J Orthop Spine Trauma. 2024 December; 10(4): 174-6. DOI: 10.18502/jost.v10i4.17370

Case Report

Diagnosis and Management of Freeman-Burian Syndrome: A Case Report

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Received: 11 August 2024; **Revised:** 02 October 2024; **Accepted:** 05 November 2024

Abstract

Background: Freeman-Burian syndrome (FBS) is a rare genetic disorder characterized by facial deformities, arthrogryposis, and difficulties in orthopedic management.
Case Report: A case study of a nine-month-old female patient with FBS is presented, who exhibited facial abnormalities and contractures of the hands and feet. Non-operative treatment, including stretching, massage, and splinting, was initially advised. At nine months, bilateral Achilles tenotomy was performed under local anesthesia due to anesthetic risks. Serial casting and bracing were used to maintain the correction.
Conclusion: The authors recommend prompt treatment, especially with non-operative methods, and early training of parents in non-operative therapy for optimal results, as multiple surgeries and anesthetic complications can lead to suboptimal outcomes. Massage, stretching, and achieving stable plantigrade feet are crucial for independent walking in patients with FBS.

Keywords: Craniocarpotarsal Dysplasia; Freeman-Burian Syndrome; Freeman-Sheldon Syndrome; Whistling Face Syndrome

Citation: Arabzadeh A, Azaditalab H, Alitaleshi H, Abbaszadeh M. **Diagnosis and Management of Freeman-Burian Syndrome: A Case Report.** *J Orthop Spine Trauma* 2024; 10(4): 174-6.

Background

Freeman-Burian syndrome (FBS) is an extremely rare congenital autosomal dominant combined skeletal and muscular dysplasia with craniocarpotarsal manifestations that presents many difficulties in orthopedic management (1). There are also anesthetic concerns about malignant hyperthermia and difficult intubation (2, 3). FBS was first reported by Freeman and Sheldon (4) and Burian (5).

Case Report

A nine-month-old female child was born to non-consanguineous and healthy parents. Her mother was 34 years old, and her father was 42 years old. There was no known family history of any congenital malformation. During pregnancy, her mother did not suffer from any disease and did not use any drug other than vitamin or mineral supplements.

The child was referred with severe and rigid bilateral clubbed feet (Figures 1B and 2A) and windblown ulnar deviated hand, clasped thumb, overlapping fingers (Figures 1, 3A, and 3B), absent palmar creases (Figure 3C), and multi-joint contracture (Figure 1). On visits to some pediatricians and orthopedists, no specific treatment was performed due to her microcephaly and the possibility of a poor prognosis. Nevertheless, treatment was started with us without wasting time since she had achieved some developmental milestones and a head circumference above 35 cm, yet there was the presence of moderate failure to thrive.

Furthermore, she presented a mask-like face, midface hypoplasia, hypertelorism, microphthalmia, deep-set eyes, ptosis, blepharophimosis, and strabismus. Other findings were microstomia with the typical facial appearance of a whistler, an H-shaped cutaneous dimple on the chin, an abnormally long philtrum, micrognathia, and a low-set ear (Figure 1). These signs suggested a syndrome with difficult management that was explained to the parents, and they were referred to genetic counseling for a definitive diagnosis.

Figure 1. The gross appearance of the Freeman-Burian syndrome (FBS); A) Fifteen-month-old; B) Four-year-old child showing long philtrum, an H-shaped dimpling of the chin, whistling mouth appearance, bilateral windblown ulnar deviated hand, and bilateral club foot

The report of genetic analysis noted the identification of a pathogenic mutation in the gene of myosin heavy chain (MYH3) in a heterozygous form, which explains the child's symptoms and is the cause of FBS with autosomal dominant inheritance.

At first, her parents were advised to do regular stretching, massage, and splinting of rigid hands. At the earliest opportunity, at the nine-month age, bilateral Achilles tenotomy was performed using sedation with a local anesthetic due to the high risk of general anesthesia.

