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Freeman-Sheldon Syndrome Presenting with Unilateral Congenital Hip Dislocation and Bilateral Wrist Flexion Contractures: A Detailed Rare Case Report with Familial Occurrence and Literature Review

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ABSTRACT
Freeman-Sheldon syndrome (FSS), a rare autosomal dominant disorder (distal arthrogryposis type 2A), is characterized by distinctive facial features and distal limb contractures. We present a detailed case of an 11-year-old male diagnosed with FSS exhibiting a less common combination of unilateral congenital hip dislocation and prominent bilateral wrist flexion contractures. Characteristic facial features included significant microstomia with pursed lips, a distinct V-shaped chin dimple, hypertelorism, deep-set eyes with down-slanting palpebral fissures, a high-arched palate, and dental crowding. Limb examination revealed bilateral camptodactyly, marked ulnar deviation of the fingers ("windmill vane hand"), thumb-in-palm deformity, and severely limited wrist movement. Orthopedic assessment revealed a right congenital hip dislocation confirmed radiographically, accompanied by a right hip flexion contracture (positive Thomas test), instability (positive Staheli test), and rectus femoris tightness (positive Ely test), with significant limitation in abduction and external rotation. The patient's early development was notable for feeding difficulties and significant gross motor delays. Notably, the patient's father presented with similar hand deformities and characteristic facial features, along with a history of bilateral foot surgery, strongly suggesting familial inheritance. Despite these challenges, the patient demonstrates good functional adaptation with a DASH score of 4.2 and participation in sports. This case underscores the phenotypic variability of FSS, highlights the importance of meticulous clinical examination, detailed developmental and family history, and contributes to the understanding of less common musculoskeletal associations.

Keywords: Freeman-Sheldon Syndrome, Distal Arthrogryposis, Congenital Hip Dislocation, Wrist Flexion Contracture, Familial Inheritance, Developmental Delay, Case Report
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INTRODUCTION

Freeman-Sheldon syndrome (FSS) is a rare autosomal dominant disorder primarily attributed to mutations in the *MYH3* gene, which encodes embryonic skeletal muscle myosin heavy chain. The syndrome is characterized by a distinctive and relatively consistent pattern of facial anomalies, including microstomia, pursed lips resembling a "whistling face," and a deep-set chin crease often described as H-shaped or V-shaped. Distal limb contractures, such as camptodactyly, ulnar deviation of the fingers, and talipes equinovarus, are also hallmark features. However, the clinical expression of FSS exhibits significant variability, leading to the recognition of a spectrum of musculoskeletal involvement. We present a detailed case of an 11-year-old male with a clinical diagnosis of FSS, notable for the presence of a unilateral congenital hip dislocation and significant bilateral wrist flexion contractures, accompanied by a comprehensive account of his birth, developmental, and family history, including similar findings in his father (1,2). This case aims to enhance the understanding of the phenotypic breadth of FSS and emphasize the importance of thorough clinical assessment in recognizing its diverse presentations.

CASE PRESENTATION

An 11-year-old male, MKDS, from Kediri, Indonesia, presented for orthopedic evaluation due to congenital bilateral wrist stiffness and an unbalanced gait. Born full-term via vacuum extraction, his early development was notable for feeding difficulties due to a short lingual frenulum and maternal milk insufficiency, requiring formula feeding. Gross motor milestones were significantly delayed, with independent sitting at 12 months and ambulation at 3 years. Despite these delays, language and feeding development were typical, and he reports independent ambulation and physical activity participation. His birth history included maternal hypertension during

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pregnancy, and he has no history of seizures or allergies. Immunizations are complete.

Physical Examination:

The patient was alert and cooperative. Anthropometric measurements revealed a height of 131 cm (below the 5th percentile) and a weight of 21 kg (below the 5th percentile), indicating underweight status. Facial examination demonstrated phenotypic features of Freeman-Sheldon Syndrome, including microstomia with pursed lips, a V-shaped chin dimple, hypertelorism, deep-set eyes with down-slanting palpebral fissures, a high-arched palate, and dental crowding (Fig. 1).

