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Pena-Shokeir Syndrome: A Case Report of Two Siblings with Type 1. First Case from Africa

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Abstract: Pena-Shokeir Syndrome is a rare genetic disorder, categorized into Type 1 and Type 2. PSS Type 1, characterized by pulmonary hypoplasia, joint contractures, and facial anomalies, typically results in intrauterine or early neonatal death. Approximately 100 cases of PSS Type 1 have been reported. This case report describes two siblings affected by PSS Type 1, born to a mother with a history of 3 miscarriages and with a healthy first child. It underscores both the clinical and genetic aspects of this rare syndrome.

Keywords: Pulmonary Hypoplasia, Genetic Disorder, Joint Contractures (Arthrogryposis), Facial Anomalies, Intrauterine Death.

Case Report

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1. INTRODUCTION

PSS Type 1 is a severe genetic disorder marked by multiple congenital anomalies, especially pulmonary hypoplasia, which significantly contributes to early death in affected neonates [1, 2]. The syndrome presents with characteristic features such as pulmonary hypoplasia, arthrogryposis, and facial abnormalities and is extremely rare (occurring less than 1 in 1,000,000 births) [3].

PSS Type 2, also known as cerebro-oculo-facio-skeletal syndrome, presents with specific neurological features, including microcephaly and severe developmental delay, ocular abnormalities, such as congenital cataracts and microphthalmia, skeletal abnormalities including arthrogryposis, and is distinguished from PSS Type 1 by the absence of pulmonary hypoplasia [2-4].

PSS Type 1 follows an autosomal recessive inheritance pattern [3]. In some cases, maternal anti-AChR antibody titers are increased despite the absence of any clinical symptoms of myasthenia gravis in the mothers. The recurrence risk was very high in these cases, and all subsequent pregnancies were affected [5].

There are also reports of mothers with a history of intrauterine death in previous pregnancies, followed by the birth of a child with PSS Type 1, and cases of recurrent PSS Type 1 across multiple pregnancies [6, 7].

2. CASE PRESENTATION

We present two siblings, a male, and a female, both diagnosed with PSS Type 1, born 1.5 years apart. The mother, aged 40 and 41, had a history of three miscarriages before delivering a healthy first child.

Family History

There is no consanguinity between the parents. Both parents are healthy.

- **First Child (born 05/08/2019):** A healthy girl was born at 40 weeks gestation, weighing 3.5 kg, with no complications.
- **Second Child (born 06/24/2021):** The mother was 40 years old and had polyhydramnios. The male infant was born at term (40 weeks), weighing 3.7 kg (75th-90th percentile), with a height of 47 cm (25th-50th percentile) and a head circumference of 36 cm (50th-75th percentile). The infant did not initiate spontaneous breathing after birth and required intubation.

Key findings:

- Pulmonary hypoplasia: Markedly reduced lung volume, occupying less than half of the thoracic cavity (Figure 1A).
- Joint contractures: Deformities of the rib cage and vertebral positional abnormalities, congenital malformations of the fingers, and jaw joint rigidity.

- Facial anomalies: Cleft palate (no cleft lip) and micrognathia.
- Additional findings: Large umbilical hernia, abdominal distension, absence of sucking reflex, and complete hoarseness. Despite intensive care, the infant died after 32 days from respiratory failure.

- **Third Child (born 07/01/2022):** The mother was 41.5 years old and had polyhydramnios. A female infant was delivered via cesarean section at 38 weeks gestation, weighing 3.7 kg (75th-90th percentile), with a height of 50 cm (50th-75th percentile) and a head circumference of 36 cm (75th-90th percentile).
  - Pulmonary hypoplasia: Markedly reduced lung volume, occupying less than half of the thoracic cavity (Figure 1B).
  - Joint contractures: Rib cage deformity, vertebral positional abnormalities, and camptodactyly in the fingers and toes (Figures 2A, 2B, 2C and 3A, 3B). Jaw joint rigidity made intubation difficult.
  - Facial anomalies: Micrognathia and short neck.
  - Additional findings: Diastasis recti, abdominal distension, absence of sucking reflex, difficulty swallowing, and complete hoarseness. The infant required mechanical ventilation, developed atelectasis, and died from septicemia at 63 days.

