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## CASE REPORT

# Idiopathic Pulmonary Hemosiderosis Characterized by Recurrent Infections and Anemia

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**SUMMARY**

***Background:*** **Idiopathic pulmonary hemosiderosis (IPH) is a rare condition characterized by recurrent alveolar bleeding, hemosiderin deposition, and pulmonary fibrosis, predominantly affecting children. Its diagnosis and management are complex.**
***Methods:*** **A case involving a 3-year-old female patient with iron deficiency anemia and recurrent pneumonia was analyzed supported by laboratory and imaging investigations. Clinical symptoms included nausea, fever, and pallor.**
***Results:*** **Initial evaluations indicated moderate anemia (HGB 73 g/L) and signs of infection, with imaging revealing diffuse ground-glass opacities. Following the exclusion of other conditions, a diagnosis of IPH was established, and comprehensive treatment resulted in notable clinical improvement.**
***Conclusions:*** **This case underscores the importance of multidisciplinary collaboration in diagnosing and managing IPH, particularly in pediatric patients, to enhance outcomes and quality of life.**
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**KEYWORDS**

idiopathic pulmonary hemosiderosis, iron deficiency anemia, infection

## INTRODUCTION

Idiopathic pulmonary hemosiderosis (IPH) is a rare and complex disorder characterized by recurrent episodes of alveolar bleeding, leading to the abnormal deposition of hemosiderin in lung tissue and subsequent pulmonary fibrosis [1]. It primarily affects children, and its etiology remains largely unclear, complicating both diagnosis and treatment.

This report presents a case of a 3-year-old female patient with IPH, highlighting the clinical manifestations, diagnostic challenges, and treatment strategies employed. Through this case, we aim to enhance understanding of IPH and reinforce the importance of a multidisciplinary approach in managing pediatric patients with recurrent anemia and pulmonary complications.

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## CASE PRESENTATION

**General information**

The patient is a 3-year and 4-month-old female, admitted on December 19, 2024, with complaints of nausea for three days and fever accompanied by pallor and poor appetite for one day. The family reported that the patient had been experiencing nausea without vomiting or diarrhea. On December 19, she presented with a fever peaking at 39°C, along with pallor, fatigue, and poor appetite. Blood tests from an external facility indicated hemoglobin (HGB) of 86 g/L (↓) and platelet count (PLT) of 503 x $10^9$/L (↑). That evening, she appeared lethargic, with increased heart rate and respiratory rate, prompting her transfer to our emergency department for "moderate anemia and respiratory infection".

The patient was alert but appeared anemic, with pale skin and mucous membranes, reddened throat, mildly enlarged tonsils, and rough breath sounds in both lungs, with no wheezing noted. Since the onset of symptoms, the patient had been lethargic, with poor appetite and sleep. No significant abnormalities were noted in her bowel or bladder habits. After admission, she experienced one episode of fever (temperature 38.5°C), which returned to normal after administering antipyretics. She continued to exhibit poor appetite and fatigue, with no signs of tea-colored urine, blood in stool, gum bleeding, or nasal bleeding, although her overall condition remained suboptimal.

**Relevant medical history**

In July 2024, the patient was treated for anemia. Laboratory results showed negative direct antiglobulin tests and indicated iron deficiency: serum iron at 3.24 μmol/L (↓), transferrin saturation at 5.48% (↓), and normal levels of serum folate and vitamin B12. Tests for thalassemia and G-6-PD deficiency performed on July 13, 2024, were negative. Following iron supplementation, the patient's hemoglobin showed an upward trend without evidence of hemolysis, leading to a diagnosis of iron deficiency anemia. After discharge, she continued oral iron therapy, resulting in improved hemoglobin levels.

In October 2024, she was readmitted for pneumonia, after which her hemoglobin levels decreased again. Combined treatment with anti-infectives and iron supplementation restored HGB to 122 g/L by November 24.

**Laboratory tests and imaging studies**

December 19.

**Complete blood count**

White Blood Cell Count (WBC): 15.28 x $10^9$/L (↑), Neutrophil Percentage (NEUT%): 83.1% (↑), Lymphocyte Percentage (LYMPH%): 12.5% (↓), Red Blood Cell Count (RBC): 3.1 x $10^{12}$/L (↓), HGB: 73 g/L (↓), PLT: 242 x $10^9$/L, Absolute Reticulocyte Count (RET#): 324.6 x $10^9$/L (↑), Reticulocyte Percentage (RET%): 10.54% (↑).

**Inflammatory markers**

High-Sensitivity C-Reactive Protein (hs-CRP): 49.48 mg/L (↑), Interleukin-6 (IL-6): 26.38 pg/mL (↑), Procalcitonin (PCT): 2.920 ng/mL (↑).

Red Blood Cell Morphology (Figure 1): Mature red blood cells displayed significant size variation, with some showing enlarged central pallor areas and notable polychromatic erythrocytes.

**Bone marrow smear**

Active hyperplasia noted; elevated erythroid ratio with nuclear abnormalities and mitotic figures observed. Some cells exhibited scant cytoplasm and irregular edges, with prominent eosinophils and occasional atypical lymphocytes.

**Iron metabolism indicators**

Serum Iron (FE): 2.99 μmol/L (↓), Total Iron Binding Capacity (TIBC): 37.3 μmol/L (↓), Unsaturated Iron Binding Capacity (UIBC): 34.3 μmol/L, Transferrin Saturation (TS): 8.02% (↓), Transferrin (TRSF): 1.96 g/L (↓), Ferritin: 296.20 ng/mL (↑).

**Liver and kidney function, myocardial enzymes, electrolytes, blood sugar, serum folate, and vitamin B12**

All within normal limits.

December 23.

**Chest CT scan with 3D reconstruction (Figure 2A)**

The scan revealed diffuse ground-glass opacities in both lungs, suggesting possible diffuse alveolar hemorrhage. Consideration of idiopathic pulmonary hemosiderosis (IPH) is recommended, along with further clinical correlation. Cardiac chamber density was reduced, indicating anemia.

**Cytological examination**

Sputum analysis showed no hemosiderin.

December 26.

**Allergen inhalation panel**

Dust mites: Level 6.

Food-specific IgG antibodies: Cheese: Level 3, Cow's Milk: Level 3, Goat's Milk: Level 3.

**Autoantibody tests**

Antiphospholipid antibodies (APLA), anti-glomerular basement membrane antibodies (GBM), and anti-neutrophil cytoplasmic antibodies (ANCA) were all negative. Immunoglobulin levels and rheumatological panel results were normal.

**Diagnosis and differential diagnosis**

**Iron deficiency anemia**

The patient received treatment for anemia in July 2024, with iron metabolism tests suggesting iron deficiency anemia. After treatment with oral iron supplements, hemoglobin levels increased. In October, the patient was