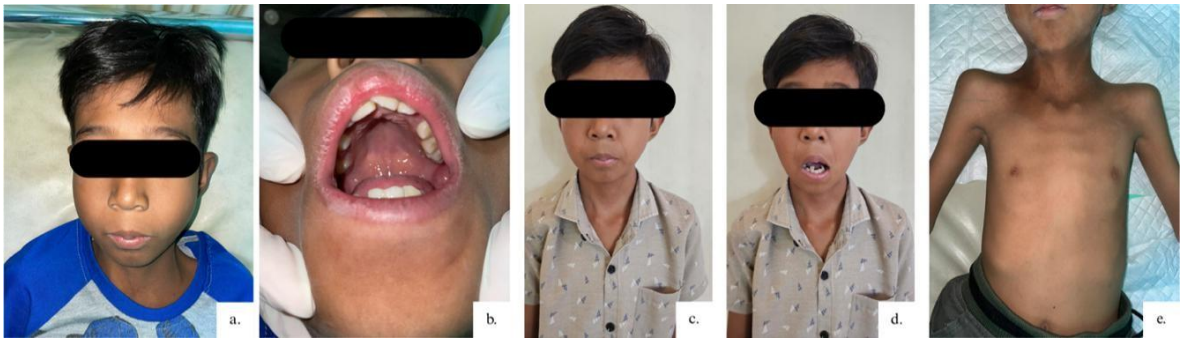

Figure 1. Anterior view (a) demonstrating microstomia with pursed lips, hypertelorism, and deep-set eyes with down-slanting palpebral fissures. Palatal view (b) showing a high-arched palate and dental crowding. Microstomia is shown in closer detail in (c) and (d). The thorax appears normal.

Examination of the bilateral upper limbs revealed fixed flexion contractures at the wrists, with severely limited extension to approximately 80 degrees from neutral. Multiple fingers exhibited camptodactyly, and there was marked ulnar deviation, creating a "windmill vane hand" appearance. Bilateral thumb-in-palm deformities were present, with restricted thumb extension and abduction. Functional assessment using the DASH score was 4.2, suggesting minimal disability. The patient reported some difficulty reaching his back for bathing but otherwise denied significant limitations in daily activities or sports such as swimming (Fig 2).

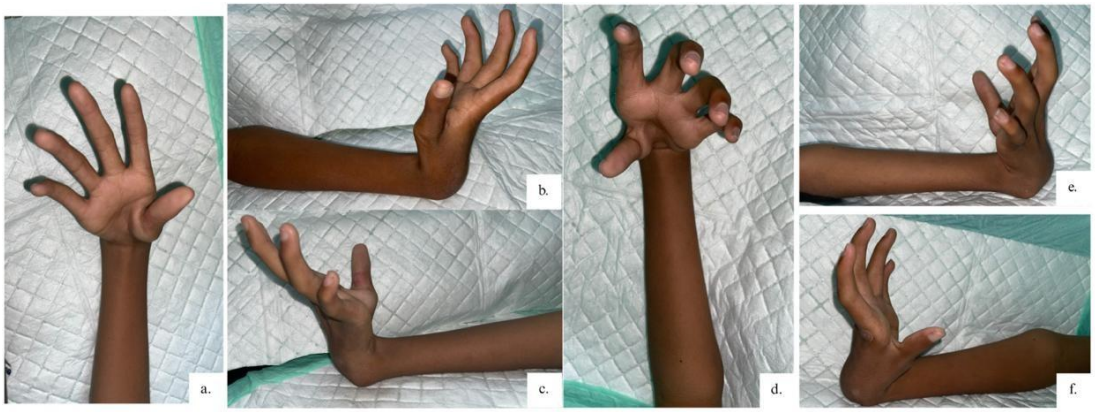

Figure 2. Bilateral upper limbs (a-f) revealed fixed flexion contractures at the wrists. Multiple fingers exhibited camptodactyly, and there was marked ulnar deviation, creating a "windmill vane hand" appearance. Bilateral thumb-in-palm deformities were present, with restricted thumb extension and abduction.

Examination of the lower limbs revealed no gross deformities of the feet. Spinal inspection demonstrated mild scoliosis. Right hip assessment showed a positive Thomas test, indicating a flexion contracture, a positive Staheli test suggestive of instability, and a positive Ely test, indicating rectus femoris tightness. Hip abduction and external rotation were restricted to approximately 20 degrees from midline. Leg length measurements revealed both an apparent discrepancy of 3 cm (right 69 cm, left 72 cm) and a true discrepancy of 3 cm (right 65 cm, left 68 cm), with equal femoral lengths of 31 cm. Distal neurovascular status was intact throughout all extremities (Fig 3).