Key findings:

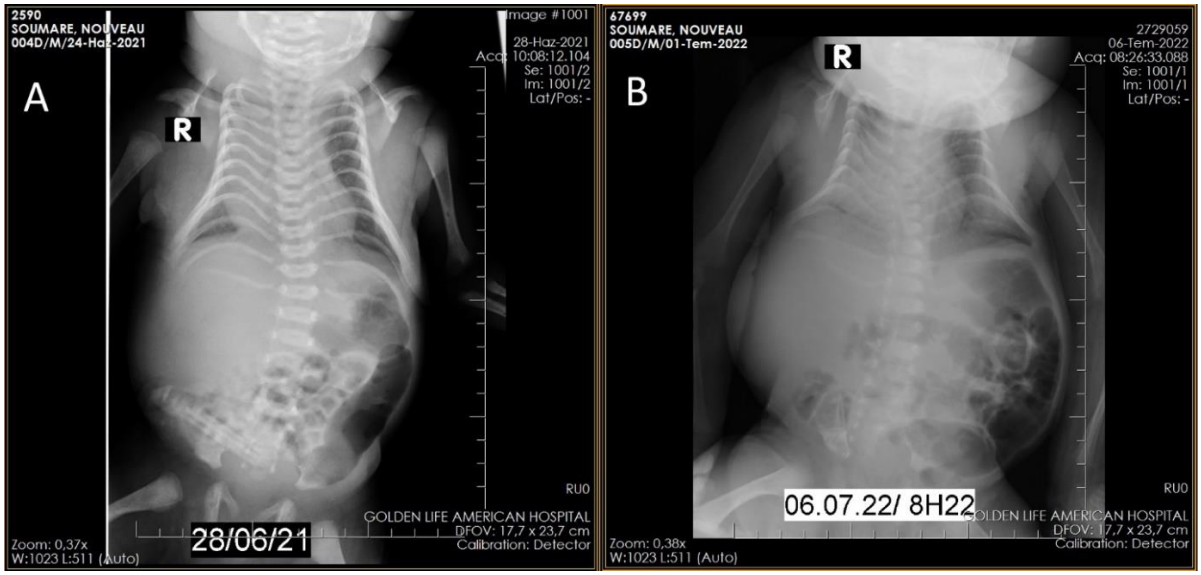

Figure 1-A (for second child): The lungs occupy almost only 1/2 of the thoracic cavity, extremely large deformity of the rib cage and vertebral positional abnormalities; Figure 1-B (for third child): The lungs occupy almost only 1/2 of the thoracic cavity, extremely large deformity of the rib cage and vertebral positional abnormalities

Figure 2-A: Micrognathia, short neck, Figure 2-B: Camptodactyly (Joints contractures in the fingers), Figure 2-C: Camptodactyly (Joint contracture in the big toe)

