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CASE REPORT OF JUVENILE HYALINE FIBROMATOSIS

General Surgery

Dr.Irugu kishan Junior resident , Sri Siddhartha medical college and hospital

Dr.Shivakumar.T* Professor ,Sri Siddhartha medical college and hospital*Corresponding Author

ABSTRACT

Juvenile Hyaline Fibromatosis (JHF) is a rare genetic disorder characterized by the deposition of hyaline material in soft tissues, leading to skin nodules, gingival hypertrophy, and joint contractures. This case report details the clinical findings, histopathological features, and genetic implications of a 22-year-old male diagnosed with JHF. The patient presented with multiple non-tender, firm nodules on the scalp, without other systemic symptoms. Histopathological examination from two separate instances (2005 and 2024) confirmed the presence of hyalinized stroma and fibroblasts without mitotic activity, leading to a diagnosis of JHF. This case highlights the essential role of histopathology in diagnosing JHF, given its non-specific clinical presentation. Genetic counseling was recommended due to the identification of potential CMG-2 gene mutations. This case adds to the limited literature on JHF and underscores the importance of considering this rare diagnosis in patients with similar dermatological presentations.

KEYWORDS

Juvenile Hyaline Fibromatosis, histopathology, genetic counseling, CMG-2 mutation, dermatological presentation.

INTRODUCTION

Juvenile Hyaline Fibromatosis (JHF) is a rare genetic disorder, primarily affecting children and young adults, characterized by the systemic deposition of a clear hyaline material in the skin, bones, and internal organs. The condition typically manifests with multiple skin nodules, gingival hypertrophy, joint contractures, and osteolytic bone lesions. The clinical presentation of JHF can vary greatly in severity, often leading to progressive disability and, in severe cases, early mortality due to organ dysfunction caused by extensive deposition of the hyaline material [1].

The genetic underpinnings of JHF have been linked to mutations in the capillary morphogenesis gene 2 (CMG-2), also known as the ANTXR2 gene. This gene is vital for the regulation of endothelial cell intercellular junctions and cytoskeletal organization. Mutations in ANTXR2 disrupt cellular adhesion and tissue integrity, leading to the pathological accumulation of hyaline material. This discovery not only offers insights into the etiology of JHF but also paves the way for potential genetic-based interventions [2].

Histopathologically, JHF is characterized by the deposition of amorphous, eosinophilic, hyaline material in the dermis. This material is usually accompanied by a proliferation of fibroblasts and a variable inflammatory response. These findings are crucial for diagnosis, particularly in distinguishing JHF from other fibromatoses and connective tissue disorders that may present with similar clinical features [3].

The rarity and complexity of JHF pose significant challenges in its management and treatment. Current therapeutic options are largely symptomatic and include surgical removal of the nodules to relieve pain or restore function, and physiotherapy to prevent joint contractures. However, these interventions do not address the underlying genetic cause or halt the progression of the disease [4].

In terms of epidemiology, JHF is extremely rare with just over a hundred cases reported worldwide. The disorder affects both genders equally and has been reported in various ethnic groups, suggesting a widespread genetic dispersion. Understanding the epidemiology of JHF is critical for developing effective management strategies and for genetic counseling of affected families [5].

The impact of JHF on quality of life can be profound. Physical deformities and functional impairments can lead to psychological stress and social stigmatization for patients. Moreover, the progressive nature of the disease can place a significant emotional and financial burden on families. Comprehensive care, therefore, involves not only medical but also psychosocial support [6].

Research into JHF has been limited, largely due to its rarity. Studies have primarily focused on case reports and small case series, which highlight the clinical variability of the disorder. There is a clear need for more systematic research to understand the natural history of JHF, the full spectrum of clinical manifestations, and the outcomes of various therapeutic interventions [7].

Advances in genetic testing and molecular biology offer hope for a better understanding of JHF. The identification of the CMG-2 gene as responsible for JHF provides a target for genetic testing, which can aid in the early diagnosis and management of the disease. Moreover, understanding the molecular mechanisms underlying the disorder could lead to the development of targeted therapies, potentially offering more effective treatment options [8].

The broader relevance of studying rare diseases like JHF extends beyond the immediate impact on affected individuals [9]. Rare diseases often provide unique insights into more common diseases and into biological processes in general [10]. The study of JHF, for instance, enhances our understanding of tissue remodeling and fibrosis, which has implications for a range of more prevalent fibrotic diseases.

This study aims to provide a comprehensive overview of Juvenile Hyaline Fibromatosis, focusing on its clinical, histopathological, and genetic aspects. By documenting and analyzing a case of JHF, this research hopes to contribute to the scant literature and improve understanding of the disease, ultimately aiding in the development of more effective diagnostic and therapeutic strategies. Our study emphasizes the need for increased awareness and research into rare diseases, which despite their rarity, have significant implications for medical science and patient care.

CASE REPORT

A 22-year-old male, presented with multiple swellings on his scalp that he had first noticed several years prior. These swellings had been gradually increasing in size but were not accompanied by pain or any other discomfort. The patient had no significant medical history and no familial history of similar conditions.

CLINICAL EXAMINATION

Upon physical examination, several firm, non-tender nodules were palpated on the scalp. These nodules varied in size and were not associated with erythema or warmth, suggesting a non-inflammatory nature. There were no signs of systemic illness, and the rest of the physical examination was unremarkable. Given the unusual presentation and chronic progression, a biopsy was recommended to ascertain the underlying pathology.