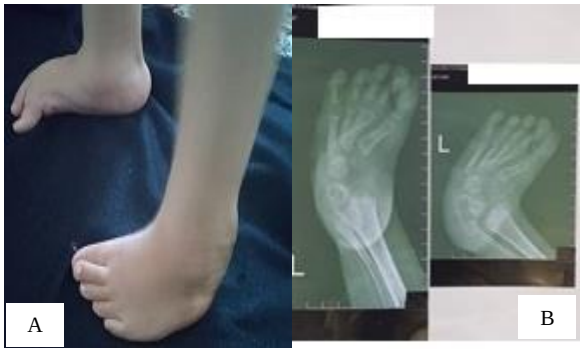

Figure 2. Foot deformity of the Freeman-Burian syndrome (FBS); A) Talipes equinovarus deformity; B) Tarsal coalition in foot radiography

Besides, serial casting was accomplished, followed by a long period of bracing to maintain the correction.

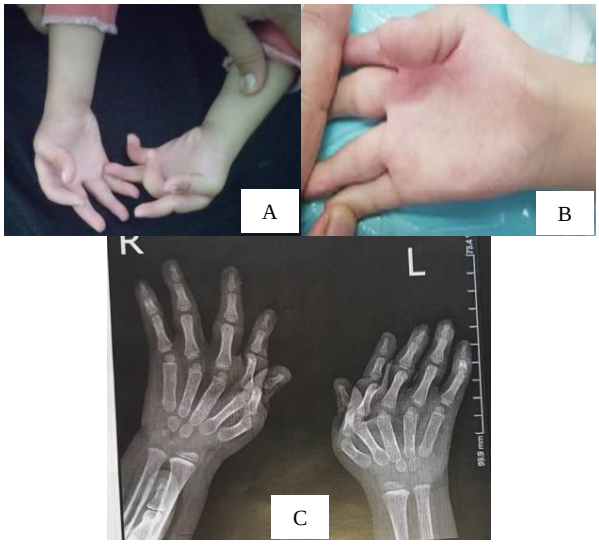

Figure 3. Hand deformity of the Freeman-Burian syndrome (FBS); A) Windblown ulnar deviated hand, and clasp thumb; B) Absence of palmar creases and wrinkles; C) Ulnar deviation of wrists and fingers in hand radiography

Now she is four years old, and some recurrence of foot deformity occurs; later X-ray shows tarsal coalition (Figure 2B) but walks independently with retarded locomotion. Her clasped thumb tends towards bony deformity, and she will need surgical first web contracture release. This procedure can be scheduled if her parents provide informed consent. Her speech was nasal but comprehensible and had intact neuro-cognitive function.

Discussion

The current study describes a case of FBS, a rare genetic disorder characterized by facial deformities and arthrogryposis. The patient had facial deformities, including microstomia, an H-shaped cutaneous dimple on the chin, and a long philtrum, fulfilling the Stevenson et al. diagnostic criteria for FBS (6). Additionally, she had contracture of the distal joints of hands and feet, including bilateral windblown ulnar deviated hands, clasped thumb, and bilateral rigid talipes equinovarus.

Due to the rarity of the disease (about 0.9 per million), the diversity of its manifestations and its overlap among different types of arthrogryposis, and the lack of clarity in the literature, diagnosis and management of FBS are difficult and controversial (3). In our case, the diagnosis was made based on facial deformities and arthrogryposis, combining the report of genetic analysis.

The etiology of FBS, in this case, had a genetic basis, possibly a mutation in the gene of embryonic MYH3. Mutation in the gene of MYH3 is a known pathogenic cause of inhibition of adenosine triphosphate (ATP) binding to myosin (7) that results in impaired muscle contraction and myo-physiologic development with fibrosis and contracture and recurrence of deformities (8).

The management of FBS is intricate and controversial, and the reported results of treatment and long follow-ups are insignificant and less published (1). However, optimal management is probably best obtained by fibrous tissue stretching and releasing through a combination of physiotherapy and surgery to decrease contractures (3).

In this case, the patient's rigid foot deformities were managed with Achilles tenotomy, followed by weekly serial casting according to the Ponseti method, and then with bracing. Achilles tenotomy was performed using sedation with a local anesthetic due to the high risk of general anesthesia in patients with FBS, including difficult intubation, malignant hyperthermia, and postoperative pulmonary complications. Even though some recurrence of foot deformity occurs, she could walk independently, and our result is in accordance with the previous study (1). In the future, the ankle may need fusion.