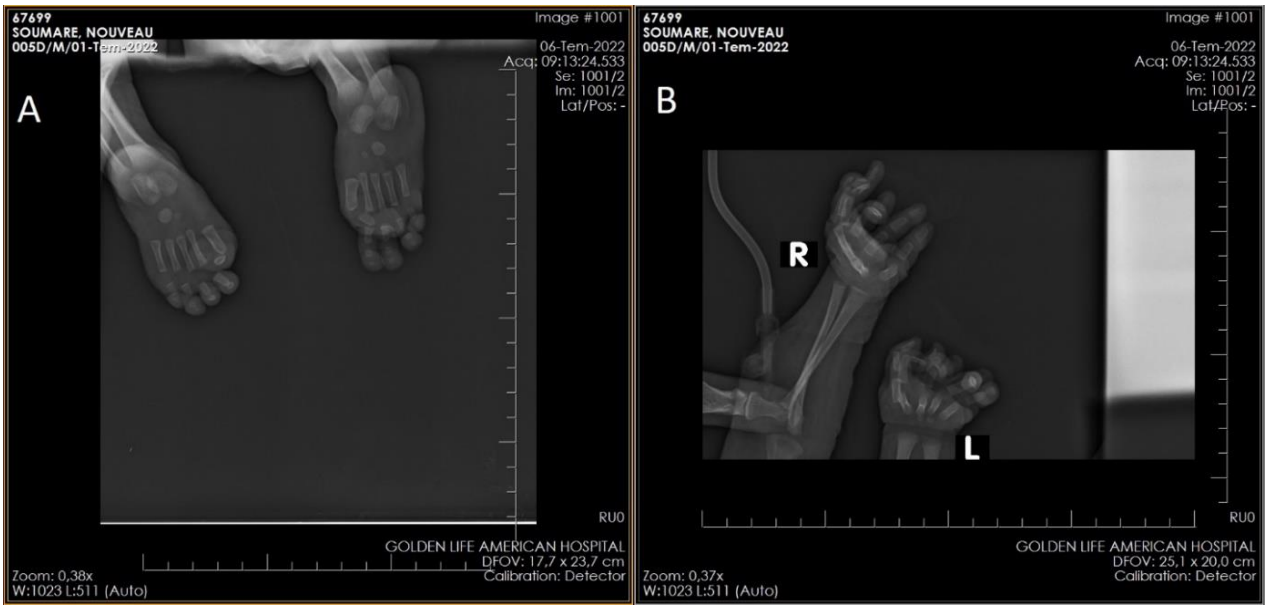

Figure 3-A: Camptodactyly (Joint contracture in the big toe); Figure 3-B: Camptodactyly (Joints contractures in the fingers)

3. DISCUSSION

PSS Type 1 is characterized by severe pulmonary hypoplasia, which directly leads to respiratory failure—the main cause of death in affected neonates. Additional features may include joint contractures, facial anomalies, and hypotonia, all of which contribute to significant functional impairments. The clinical features observed in the siblings are consistent with the classic presentation of PSS Type 1.

Key Clinical Findings Include:

- **Pulmonary Hypoplasia**: Both infants exhibited underdeveloped lungs with significantly reduced lung volume, a hallmark of PSS Type 1. Imaging confirmed a small thoracic cavity, exacerbating respiratory insufficiency.
- **Skeletal Abnormalities**: Rib cage deformities and vertebral positional abnormalities are common in PSS Type 1, contributing to the poor respiratory prognosis. Joint contractures, including arthrogryposis multiplex, affected the hands, feet, and jaw.
- **Facial and Musculoskeletal Abnormalities**: Micrognathia and facial dysmorphisms were observed in both infants. Jaw stiffness and difficulty with intubation further complicated respiratory management.
- **Polyhydramnios**: Excessive amniotic fluid was noted in both pregnancies, a common feature in PSS Type 1 due to impaired swallowing from hypotonia.
- **Severe Hypotonia**: Both infants exhibited marked hypotonia, a central feature of PSS Type 1, contributing to feeding difficulties and failure to thrive.

Diagnostic Findings

- **Normal liver and kidney function**: As expected in PSS Type 1, organ systems other than the musculoskeletal and respiratory systems were unaffected.
- **Normal brain imaging**: No central nervous system anomalies were noted, consistent with the selective nature of the syndrome, which primarily impacts the musculoskeletal and respiratory systems.
- **Normal echocardiography and abdominal ultrasound**: These findings suggest that cardiovascular and abdominal structures are usually spared in PSS Type 1.
- No pathology was detected in eye examinations.

Prognosis and Management

The prognosis for PSS Type 1 is extremely poor due to the severity of pulmonary hypoplasia, which leads to respiratory failure and early death. Despite the absence of significant neurological or other organ involvement, the pulmonary compromise limits survival beyond the neonatal period.

- **Palliative Care**: Given the poor prognosis, early diagnosis and palliative care are crucial. This includes managing respiratory distress, providing comfort, and addressing feeding difficulties.
- **Genetic Counseling**: Genetic counseling is essential for families with a history of PSS Type 1,

as future pregnancies have a high recurrence risk. Preimplantation genetic diagnosis (PGD) or prenatal screening may be options for affected families.

4. CONCLUSION

This case report highlights the distinctive clinical features and poor prognosis associated with PSS Type 1. The recurrence of PSS in siblings underscores the critical need for early diagnosis, genetic counseling, and palliative care. Early recognition of key features such as pulmonary hypoplasia, joint contractures, and craniofacial abnormalities is essential for the timely diagnosis and management of affected neonates. Genetically, the mother in this case experienced five pregnancies: two resulted in confirmed PSS Type 1, while three ended in miscarriages, likely due to the same condition. This pattern is difficult to explain by autosomal recessive inheritance alone, suggesting the need for further investigation into the genetic mechanisms underlying PSS Type 1.

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