offer the potential to improve outcomes in affected infants. Genetic counseling is vital given the autosomal recessive inheritance pattern and familial clustering evident in this case.

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Legend Figures

Figure 1:

Figure 2: