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Case Report

A Rare Case of Shwachman-Diamond Syndrome: Diagnostic Challenges and Management

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Abstract

Background: Rare inherited bone marrow failure syndromes pose significant diagnostic challenges in pediatric practice due to their variable and overlapping clinical presentations. Shwachman-Diamond syndrome (SDS) is one such rare autosomal recessive disorder characterized by exocrine pancreatic insufficiency, bone marrow dysfunction, skeletal abnormalities, and variable immune deficiency. Due to its low prevalence and heterogeneous clinical presentation, SDS is frequently underrecognized or misdiagnosed, especially in pediatric patients. *Objective*: To review the diagnostic and therapeutic process of a pediatric patient with SDS, with the aim of enhancing clinical awareness and understanding of this rare multisystem disease. *Methods*: A detailed analysis was conducted of the patient's clinical manifestations, physical examination findings, laboratory results, imaging data, and genetic testing, alongside a review of the therapeutic regimen and follow-up. Results: The patient exhibited hallmark features of SDS, including short stature, recurrent respiratory infections, and persistent neutropenia. Genetic analysis revealed an SBDS (NM_016038.4): c.258+2T>C (intron 2/4) mutation, confirming the diagnosis. Supportive and symptomatic treatments were administered, including infection prevention, nutritional support, and regular monitoring of hematologic status. *Conclusion*: This case underscores the importance of considering SDS in children with unexplained cytopenias and recurrent infections. Genetic testing plays a pivotal role in achieving a definitive diagnosis. Early recognition and appropriate management can improve outcomes and provide valuable reference for clinicians encountering similar cases.

Keywords

Shwachman-Diamond Syndrome, Pediatric, Genes

1. Introduction

Shwachman-Diamond syndrome (SDS) is a rare hereditary multisystem disorder classified as a ribosomopathy, first described by Shwachman and Diamond in 1964 [1-3]. The estimated incidence is approximately 1 in 75,000 live births, with a male-to- female ratio of about 1.7:1. The disease is primarily characterized by pancreatic exocrine insufficiency, bone marrow dysfunction, and skeletal abnormalities [1, 4, 5]. SDS is closely associated with mutations in the SBDS gene, making genetic testing a key diagnostic tool [5]. In recent years, the rapid advancement and widespread application of genetic sequencing technologies have significantly improved SDS diagnosis. Despite these advancements, the clinical heterogeneity and complexity of SDS often lead to diagnostic confusion with other conditions, such as cystic fibrosis and congenital neutropenia [1, 7]. Furthermore, most systematic studies on SDS diagnosis and management have focused on

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adult populations, particularly on digestive and hematologic manifestations, with limited pediatric case reports [6-8]. To address these challenges, this study retrospectively analyzed the diagnostic and therapeutic course of a pediatric SDS case diagnosed at a tertiary hospital in Guangzhou in December 2024. By integrating recent literature, we systematically explored the clinical features, differential diagnosis, and treatment strategies of SDS. This study aims to enhance clinicians' understanding, optimize diagnostic and management approaches, reduce underdiagnosis and misdiagnosis, and contribute to the standardization of SDS diagnosis and treatment.

2. Case Report

A 4-month-old female infant with short stature was admitted to the pediatrics department of our hospital on December 18, 2024, due to intermittent fever and neutropenia for three weeks. Since November 28, she had experienced recurrent fever of unknown origin, with a peak temperature of 39°C. The fever temporarily subsided after oral administration of acetaminophen but recurred every 4–5 hours, without overt signs of infection. From December 1 to December 16, she was treated at an external hospital, where laboratory tests revealed neutropenia and anemia, with a hemoglobin level of 91 g/L. During this period, she received intravenous imipenem for antimicrobial therapy, acetaminophen for fever control, and oral shark liver oil tablets as an adjunctive immune modulator. The patient was the second child of non-consanguineous parents, born full-term with a normal birth weight. Her older sister had normal development, and the parents reported no known family history of genetic disorders.

On physical examination, the patient's temperature was 36.5°C, pulse 146 beats/min, and respiratory rate 34 breaths/min. Her length was 58.0 cm (-3SD), and weight was 5.0 kg (-3SD). She exhibited normal mental status and appetite, but pallor was noted. Genital examination revealed normal female external genitalia. Cardiac, pulmonary, abdominal, and neurological examinations were unremarkable. During hospitalization, the patient experienced fever, with a peak temperature of 38.7°C.