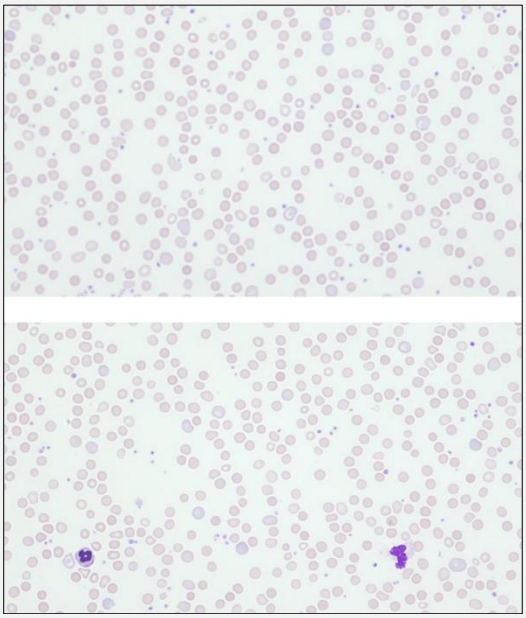

**Figure 1. Two fields of view showing the typical red blood cell morphology of the patient under the microscope.**

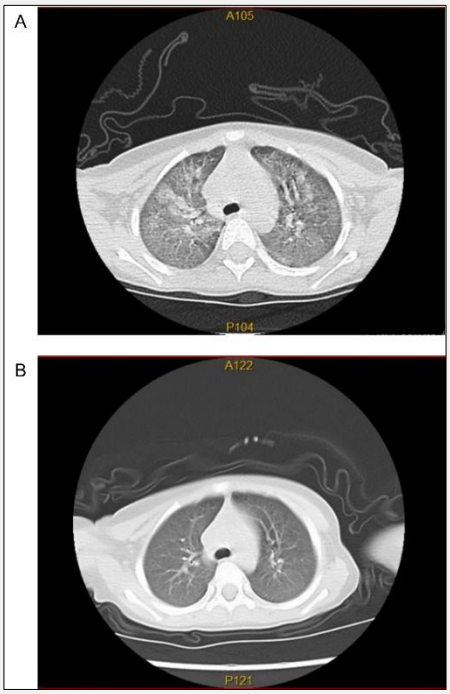


**Figure 2. A Chest CT scan image from December 23 (pre-treatment). B Chest CT scan image from december 29 (post-treatment).**

hospitalized for pneumonia, and following infection, hemoglobin levels dropped again. After anti-infective and iron therapy, HGB was then increased. Current tests indicate decreased serum iron and transferrin saturation, but a decrease in TIBC with normal UIBC does not fully support the diagnosis of iron deficiency anemia.

**Thalassemia**
The patient's mother is from Guangdong and the father from Fujian, both without anemia symptoms. The patient responded well to iron treatment in the past. Recent tests for thalassemia genes showed no abnormalities.

**Glucose-6-phosphate dehydrogenase deficiency**
The patient experienced a rapid drop in hemoglobin but showed no symptoms such as tea-colored urine, jaundice, or splenomegaly. Testing in July 2024 did not detect G6PD gene mutations.

**Aplastic anemia**
While the patient has moderate anemia, multiple tests of granulocyte and megakaryocyte lines were normal, and reticulocyte counts were significantly elevated, which does not support this diagnosis.

**Other hemolytic diseases**
There is no clear evidence of hemolysis, but acute hemolysis following infection due to other genetic mutations cannot be ruled out. Further genetic screening may be necessary.

**Idiopathic pulmonary hemosiderosis**
The patient is a young female with an acute onset and multiple hospitalizations, presenting with recurrent pneumonia and anemia. There are no gastrointestinal bleeding symptoms such as blood in stool or vomit. Chest CT scan showed diffuse ground-glass opacities in both lungs, suggesting possible diffuse alveolar hemorrhage. Considering blood tests, morphological and immunological evaluations, and imaging findings, the diagnosis of idiopathic pulmonary hemosiderosis is considered.

**Treatment progress**
After admission, the patient received anti-infective therapy, low-flow oxygen, and leukocyte-reduced red blood cell transfusions, resulting in slight improvement in anemia. On december 24, she exhibited a cough with minimal sputum and reported persistent fatigue. Auscultation revealed moist rales in both lungs.
Given her history of two previous hospitalizations, the recurrence of fever and anemia, and the lack of gastrointestinal bleeding symptoms, jaundice, splenomegaly, or hemolysis indicators, along with CT findings suggesting diffuse alveolar hemorrhage, a diagnosis of IPH was considered. Sputum samples were collected to identify hemosiderin-laden macrophages.
Methylprednisolone was administered to suppress the immune response, along with nebulized treatment to reduce respiratory inflammation. Oral iron supplementation and low-flow oxygen support continued. Acetylcysteine was prescribed to prevent lung fibrosis, along with vitamin and calcium supplementation. Based on allergy results, the patient was advised to avoid allergens, with plans to taper steroids to oral administration and schedule follow-up imaging.
By December 29, the patient’s condition improved significantly. A follow-up chest CT showed notable absorption and improvement of lung lesions (Figure 2B), with clinical symptoms also enhancing. The patient was approved for discharge the next day, instructed to continue oral prednisone, calcium, vitamin D, and acetylcysteine, along with ongoing iron supplementation and outpatient follow-up.