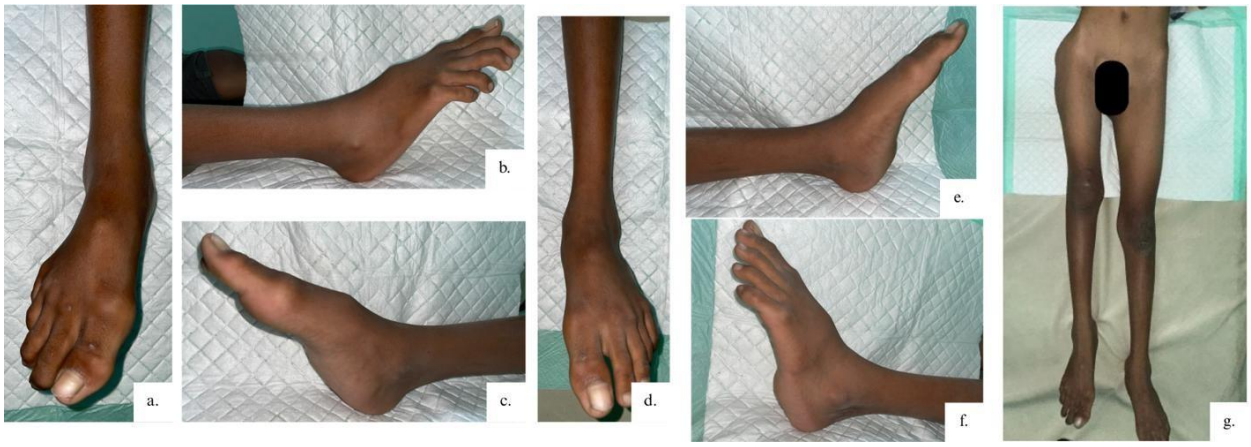

Figure 3. Bilateral feet appeared normal (a-f). Leg length discrepancy was observed (g).

Investigations:

Radiographic evaluation of the pelvis (anteroposterior projection) revealed superior and posterior displacement of the right femoral head relative to the acetabulum, consistent with a congenital dislocation of the hip. The right hip showed following changes in the right hip; decrease femoral epiphysis height, horizontal proximal femoral physis, and the coxa brevia. Bilateral wrist radiographs demonstrated fixed flexion contractures, with no evidence of bony abnormalities, including fusions or dysostosis (Fig 4). Nerve conduction velocity (NCV) studies of the bilateral hands yielded normal results, indicating no primary neurological contribution to the observed wrist contractures. Genetic testing for mutations in the *MYH3* gene was not performed in this case due to resource limitations and the strong clinical and familial presentation.

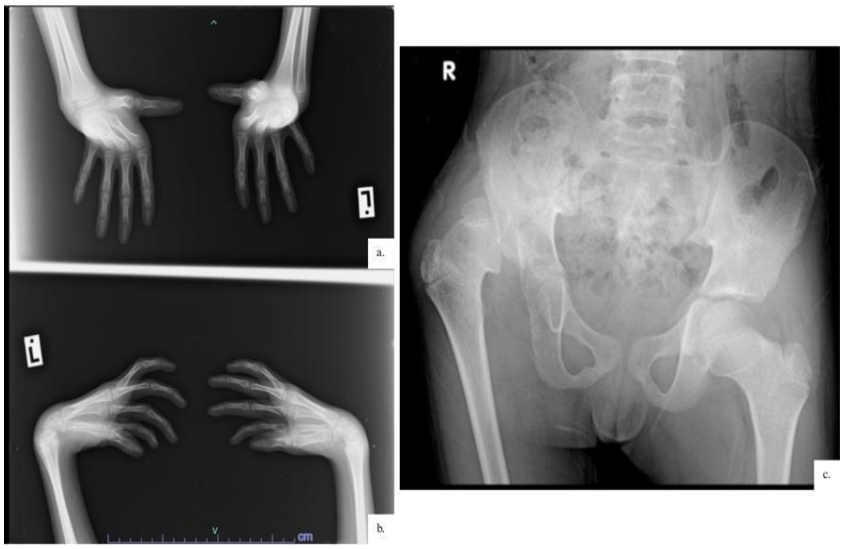

Figure 4. Bilateral hand radiographs (Manus) are shown in (a-b). An anteroposterior (AP) radiograph of the pelvis is shown in (c).

