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Case Report **Pediatrics**

Hyaline Fibromatosis Syndrome: A Case Report and Review of Literature

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Abstract

Background: Hyaline fibromatos is syndrome (HF) is a rare condition characterized by hyaline deposits in the papillary dermis that lead to joint contractures, motor impairment, thickened skin, and hyperpigmented macules. Severe cases may present with protein-losing enteropathy (PLE), increasing the risk of mortality. The diagnosis of HFS involves clinical evaluation, genetic analysis of ANTXR2 variants, skin and intestinal biopsies, skeletal x-rays, and molecular genetic testing. Treatment focusses on the management of symptoms and includes various interventions such as splinting, excision of lesions, hydration, and pharmacotherapy. ***Case presentation:*** We present the case of a 2-month-old female child with HFS, born prematurely to consanguineous parents. The child exhibited characteristic symptoms, including excessive crying, limb deformities, and congenital hypothyroidism. Despite symptomatic management and prenatal diagnosis counseling, the child succumbed to sepsis after a month. ***Conclusions :*** HFS presents significant challenges in clinical management, particularly in severe cases where complications such as protein-losing enteropathy can lead to fatal outcomes. Early diagnosis through comprehensive genetic and clinical evaluation is crucial for appropriate management and counseling of affected individuals and their families.

Keywords: Hyaline Fibromatosis Syndrome; infantile systemic hyalinosis; genetic analysis; ANTXR2 variants; protein-losing enteropathy; joint contractures; motor impairment; prenatal diagnosis.

INTRODUCTION

Hyaline Fibromatosis Syndrome (HFS), also known as infantile systemic hyalinosis, is a condition characterized by hyaline deposits in the papillary dermis, causing discomfort, joint contractures, motor impairment, thicker skin, and hyperpigmented macules. It can lead to protein-losing enteropathy (PLE) complications, with severe cases posing a high risk of death [1]. The diagnosis of HFS is typically confirmed through a comprehensive approach. This involves assessing clinical features, identifying variants in the anthrax toxin receptor 2 (ANTXR2) gene, conducting skin and intestinal biopsies, and examining skeletal x-rays [2]. Treatment for symptoms of a medical condition can involve the following: gentle handling, splinting, consultation with pain management specialists, excision of airway lesions, difficulties with endotracheal intubation, excision of perianal masses, treatment for skin nodules, hydration, and albumin infusions, physiotherapy for joint contractures, non-steroidal anti-inflammatory drugs, opiates, and gabapentin [1]. Infection or complications PLE can be fatal. A milder phenotype, possibly with a later onset and possible survival into maturity. From mild to severe/deadly, a clinical classification system for HFS has been developed. Sepsis and organ failure are associated with the most severe forms [3].

CASE PRESENTATION

History: A 2-month-old child (Figure 1), born to a consanguineous couple as depicted in Figure 2 (Pedigree), was brought in with complaints of excessive crying and deformity of both limbs, accompanied by spasms. Furthermore, any attempt at manipulation by the parents results in excessive crying, with no alleviation from stiffness. She is the late product of an emergency cesarean section at 32 weeks due to placental abruption at 8 months. Upon birth, the baby was admitted to the neonatal intensive care unit (NICU) for 18 days due to prematurity, with a weight of 1000g (less than the third percentile). Following discharge from the NICU, her mother noticed abnormal positioning, tenderness in both limbs, and excessive

crying during handling. She is a known case of congenital hypothyroidism without goiter. Upon detailed inquiry, it was revealed that there were frequent episodes of upper respiratory tract infections and diarrhea since birth. In addition, there is a history of similar complaints in another older sibling, who passed away at the age of 1 year, 12 years ago, with multiple abnormalities and cardiac problems.