## DISCUSSION

Idiopathic pulmonary hemosiderosis (IPH) is a rare chronic lung disease characterized by recurrent alveolar bleeding and abnormal deposition of hemosiderin in lung tissue, ultimately leading to pulmonary interstitial fibrosis. Despite its low incidence, the disease significantly impairs lung function and quality of life, and its complex etiology presents diagnostic and therapeutic challenges.
The exact cause of IPH remains unclear, but existing research suggests that its onset may involve interactions among multiple factors [2]. Abnormal alveolar development is considered one potential pathological basis, with some patients exhibiting ultrastructural abnormalities in alveolar epithelial cells and the basement membrane, leading to impaired alveolar-capillary barrier function and increased vascular permeability, which can trigger recurrent bleeding. Additionally, immune abnormalities play a critical role; some patients may have detectable anti-alveolar basement membrane antibodies that directly damage capillary walls through complement activation, resulting in vascular rupture and bleeding [3]. Recent studies have also found that environmental exposure and allergic reactions may participate in the disease process [4]: long-term exposure to heavy metal dust or harmful chemical gases can damage pulmonary endothelial cells through oxidative stress, increasing the risk of bleeding. Furthermore, milk protein allergy has been linked to some cases - patients often experience a significant reduction in symptom frequency upon discontinuation of milk, suggesting that certain components in milk may activate pulmonary inflammatory responses via immune pathways, leading to increased vascular permeability [5].
The pathological process of IPH centers around a cycle of "bleeding-deposition-fibrosis" [2]. After repeated bleeding in the pulmonary capillaries, red blood cells are engulfed and degraded by alveolar macrophages, leading to the formation and deposition of hemosiderin granules in lung tissue. This process not only directly

obstructs gas exchange but also activates fibroblasts to release cytokines such as transforming growth factor-beta (TGF-β), promoting pulmonary interstitial fibrosis and potentially leading to restrictive ventilatory dysfunction. Notably, long-term iron deposition can induce pulmonary hypertension and right heart failure, further exacerbating the patient's condition [6].

Diagnosis of IPH requires a combination of clinical presentation, laboratory tests, and imaging features, ultimately confirmed through pathology [7]. Iron deficiency anemia is an important clue, with complete blood counts typically showing microcytic, hypochromic anemia, decreased ferritin, and elevated TIBC. Early chest X-rays may reveal diffuse ground-glass opacities, while high-resolution CT scans can more clearly display reticular fibrosis and honeycombing changes. Currently, the diagnosis relies on the detection of hemosiderin-laden cells, although this method has lower sensitivity and requires multiple samples. Lung biopsy, while the "gold standard," is limited in clinical use due to its invasive nature and is usually reserved for difficult cases.

Currently, the treatment of IPH focuses on controlling acute bleeding, reducing iron deposition, and delaying fibrosis, but there are no specific therapies available [8]. The prognosis varies significantly among individuals; some pediatric patients may achieve long-term remission with standardized treatment, while adults often experience chronic progression, ultimately dying from respiratory failure or cor pulmonale. Poor prognostic factors include younger age at onset, underlying comorbidities, and poor treatment response.

## CONCLUSION

Due to its rarity and complexity, IPH remains a challenging area of research within the field of respiratory diseases. This case illustrates how the integration of resources from laboratory medicine, medical imaging, and other disciplines can assist clinicians in timely identifying the causes of recurrent infections and anemia in patients, leading to the diagnosis of IPH. This approach provides a basis for optimizing treatment plans and implementing early preventive interventions against pulmonary fibrosis, which is crucial for improving patient prognosis and subsequent quality of life. We hope that by reviewing this case, we can outline the clinical manifestations, differential diagnosis, and treatment strategies for IPH, while also providing a reference for exploring the causes of recurrent anemia accompanied by pulmonary lesions in children.

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**Declaration of Interest:**
The author declares that there is no conflict of interests.

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