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A detailed family history indicated the patient's father had a lifelong history of bilateral hand deformities, characterized by camptodactyly, ulnar deviation of the fingers, thumb-in-palm deformity, and restricted wrist movement. The father elected against surgical intervention for his hand deformities. He underwent bilateral Achilles tendon lengthening in 1992 to address gait abnormalities associated with bilateral foot deformities. The father also reported a history of microstomia and childhood shortness of breath. He was formula-fed and described as underweight during childhood. Despite his hand limitations, he currently works as a truck driver, reporting initial challenges but now managing without significant functional impairment (Fig 5).

Figure 5. Figure. Anterior facial view showing resemblance to the child (a). Bilateral upper limbs with wrist flexion contractures, finger camptodactyly, ulnar deviation ("windmill vane hand"), and thumb-in-palm deformities with limited thumb extension and abduction, similar to the child (b-d).

DISCUSSION

Freeman-Sheldon syndrome (FSS) is primarily caused by variants (mutations) in the MYH3 gene, located on chromosome 17. This gene encodes myosin-3, a protein crucial for muscle contraction, especially during fetal development. Mutations in MYH3 disrupt myosin-3 function, leading to prolonged muscle contraction and impaired relaxation. This results in restricted fetal muscle movement, causing the characteristic contractures and deformities of FSS, especially facial muscle development. However, a small percentage of individuals with clinical FSS do not have identifiable MYH3 mutations, indicating potential genetic heterogeneity. Recent research has identified mutations in the NALCN gene in some clinically diagnosed FSS cases. This suggests that other genetic factors or non-genetic mechanisms may contribute to the FSS phenotype. The research regarding NALCN's role in FSS is still very limited. Genetic testing is essential for accurate FSS diagnosis. The genetic heterogeneity of FSS has implications for genetic counseling and patient management. Further research is needed to fully understand the genetic and non-genetic factors contributing to FSS (1,3,4).

Freeman-Sheldon syndrome is characterized by multiple congenital contractures, particularly affecting the distal joints of the limbs, including the wrists. Contracture flexion of the wrist, occurring on both sides (bilateral), is a recognized feature of this syndrome (5). In Freeman-Sheldon syndrome, the hands often present with a combination of deformities, including ulnar deviation of the fingers (where the fingers angle towards the little finger), camptodactyly (permanent bending of the fingers), and contractures of the wrists(2). The term "arthrogryposis" itself refers to multiple congenital joint contractures, and Freeman-Sheldon syndrome is classified as a type of distal arthrogryposis, meaning the contractures primarily affect the extremities, such as the hands and feet (6). The underlying cause of these contractures in Freeman-Sheldon syndrome lies in mutations of the MYH3 gene, which affects the development of muscle fibers during fetal development, leading to stiffness and restricted movement in the joints . This can result in the wrists being fixed in a flexed position bilaterally from birth (7). Management of hand deformities, including wrist contractures, in Freeman-Sheldon syndrome often involves a multidisciplinary approach with orthopedic surgery, splinting, and physical and occupational therapy aimed at improving function and range of motion (8).

The examination of the patient's bilateral upper limbs, revealing fixed flexion contractures at the wrists, camptodactyly of multiple fingers, marked ulnar deviation resulting in a "windmill vane hand" appearance, and bilateral thumb-in-palm deformities with restricted thumb movement, is consistent with the well-documented characteristics of Freeman-Sheldon syndrome, particularly the involvement of distal joints as highlighted in the literature (2,5)