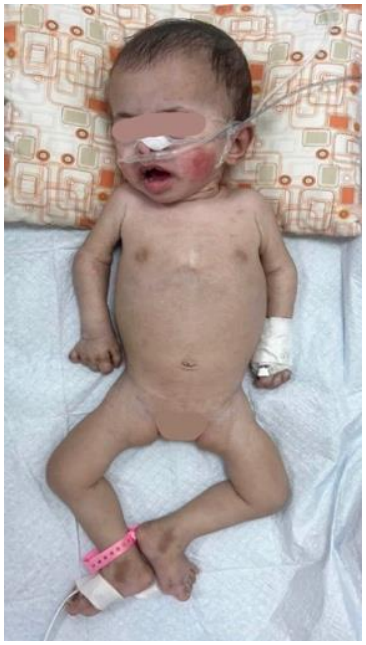

Figure 1: Clinical Photograph of baby

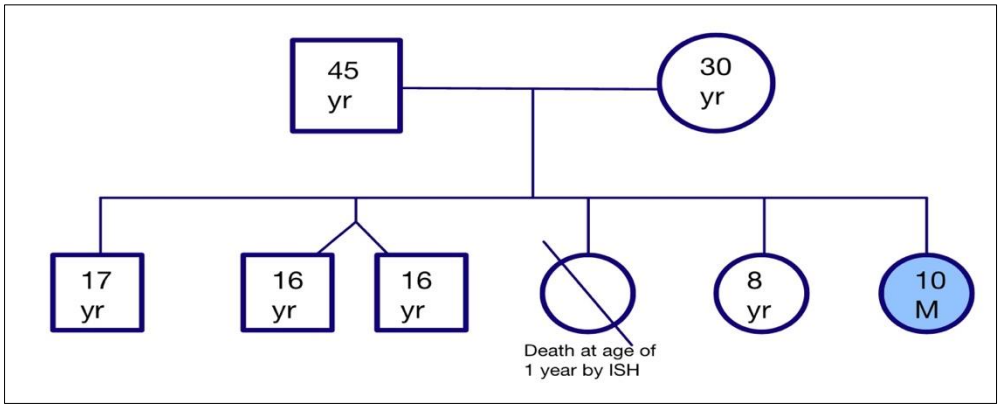

Figure 2: Pedigree chart

Clinical examination: Clinical examination revealed a well-looking and active child with no signs of dehydration. The child weighed 4.59 kg (below the 3rd centile) and measured 45 cm in height (below the 3rd centile). Blood pressure was measured at 100/50. Bilateral tenderness was observed in both limbs, along with limited movement. Additionally, the child exhibited bilateral adduction and internal rotation of the shoulders, extended pronation of the elbows, flexed wrists, and flexion deformity of the hips and knees. Her neck appeared short and thick, with an erythematous plaque present over the auricular area and the back of the neck, accompanied by a mild deviation to the right side. Excessive eye discharge was observed. Cautery marks were observed on the back along with Mongolian spots. Hypertrophic gums were evident, and the lower lip appeared to be everted due to a prominent gingival mass. Additionally, fleshy nodular excrescences around the anus were noted (Figure 3: A-I).

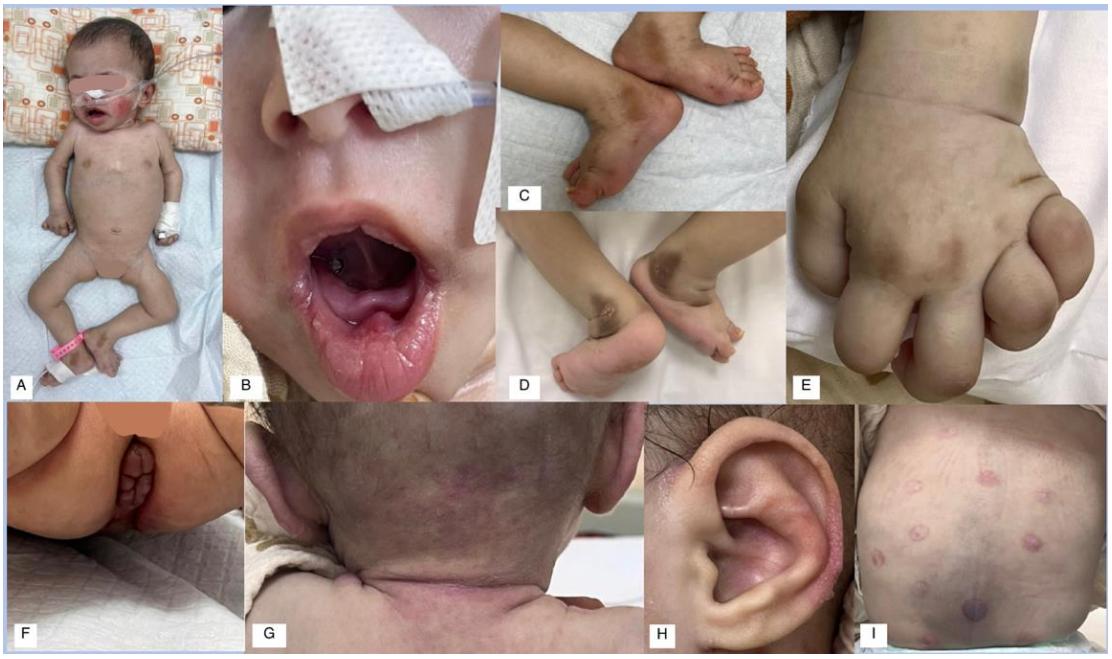

Figure 3:
A: Clinical photograph showing deviation of neck to right, flexion deformity of both hips and knees and extension attitude of both the elbows.
B: Photograph of hypertrophied gums. The lower lip is everted due to prominent gingival mass.
C&D: Photograph of ankle with foot depicting hyper pigmented patches, swollen ankle and foot.
E: Photograph showing swollen hand with clawing of fingers and hyper pigmented patches in the creases.
F: Photograph of perineum depicting perianal fleshy excrescence/nodule
G & H: Photograph of erythematous plaque in the auricular area and neck.
I: Photograph of cautery marks in the back and Mongolian spots

Laboratory findings: Laboratory hematology results were within normal limits. Clinical chemistry analysis indicated decreased levels of Albumin (16.33 g/L; reference range: 35-50 g/L), calcium (1.65 mmol/L; reference range: 2.20-2.60 mmol/L), serum creatinine (15 umol/L; reference range: 53-97 umol/L), and potassium (3.6 mmol/L; reference range: 3.5-5.0 mmol/L). TSH levels were low (0.104 uIU/mL; reference range: 0.4-4.0 uIU/mL).

