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Hyaline fibromatosis: Two case reports and literature review

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ABSTRACT

Hyaline fibromatosis (HF) is a rare genetic disease, with two types that have an early onset. The disease is distinguished by hyaline deposition at different areas in the body, osteolytic bony lesions, and gingival hypertrophy. There are two variants of the disease, juvenile and infantile HF. In this report, we present two cases of HF that were seen in National Guard Hospital within Riyadh – Kingdom of Saudi Arabia.

Keywords: Juvenile; Hyaline; Infantile; Fibromatosis; Autosomal

1. INTRODUCTION

Hyaline fibromatosis (HF) is an uncommon autosomal recessive disease, with two variants that share an early presentation in the first years of life. There are two expressions of the disease, the less severe form juvenile hyaline fibromatosis (JHF) and the potentially lethal form infantile hyaline fibromatosis (ISH) (Marques et al., 2016). The disease is characterized by abundant hyaline deposition at different sites in the body giving cutaneous, mucous, internal involvement, and osteolytic bony lesions (Mantri et al., 2016). We reported two cases of HF that were seen in the Oral and Maxillofacial Surgery Department in National Guard Hospital within Riyadh – Kingdom of Saudi Arabia.

2. CASE REPORT 1

A 33-month-old baby boy case of hyaline fibromatosis was confirmed by molecular testing. A homozygous pathogenic variant in ANTXR2 was also found in the mother. The baby is born to a non-consanguine marriage. The patient presented to the hospital with symptoms of respiratory distress while sleeping, manifested by daily snoring, apnea attacks, and mouth breathing, that was later found to have hypertrophied adenoids. Moreover, he is a known case of valvular heart disease. Relatively, the head and neck area had no dysmorphic features except for a scalp cutaneous nodule in the occipital region and bilateral ear nodules (Figure 1). No organomegaly in the abdomen has been reported, though feeding is limited to a Nasogastric tube (NGT) due to the gastroesophageal reflux. Joint stiffness with chronic pain and limitation in mobility; affect the lower limbs more. In addition to that, a history of diarrhea has been documented and history of aspiration pneumonia. Intraoral examination showed heavy fibrotic lesions on both the right and left buccal

mucosa with gingival hyperplasia, mostly in the lower arch. A retention cyst was noted around the erupting primary maxillary incisor as shown in (Figure 2), and no obvious abnormality was noted in the tongue. Gingivectomy was done for the lower arch and histopathologic examination of the resected gingival tissue showed pseudoepitheliomatous hyperplasia, dermal/submucosal hyaline material deposition, ecstatic blood vessels and slit-like stellate cells (Figure 3 & 4). The CT revealed moderate adenoid hypertrophy, but the neck CT revealed a patent airway. The Complete Blood Count (CBC) revealed normal levels, except for the high WBC.