In the management of the windmill vane hand in our case, non-operative treatment started as soon as possible to improve the position of the finger. Her clasped thumb tends to bony deformity, and we planned for surgical first web contracture release before four years old to reduce the progression of skeletal deformities and maladaptive learning behaviors (9).

Because of the presence of fibrous tissue bands and their tendency to reform, recurrence of deformities is the rule, even with the operation. However, for those who have nothing, small improvements are great, too. However, their disabilities were diminished with simple massage and stretching, especially if undertaken as soon as possible, and our results are similar to those of other studies (1).

Since this patient had near normal neuro-cognition and, on the other hand, she had social avoidance and poor self-image, she was advised to seek psychological assistance to potentiate her functioning, overall health, and independent life.

Conclusion

We recommend prompt treatment, particularly with non-operative methods, for a better prognosis. Early and closely supervised training of parents in non-operative therapy is crucial for optimal results, as multiple surgeries and anesthesia complications can lead to suboptimal outcomes. Parents should be advised to start massage and stretching, especially for complex hand deformities, and every effort should be made to achieve stable plantigrade feet for independent walking.

Conflict of Interest

The authors declare no conflict of interest in this study.

Acknowledgements

The authors thank Dr. Elham Harati, who provided a

careful and critical review of the manuscript, guidance in the literature review, and technical assistance.

Informed consent to publish the patient's pictures was obtained from her parents, and efforts was made to conceal her name and identity.

This study received no funding.

References

1. Poling MI, Dufresne CR, McCormick RJ. Identification and recent approaches for evaluation and management of rehabilitation concerns for patients with Freeman-Burian syndrome: Principles for global treatment. *J Pediatr Genet*. 2020;9(3):158-63. doi: 10.1055/s-0040-1710339. [PubMed: 32714615]. [PubMed Central: PMC7375843].
2. Fisher K, Qasem F, Armstrong P, McConachie I. Anesthetic considerations in a parturient with Freeman-Sheldon syndrome. *Int J Obstet Anesth*. 2016;27:81-4. doi: 10.1016/j.ijoa.2016.02.001. [PubMed: 27016877].
3. Poling MI, Dufresne CR, Chamberlain RL. Freeman-Burian syndrome. *Orphanet J Rare Dis*. 2019;14(1):14. doi: 10.1186/s13023-018-0984-2. [PubMed: 30630514]. [PubMed Central: PMC6327538].
4. Freeman EA, Sheldon JH. Cranio-carpo-tarsal dystrophy. *Arch Dis Child*. 1938;13(75):277-83. doi: 10.1136/adc.13.75.277. [PubMed: 21032118]. [PubMed Central: PMC1975576].
5. Burian F. The "whistling face" characteristic in a compound cranio-facio-corporal syndrome. *Br J Plast Surg* . 1963;16:140-3. doi: 10.1016/s0007-1226(63)80095-8. [PubMed: 14017017].
6. Stevenson DA, Carey JC, Palumbos J, Rutherford A, Dolcourt J, Bamshad MJ. Clinical characteristics and natural history of Freeman-Sheldon syndrome. *Pediatrics*. 2006;117(3):754-62. doi: 10.1542/peds.2005-1219. [PubMed: 16510655].
7. Al-Haggar M, Yahia S, Damjanovich K, Ahmad N, Hamada I, Bayrak-Toydemir P. p.R672C mutation of MYH3 gene in an Egyptian infant presented with Freeman-Sheldon syndrome. *Indian J Pediatr*. 2011;78(1):103-5. doi: 10.1007/s12098-010-0230-y. [PubMed: 20924721].
8. Tajsharghi H, Kimber E, Kroksmark AK, Jerre R, Tulinius M, Oldfors A. Embryonic myosin heavy-chain mutations cause distal arthrogryposis and developmental myosin myopathy that persists postnatally. *Arch Neurol*. 2008;65(8):1083-90. doi: 10.1001/archneur.65.8.1083. [PubMed: 18695058].
9. Gavaskar KG, Chowdary N. Surgical management of windblown hand: Results and literature review. *J Child Orthop*. 2009;3(2):109-14. doi: 10.1007/s11832-009-0163-z. [PubMed: 19308621]. [PubMed Central: PMC2656951].