Table 1. *Changes in blood count and infection indicators.*

	categories				
Time	**C-reactive protein**	**White blood cell**	**Neutrophil**	**Procalcitonin**	**Hemoglobin**
Dec. 18	29.0 mg/L	7.90×10^9/L	0.07×109/L	4.15 ng/ml	94.0 g/L
Dec. 21	11.2 mg/L	9.56×10^9/L	0.83×109/L	2.45 ng/ml	95.0 g/L
Dec. 24	8.7 mg/L	7.10×10^9/L	0.15×109/L	0.29 ng/ml	92.0 g/L
Dec. 26	2.0 mg/L	7.62×10^9/L	0.48×109/L		96.0 g/L

Variations in blood counts and infection markers during hospitalization are summarized in Table 1. Peripheral blood genetic testing revealed the following abnormalities: neutropenia (HP: 0001875), recurrent respiratory tract infections (HP: 0011947), neutrophil abnormalities (HP: 0001874), and immune system dysfunction (HP: 0002715). A pathogenic variant in SBDS (NM_016038.4: c.258+2T>C, intron 2/4) was identified. The Sanger sequencing results are shown in Figure 1.

Imaging studies revealed multiple abnormalities. A lung X-ray demonstrated diffuse haziness in both lower lungs (Figure 2). Neck ultrasound showed lymph node enlargement (Figure 3), while abdominal CT indicated intestinal stasis (Figure 4).

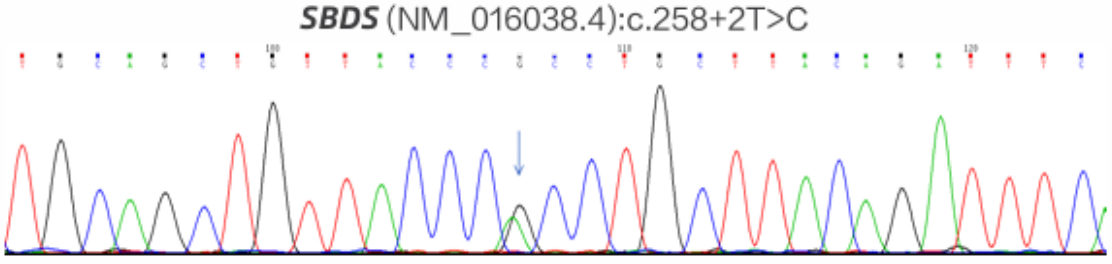

Figure 1*. Sanger sequencing profiles of the SBDS gene.*

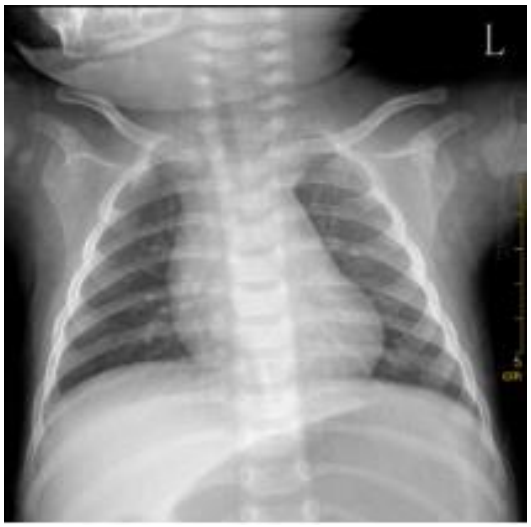

Figure 2. *Lung X-ray results.*

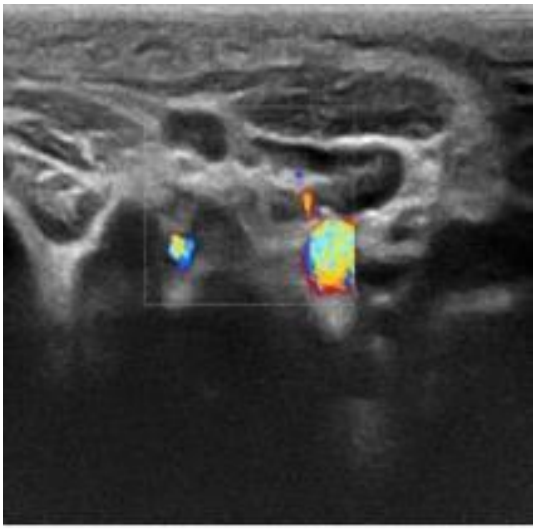

Figure 3. *Neck ultrasound results.*

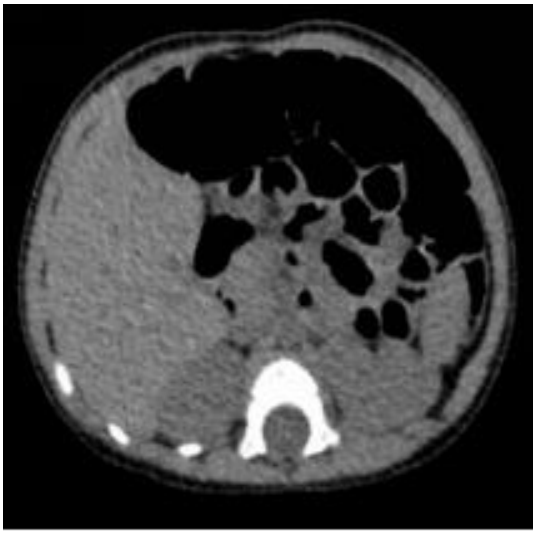

Figure 4. *Abdominal CT results.*

The child was treated with ceftriaxone for infection control, budesonide nebulization, human granulocyte colony-stimulating factor (G-CSF) to promote neutrophil production, supplementation with fat-soluble vitamins and micronutrients, and iron protein succinate oral solution to correct anemia. The child was discharged on December 27 following stabilization of body temperature and recovery of neutrophil count.