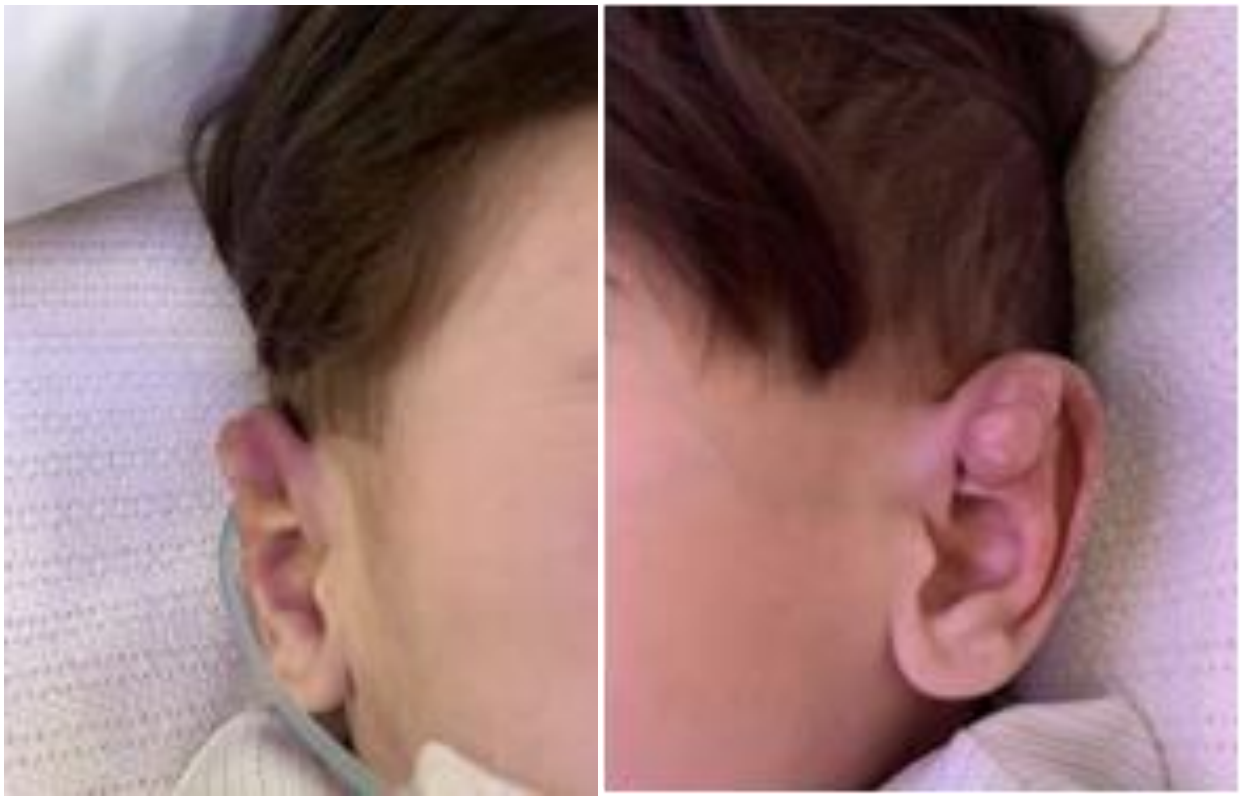

Figure 1 Bilateral Ear Nodules

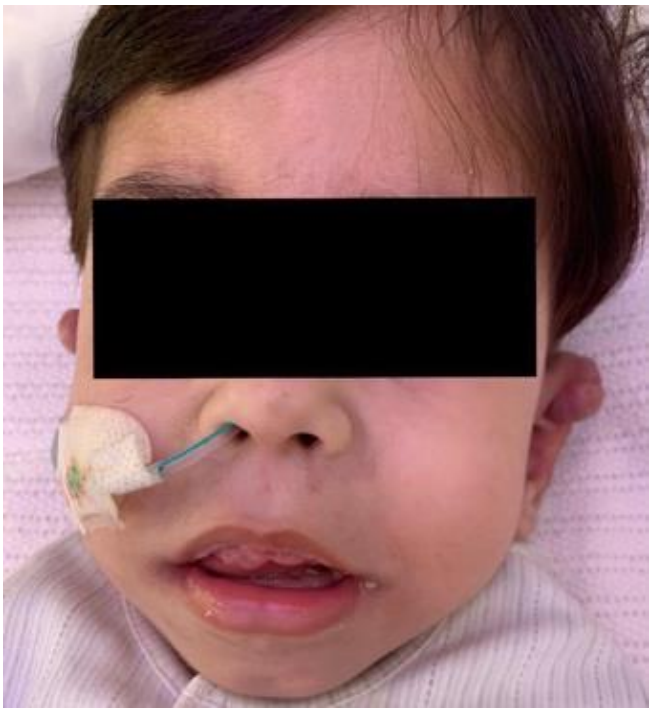

Figure 2 Gingival Hyperplasia and retention cyst around the erupting primary maxillary incisor

