Juvenile Hyaline Fibromatosis: A 10-year Follow-up

Esra Baltacioglu, Esra Guzeldemir, Erkan Sukuroglu, Kadriye Yildiz, Pinar Yuva, Güven Aydin, Naci Karacal

Abstract
Juvenile hyaline fibromatosis (JHF) is a rare hereditary disease with an autosomal recessive transmission. JHF is characterized by papulonodular skin lesions, osteolytic bone lesions, flexural joint contractures, and gingival hyperplasia and usually diagnosed in infancy or early childhood. JHF is thought to be a disorder of collagen metabolism and characterized by homogenous amorphous eosinophilic material and fibrous tissue. We report the case of a 14-year-old male child with multiple papulonodular skin lesions, progressive flexion contractures of joints, and severe gingival hyperplasia, with a 10-year follow-up. Although the lesions were totally removed thrice during the last 10 years, they recurred rigorously.

Key Words: Gingival hyperplasia, gingivectomy, juvenile hyaline fibromatosis

Introduction
Juvenile hyaline fibromatosis (JHF) is a rare mesenchymal dysplasia that is inherited in an autosomal recessive transmission with unknown etiology. JHF is characterized by tumorous and papulonodular skin lesions, osteolytic bone lesions, flexural joint contractures, and gingival hyperplasia.[1] The skin lesions may consist of multiple, large cutaneous nodules or tumors involving head, commonly the scalp, ears, nose, lower lips, neck, and perianal regions. Gingival hyperplasia which can in turn lead to malnutrition, recurrent infections, and even death is a substantial finding. JHF is usually diagnosed in young infants and in children younger than 5 years.[2] We here in report a severe case of JHF with a 10-year follow-up.

Case Report
In 2003, a 14-month-old male child was referred to a dermatology clinic. The patient was born to third-degree consanguineous parents following normal pregnancy. His parents noticed limitation in moving his limbs after 2 months of his birth. When he was 6 months old, contractures of the knees and elbows and limitation of movement of the shoulders, wrists, ankles, interphalangeal joints, spine, hands, and hips were noticed.[3] Findings of his first evaluation included pink, confluent papules on the paranasal folds, chin, gluteal sulcus, and gluteofemoral regions, nodular lesions on his bilateral periauricular and perianal regions, joint contractures on his shoulders, knees, and elbows, and severe gingival hypertrophy.[4] Histopathological examination of a gingival biopsy revealed focal epithelial atrophy, proliferation of fibroblasts, superficial edema, and telangietasia. No mitotic activity or nuclear pleomorphism was observed. Immunohistochemical studies showed that the spindle-shaped cells were...
positive for vimentin but negative for alpha-smooth muscle actin, S-100 protein. The patient was diagnosed with JHF by dermatologists based on these clinic and histopathological findings.

In 2004, severe gingival hyperplasia was noticed [Figure 1a and b] and excised by cut cautery, and the other lesions were totally removed by scalpel under general anesthesia by a plastic and reconstructive surgeon.[3] The results of the histopathological examination showed an abundance of amorphous, homogeneous, eosinophilic extracellular matrix that contained spindle-shaped cells. The hyaline material was periodic acid-Schiff positive and did not stain with Congo red; the diagnosis was confirmed as JHF. As the literature review revealed that systemic steroid therapy and radiotherapy had only modest success and long-term risks, the patient was planned to be seen on follow-up visits frequently.

In 2008, when he was 6 years old, he was referred to the Department of Periodontology for the evaluation of severe gingival hyperplasia. He had compromised oral hygiene and mastication and feeding and sucking difficulties, which lead to malnutrition caused by gingival overgrowth. Physical examination revealed multiple papular lesions on the neck, nodular lesions on the perianal region, flexion contracture of the joints, and limited motion of the right shoulder. Nodules in both ears and nodular and confluent, pink lesions in the nose were noted [Figure 2a]. Intraoral examination of the patient revealed diffuse gingival hyperplasia which presented with hyperemic, edematous, and inflammatory gingiva and spontaneous gingival bleeding. He also had multiple mucosal nodules and fibrous lesions on the buccal and labial mucosa [Figure 1c].

A periodontal surgery was planned for removing excessive gingival tissue and contouring the texture of the gingiva. Since he was 6 years old, the patient underwent gingivectomy operation (periodontal surgery) by scalpel under the general anesthesia. During the surgery, excessive hemorrhage was experienced. The severe periodontal destruction was observed especially in the posterior region where intense and larger gingival hyperplasia was seen as compared to other sides. Involved teeth were removed at the posterior region. Recovery from general anesthesia and postoperative healing was uneventful. Figure 3 shows postoperative 10th day. However, the gingival hyperplasia was recurred in a month and persisted.

The maintenance visits were scheduled; however, the patient did not show up. When we called the patient, his parents reported that he was not able to remove his body easily; they did not accept to bring him to the hospital. At the phone call, it was learned that the patient was operated once again in 2010 and all excessive tissues in his body were removed; nevertheless, the results could not be maintained and the recurrence was seen in 1½ years later and we informed that another operation was planned for him in November 2012.