3. Discussion

The diagnosis of SDS relies on both clinical and molecular assessments. Clinical diagnosis requires evidence of hematopoietic dysfunction, with at least two abnormal results detected within a 3-month period. Approximately 80% of affected children present with neutropenia ($<1.5\times10^9$/L), while some also exhibit anemia (hemoglobin below the age-specific lower limit) or thrombocytopenia ($<150\times10^9$/L) [9, 13]. Additionally, around 75% of children with SDS develop exocrine pancreatic insufficiency, characterized by reduced pancreatic enzyme secretion, which may result in digestive abnormalities such as steatorrhea and malnutrition [10, 12]. The combination of hematopoietic abnormalities and pancreatic dysfunction significantly improves the clinical recognition of SDS. Molecular diagnosis relies on identifying pathogenic variants in the SBDS gene. Approximately 90% of SDS cases involve mutations in the SBDS gene, located on chromosome 7q11 [10, 11]. The most common mutations are c.258+2T>C and c.183_184TA>CT, with the former affecting the splice site and the latter introducing a stop codon [11, 13]. The SBDS protein plays a crucial role in ribosome maturation, RNA metabolism, and neutrophil chemotaxis [11]. The present case involves a child with short stature, recurrent infections, and neutropenia (N fluctuating from 0.07 to 0.83 $\times 10^9$/L), along with persistent anemia (Hb fluctuating from 91 to 96 g/L) for nearly one month. These clinical features align with the typical presentation of SDS and are consistent with previously reported cases. Genetic testing further confirmed the diagnosis by identifying an SBDS (NM_016038.4): c.258+2T>C, intron 2 (2/4) mutation, establishing the molecular basis of the disease. However, several challenges were encountered in the diagnostic process. Clinicians may overlook SDS in pediatric practice due to its rarity, leading to delayed suspicion and diagnosis. Furthermore, the diverse clinical manifestations and significant overlap with other hematologic and immune disorders further complicate the diagnostic process. Therefore, enhancing awareness of SDS, expanding differential diagnostic considerations, and improving knowledge of rare pediatric diseases are essential for early and accurate diagnosis, ultimately leading to optimized clinical management.

Currently, there is no specific treatment program for SDS. Symptomatic supportive treatment is mainly used [11-13]. For patients with recurrent infections, the anti-infective regimen should be adjusted based on pathogen identification to avoid unnecessary antibiotic use and prevent drug-resistant infec-

tions. In this case, the child received ceftriaxone for anti-infective therapy and budesonide nebulization to reduce lung inflammation, both of which were effective.

Poor nutrition and growth retardation are common manifestations of pancreatic insufficiency in children with SDS. Therefore, the child was supplemented with oral iron, intravenous fat-soluble vitamins, and trace elements to improve nutritional status and digestive function. Despite treatment, the child's weight and length did not increase significantly, indicating the need for long-term monitoring and intervention in growth and development. For severe granulocytopenia, short-term low-dose G-CSF subcutaneous injection can be used to elevate neutrophil levels. However, long-term use is not recommended due to the risk of MDS or AML transformation [14, 15]. Post-discharge, regular follow-up and weekly blood tests are essential to monitor the child's condition closely. In addition, the quality of life of children with SDS should be closely monitored. Due to recurrent infections and chronic conditions, caregivers often experience significant psychological and financial burdens. Therefore, comprehensive psychological support and social care should be provided to assist caregivers and enhance the child's overall quality of life.

In summary, SDS is a rare genetic disease with complex and varied clinical manifestations. Diagnosis requires a combination of clinical features and genetic test results. As there is no cure for SDS, treatment mainly focuses on symptomatic supportive measures. Individualized treatment plans should be tailored to the severity of the patient's condition. Furthermore, due to the involvement of multiple systems, multidisciplinary collaboration is essential for comprehensive management. Long-term follow-up is also necessary to optimize prognosis and improve the patient's quality of life. In the future, further studies on the pathogenesis of SDS and advancements in therapeutic techniques are expected to provide more treatment options and improve clinical outcomes.

Abbreviations

SDS	Shwachman-Diamond Syndrome
G-CSF	Granulocyte Colony-stimulating Factor
CT	Computed Tomography

Author Contributions

Xinyi Xu: Data curation, Writing – original draft
Yihui Huang: Supervision, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

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