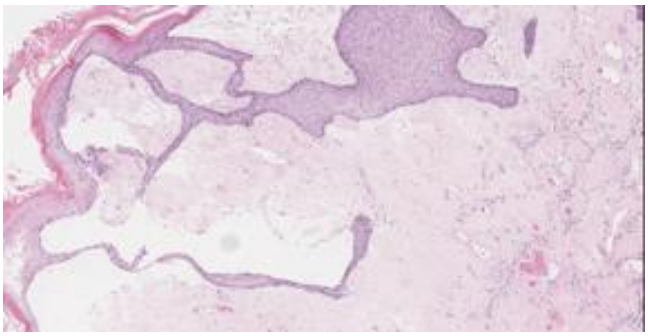

Figure 3 Histopathologic slide of the resected gingiva (H&E stain)

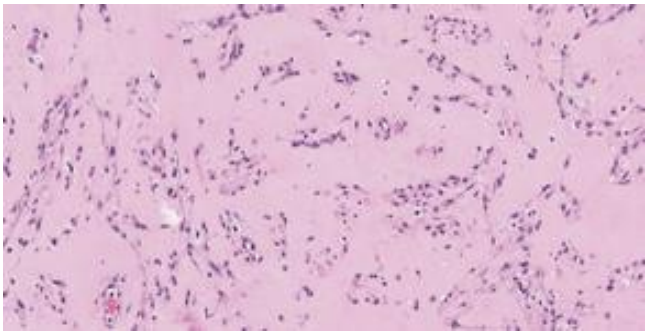

Figure 4 Higher magnification of the lesion shows eosinophilic hyalin material and the slitlikestellate cells (H&E stain)

3. CASE REPORT 2

A 29-month-old baby girl, a known case of infantile hyaline fibromatosis, was confirmed by molecular testing of a homozygous pathogenic variant in ANTXR2.

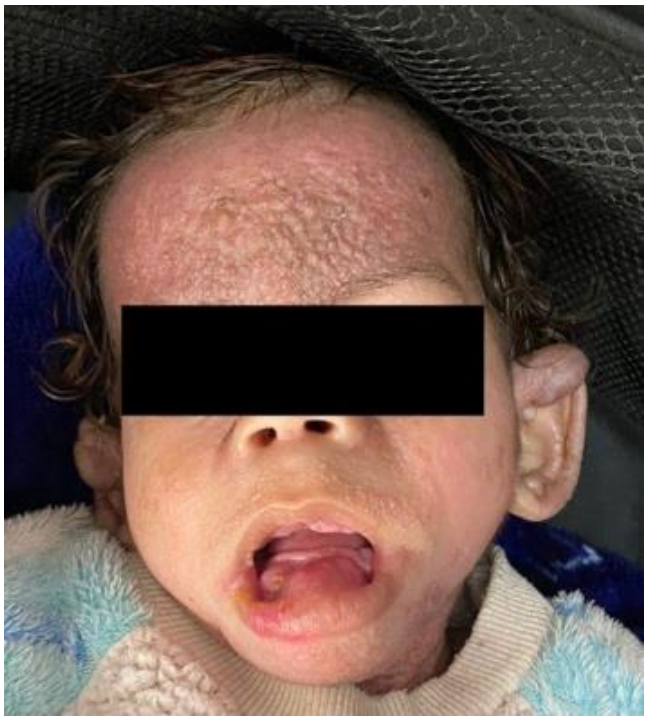

Figure 5 lower lip fibrotic non-ulcerative surfaces that are firm, on the inner surface (lower labial mucosa) from canine to canine.