Management and outcome: The baby was treated symptomatically. Parents received counseling on the importance of undergoing a prenatal diagnosis by sampling the chorionic villus in future pregnancies. Unfortunately, the child passed away at 1 years old due to sudden cardiac arrest.

DISCUSSION

HFS was meticulously described by Landing in 1986 and is among the differential diagnoses of infantile stiff skin syndromes [4]. Despite considerable research, the exact pathogenesis of these hyalinosis syndromes remains elusive. However, recent studies have indicated an increase in chondroitin synthesis by skin fibroblasts in systemic hyalinosis, offering a potential avenue for further investigation into the underlying mechanism [5]. HFS has been reported worldwide in all ethnic groups, but it exhibits a notably higher prevalence among Middle Eastern and North African populations. Regrettably, HFS carries a very poor prognosis, often leading to death within the first two years of life. Recurrent chest infections, stemming from impaired chest wall movement, emerge as the primary cause of mortality [6]. While in this case, the cause of death was sudden cardiac arrest.

Other conditions in this category include Winchester syndrome, congenital fascial dystrophy, infantile restrictive dermopathy, and juvenile hyaline fibromatosis (JHF). The clinical presentation of HFS and JHF is notably similar. Both conditions stem from defects in the ANTXR2 gene. Common clinical characteristics include pain after minimal handling of the child, progressive joint contractures affecting the upper and lower extremities, gingival hypertrophy, and the presence of fleshy subcutaneous and perianal nodules, all of which exhibit similar histological findings. Almost all characteristic clinical features of HFS were detected in our patient. Following the diagnosis of the patient.

Distinguishing between HFS and JHF poses a challenge, given their overlapping symptoms. However, ISH typically manifests early with severe and progressive forms, often resulting in death within the first two years of life and potentially leading to the development of malabsorption. Diagnosis of both conditions requires a high index of suspicion [7]. In the

case described here, the onset of the disease occurred early and manifested within the first 2 months of life. The condition exhibited a progressive course, suggesting rapid deterioration and advancement of symptoms over time.

Currently, there is no specific treatment available for HFS, and management primarily revolves around providing supportive care. Some reports have explored the use of D-penicillamine, which has shown a modest improvement in joint mobility by inhibiting the collagen mutation [8]. Surgical excision can be considered for troublesome nodules, while joint contractures require dedicated physiotherapy interventions. Despite efforts, systemic hyalinosis remains a poorly understood condition within the realm of ground substance biology, presenting both diagnostic and therapeutic challenges for treating physicians.

CONCLUSIONS

In summary, this case highlights the complex issues involved in the management of HFS, especially in severe cases with co-occurring conditions like PLE. The prognosis for people with HFS is still uncertain despite advances in therapeutic interventions and diagnostic techniques, which emphasizes the need for more studies to clarify the underlying pathophysiology and discover cutting-edge treatment approaches. Optimizing results and minimizing consequences requires early diagnosis, thorough genetic screening, and multidisciplinary care. In general, this example highlights how crucial it is to manage cases with HFS and enhance their quality of life through a coordinated strategy comprising doctors, geneticists, and supportive care providers.

REFERENCES

1. Shieh, J.T., H.E. Hoyme, & L.T. Arbour, *Hyaline fibromatosis syndrome.* 2020.
2. Patel, N.J. & J. Jankovic, *NKX2-1-related disorders.* 2016.
3. Denadai, R., *et al.*, *Identification of 2 novel ANTXR2 mutations in patients with hyaline fibromatosis syndrome and proposal of a modified grading system.* Am J Med Genet A, 2012. **158a**(4): p. 732-42.
4. Landing, B.H. & R. Nadorra, *Infantile systemic hyalinosis: report of four cases of a disease, fatal in infancy, apparently different from juvenile systemic hyalinosis.* Pediatric pathology, 1986. **6**(1): p. 55-79.
5. Finlay, A., S. Ferguson, & P. Holt, *Juvenile hyaline fibromatosis.* British Journal of Dermatology, 1983. **108**(5): p. 609-616.
6. Al-Mayouf, S., *et al.*, *Infantile systemic hyalinosis: a fatal disorder commonly diagnosed among Arabs.* Clinical and experimental rheumatology, 2005. **23**(5): p. 717.
7. Nofal, A., *et al.*, *Juvenile hyaline fibromatosis and infantile systemic hyalinosis: a unifying term and a proposed grading system.* Journal of the American Academy of Dermatology, 2009. **61**(4): p. 695-700.
8. Sahn, E.E., *et al.*, *Infantile systemic hyalinosis in a black infant.* Pediatric dermatology, 1994. **11**(1): p. 52-60.