Before fourth surgery, his physician referred the patient to a periodontology clinic. When he came for consultation in October 2012, prognosis of the disease was worse and all lesions were remarkably large compared to previous visits in 2003, 2004, and 2008 [Figure 2b]. Severe progressive flexion contractures of joints increasingly limit movement than previous visits.[8] He was almost unable to walk and had difficulties while breathing. Hard and large nodules were present over his entire scalp and in the periauricular region, in both ears and nose. He had severe gingival
hyperplasia and his mouth opening was very limited because of stiffness in the temporomandibular joint. The patient was seen in the periodontology clinic in May 2013 for the last time due to similar severe oral clinic findings, and no surgical operation was applied on the gingiva due to the difficulty of the operation. The patient was then followed up by plastic surgeons. It was learned that any improvement was observed in the patients’ clinic status, and the prognosis deteriorated.

Discussion
In the present case report, the patient was 14 months old when he was diagnosed as JHF; the diagnosis was confirmed with histopathological examination of the gingival tissue specimens.[6-9] When he was first sent to the periodontology clinic, he was 6 years old. He was suffering from severe gingival hyperplasia which resulted in feeding difficulties, impaired oral hygiene, and unaesthetic view. The recommended treatment for gingival hyperplasia due to JHF is the surgical removal of the enlarged tissues/lesions; however, recurrences are common.[4-6]

The patient underwent a clinical follow-up examination. The rapid recurrences in a month were experienced following surgery. We failed to maintain postoperative result in long term. Nevertheless, control visits were scheduled; however, he did not show up after the last visit in 2008. On phone call, his parents reported that he could not remove easily due to severe flexion contractures joint and another surgery was planned for him soon. Then, he referred to periodontology for consultation in 2012 before surgery. Severe overgrowth of lesions and nodules and very limited mouth opening were noticed. Progressive flexion contractures of joints had increasingly limited movement compared to his visit in 2008. Contractures of the joints may be resulted with disability and immobilizing and need for wheelchair in his early adulthood.[10] Bound to wheelchair may trigger ulcerations, pain, and secondary infections. Hence, the main complications related to JHF are arising from contractions of joints and gingival overgrowth.[11]

There is strong evidence for the presence of a deleterious mutation in the capillary morphogenesis gene 2 located on chromosome 4q21.[11] Unraveling of this gene mutation responsible for this condition may lead the researchers correct this fundamental defect with gene therapies in the future and results with the cure of this life-restraining disease.[12]

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

What is new?
- The present case is unique due to 10 years follow up, rapidly progressive tissue overgrowth, and severe stiffness of the joints which is life threatening.
- The treatment of gingival hyperplasia due to JHF is surgical removal of the enlarged tissues; however, recurrences are common.

References
1. Karabulut AB, Ozdem BC, Onel D, Demiryont M. Management of airway obstruction in a severe case of juvenile hyaline fibromatosis. Ann Plast Surg 2005;54:328-30.
2. Shehab ZP, Raafat F, Proops DW. Juvenile hyaline fibromatosis. Int J Pediatr Otorhinolaryngol 1999;33:179-86.
3. Karaçal N, Gülçelik N, Yildiz K, Mungan S, Kutlu N. Juvenile hyaline fibromatosis: A case report. J Cutan Pathol 2005;32:438-40.
4. Yaylı S, Uncu S, Alpay K, Yildiz K, Cimsit G, Bahadir S. A case of juvenile hyaline fibromatosis. J Dermatol 2006;33:260-4.
5. Krishnamurthy J, Dalal BS, Sunila, Guabanna MV. Juvenile hyaline fibromatosis. Indian J Dermatol 2011;56:731-3.
6. Keser G, Karabulut B, Oksel F, Calli C, Ustün EE, Akalin T, et al. Two siblings with juvenile hyaline fibromatosis: Case reports and review of the literature. Clin Rheumatol 1999;18:248-52.
7. Quintal D, Jackson R. Juvenile hyaline fibromatosis. A 15-year follow-up. Arch Dermatol 1985;121:1062-3.
8. Katagiri K, Takasaki S, Fijiwara S, Kayashima K, Ono T, Shinkai H. Purification and structural analysis of extracellular matrix of a skin tumor from a patient with juvenile hyaline fibromatosis. J Dermatol Sci 1996;13:37-48.
9. Slimani S, Haddouche A, Haid S, Ladjouze-Rezig A. Juvenile hyaline fibromatosis: Focus on radiographic features in adulthood. Rheumatol Int 2011;31:273-6.
10. Ribeiro SL, Guedes EL, Botan V, Barbosa A, Freitas EJ. Juvenile hyaline fibromatosis: A case report and review of literature. Acta Reumatol Port 2009;34:128-33.
11. Hakki SS, Ataoğlu T, Avunduk MC, Erdemli E, Gunhan O, Rahman N. Periodontal treatment of two siblings with juvenile hyaline fibromatosis. J Clin Periodontol 2005;32:1016-21.
12. Dowling O, Difeo A, Ramirez MC, Tukel T, Narla G, Bonafe L, et al. Mutations in capillary morphogenesis gene-2 result in the allelic disorders juvenile hyaline fibromatosis and infantile systemic hyalinosis. Am J Hum Genet 2003;73:957-66.