The baby was born into a non-consanguine marriage, with no history of the disease in the family presented to the hospital with symptoms of joint contracture, right-sided club foot, arthropathy, limited mobility, bilateral developmental dysplasia of the hip (DDH), osteopenia, delayed growth, flashy anal nodule, and hyperpigmentation over joint prominence with severe rash. Moreover,

history of diarrhea and vomiting has been documented. For the head and neck area, the patient had subtle dysmorphic features, long philtrum, depressed nasal bridge, low set ears, multiple skin pigmentation on the forehead, neck, chin, and facial dermatitis including the neck, and nodules (inflamed skin tag, fibroepithelial polyp) as shown in (Figure 3). Intra-oral examination showed a lower lip fibrotic non-ulcerative surface that is firm, on the inner surface (lower labial mucosa) from canine to canine as shown in (Figure 5). In addition to that, the patient had generalized gingival hypertrophy, covering all the anterior teeth completely with delayed teeth eruption. For patient management, Gabapentin 1g was prescribed for joint contracture pain and topical timolol for skin lesions. Excision of perianal skin tag was done, with a biopsy result of fibroepithelial polyp.

4. DISCUSSION

Hyaline fibromatosis syndrome is an uncommon genetic disorder caused by mutations in anthrax toxin receptor-2 gene (ANTXR2). The disease was first reported as Molluscum Fibrosum by Murray in 1873 (Casas-Alba et al., 2018; Baltacioglu et al., 2017). JHF is known to express papulonodular skin lesions, flexural joint contractures, osteolytic bone lesions, and gingival overgrowth with an early onset in first years of life (Casas-Alba et al., 2018). The disease was reported to occur more in ethnic populations like Turkish, Indian, and Moroccan, in areas where consanguinity is common. Up to date, fewer than 100 cases have been mentioned in the literature, and it has an equal female to male predilection (Baltacioglu et al., 2017; Knežević et al., 2020). Cutaneous lesions in the form of papules or nodules dispersed in the body involving the head, neck, scalp, and perianal region that grow with a recurrence tendency after surgical management (Marques et al., 2016).

Musculoskeletal involvement includes joint flexion contracture ranging from painful to limited range of movement and potentially causing disability, mandating wheelchair ambulation (Denadai et al., 2012). Gingival hyperplasia is an intraoral hallmark of the disease, as reported in our second case. Histologically, it is primarily a connective tissue disease with abnormal differentiated chondroid tissue deposition (Mayerda Silva et al., 1988). Denadai et al., (2012) proposed a modified grading system, with grade I (mild) involving skin and gingival involvement, grade II (moderate) progressing to joint and bony lesion, grade III (severe) involving internal organs, and finally, grade IV (lethal) involving organ failure and septicemia. The infantile type differs from the juvenile form with more severity in the former, causing more hyaline deposition in different organ systems, infections, failure to thrive, and early death within the first 3 years (Mantri et al., 2016). IHF presented in newborns with systemic involvement such as arthropathy, osteopenia, and short stature (Braizat et al., 2020). Regarding treatment, there are no guidelines on the treatment modality of the disorder hence esthetic, preventing orthopedic disability, and treating infections have been the focus of the treatment (Krishnamurthy et al., 2011). Moreover, the proposed treatment is gingivectomy for gingival hyperplasia. Intralesional and systemic steroids followed by surgical excision to manage the nodules and physiotherapy (Braizat et al., 2020; Knežević et al., 2020).

5. CONCLUSION

In conclusion, HF is a hereditary disease with two variants juvenile and infantile form. Both presented early in life and share common clinical features including hyaline deposition in different body parts and gingival overgrowth. We reported two cases in National Guard, Riyadh, kingdom of Saudi Arabia. Early diagnosis and proper management by multidisciplinary teams is required to improve patients' quality of life.

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Author Contributions

- Abdulatif Abuhaimed: Examination and diagnosis, manuscript writing, editing, and finalizing, communication with patient family, communication with different departments.
- Meshal Almunif: Examination and diagnosis, manuscript writing, editing.
- Mashaal Alswaidan: Examination, data collection, manuscript writing and finalizing.
- Sarah Aldosari: Data gathering, communication with patient family, manuscript writing, editing, and finalizing.
- Abdulmalik Alsahhaf: Data gathering, manuscript Writing.

Informed consent

Written & Oral informed consent was obtained from (Patient's parents) of all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there are no conflicts of interest.

Data and materials availability

All data associated with this study are present in the paper.

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