Congenital hip dislocation (CHD) is generally not considered a common feature of Freeman-Sheldon Syndrome (FSS). Most sources indicate that CHD is rare in FSS. However, it's important to acknowledge that hip involvement, including dysplasia and dislocation, has been documented in several case reports and studies. Studies finding limited hip movement in approximately 15% of FSS

patients and developmental hip dislocation as a related anomaly suggest that hip problems may be more frequent than the description "rare" implies. The variability in the clinical presentation of FSS may explain why some individuals with the syndrome experience CHD while others do not. The severity and location of contractures can play a role in the development of hip problems. Although CHD is not a hallmark of FSS, its presence in some patients suggests that the underlying pathology can, in certain cases, affect hip joint development (9–11). In this case, radiographic evaluation confirmed congenital dislocation of the right hip in this patient, a finding that, while not a hallmark of FSS, has been documented in several case reports within the literature. The observed superior and posterior displacement of the femoral head, along with changes such as decreased femoral epiphysis height and horizontal proximal femoral physis, highlights that the underlying musculoskeletal involvement in FSS can, in some instances, extend to the hip joint development.

Several studies and case reports have documented the occurrence of Freeman-Sheldon syndrome within families, providing evidence for its heritable natureM. Biri B *et al* described FSS as a rare hereditary disorder that can occur sporadically or be inherited in an autosomal dominant, and rarely autosomal recessive, manner . The article also noted that in cases with a known family history of FSS, prenatal detection might be possible through ultrasonography around the 20th week of gestation, highlighting the importance of recognizing familial patterns for early diagnosis. However, the same article also presented a case of a child with typical FSS features but no family history, suggesting a de novo mutation as the cause . Another case report from the same journal reiterated the possibility of sporadic, autosomal dominant, and rare autosomal recessive inheritance, again describing a case with no family history, thus likely representing a new mutation (12). A study characterizing genotype-phenotype relationships in 46 families with distal arthrogryposis type 2A (Freeman–Sheldon syndrome) found MYH3 mutations in 43 of these families, further establishing the genetic basis of the condition and its presence across multiple families . This research also indicated a wide phenotypic variability among individuals with the same MYH3 mutations, suggesting that even within families, the severity and specific features of FSS can differ (13). A case report reported by Ali A *et al* described a male infant with characteristic FSS signs, which were confirmed by genetic analysis revealing a de novo mutation in the MYH3 gene. The authors emphasized that while FSS is inherited in an autosomal dominant pattern, most cases occur sporadically with no family history of the disease(2). Another study discussed that while most reported cases of FSS are sporadic, there are reports indicating autosomal dominant inheritance in several families. Notably, this study also mentioned instances suggesting autosomal recessive inheritance, where affected children were born to clinically normal parents . The study presented a case of an 11-year-old girl with FSS born to consanguineous parents with no other affected family members reported, raising the possibility of autosomal recessive inheritance in this particular family (5). In this case, the father's history of similar hand deformities and characteristic facial features provides strong evidence for autosomal dominant inheritance in this family, consistent with findings in the literature. Furthermore, his history of bilateral foot surgery and Achilles tendon lengthening underscores the variable musculoskeletal involvement in FSS, a feature also noted in various case reports and studies.

CONCLUSION

This detailed case report of an 11-year-old male with Freeman-Sheldon syndrome presenting with a less common association of unilateral congenital hip dislocation and prominent bilateral wrist flexion contractures, along with a supportive family history, contributes to the understanding of the phenotypic variability of this rare disorder. The case emphasizes the importance of a comprehensive clinical evaluation, including meticulous assessment of facial features, limb involvement, developmental history, and family history, in the diagnosis of FSS. Despite significant musculoskeletal involvement and developmental delays, the patient demonstrates good functional adaptation. This report highlights the need for increased awareness of the diverse musculoskeletal manifestations of Freeman-Sheldon syndrome to facilitate accurate diagnosis and appropriate multidisciplinary management.

Learning Points

Freeman-Sheldon syndrome can present with a wider range of musculoskeletal anomalies than classically described, including congenital hip dislocation.

Detailed assessment of characteristic facial features and distal limb contractures is crucial for clinical diagnosis.

A thorough developmental history can provide insights into the functional impact of the syndrome.

A positive family history of similar features strongly supports the autosomal dominant inheritance of FSS.

Individuals with FSS can exhibit variable functional outcomes, and adaptation for daily activities and participation in sports is possible.

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Consent for Publication

Written informed consent was obtained from the patient's legal guardians for the publication of this case report and any accompanying images..

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