DIAGNOSTIC FINDINGS

Two separate histopathological analyses were conducted to diagnose the condition thoroughly:

First Histopathology Report (2005):
The sample consisted of a globular mass measuring approximately

2.5x2 cm, displaying abundant collagen interspersed with fibroblasts showing no mitotic activity. The mass was poorly delineated, which suggested a deeper tissue integration.

Second Histopathology Report (2024):
This more recent analysis confirmed the presence of grey-brown, firm, multiple soft tissue bits. Microscopy revealed non-encapsulated, nodular deposits in the dermis composed of hyalinized stroma with entrapped spindle cells. The nodules were just below the skin and showed homogenous glistening nodules noted on cut sections, characteristic of Juvenile Hyaline Fibromatosis.

GENETIC TESTING AND COUNSELING

Given the histopathological diagnosis of Juvenile Hyaline Fibromatosis, genetic testing was advised to investigate potential mutations in the CMG-2 (ANTXR2) gene, known to be associated with this condition. The patient was referred to genetic counseling to discuss the implications of the genetic findings, which confirmed the presence of mutations that were consistent with Juvenile Hyaline Fibromatosis.

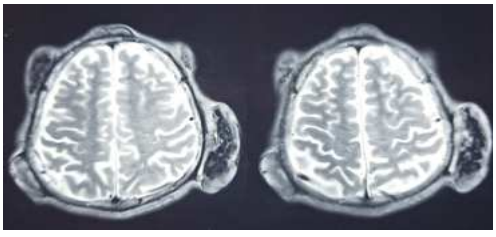
MANAGEMENT AND TREATMENT STRATEGY

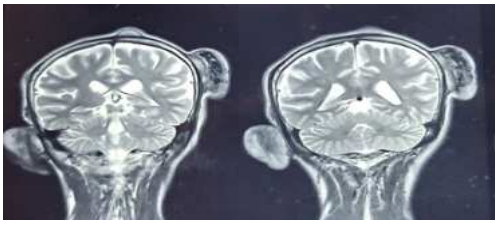
The management strategy focused on the symptomatic relief of the nodules and prevention of further complications. Surgical excision of the largest and most problematic nodules was planned to alleviate any potential physical discomfort and prevent further growth interference. Given the recurrent nature of the nodules and potential for new nodule formation, regular follow-up appointments were scheduled.

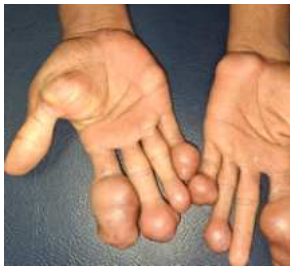
PROGNOSIS AND FOLLOW-UP

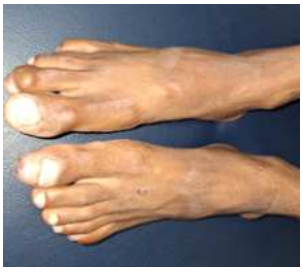
Juvenile Hyaline Fibromatosis is known for its progressive nature, with the possibility of new nodule formation and complications such as joint contractures and skin thickening. The prognosis in such cases depends significantly on the severity of the gene mutation and the extent of systemic involvement. Regular follow-up was deemed essential for managing this patient's condition effectively, focusing on monitoring for new symptoms and managing existing lesions. Long-term management would also involve physical therapy to prevent joint stiffness and contractures, a common complication as the disease progresses.

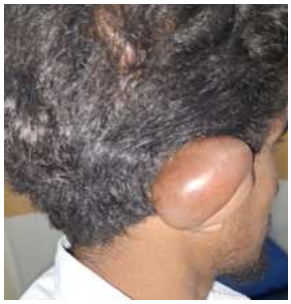
This case of Juvenile Hyaline Fibromatosis highlights the importance of considering rare genetic disorders in the differential diagnosis of non-tender, firm cutaneous nodules. It also underscores the need for a multidisciplinary approach in managing such rare conditions, involving dermatologists, geneticists, and surgeons to provide comprehensive care tailored to the individual patient's needs.

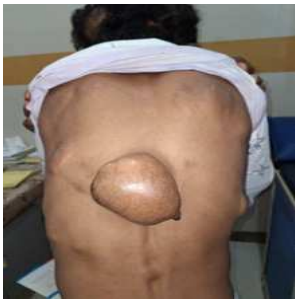


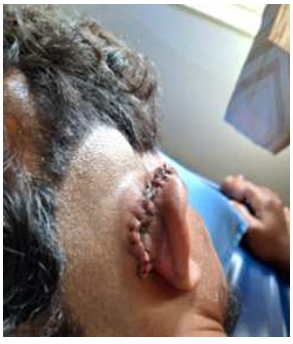


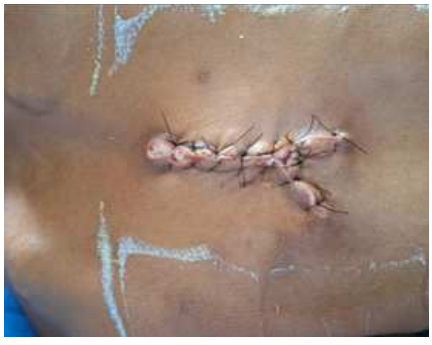












DISCUSSION

Juvenile Hyaline Fibromatosis (JHF) is a rare autosomal recessive condition with significant phenotypic variability. This discussion contextualizes our patient's presentation and management with historical and contemporary findings, highlighting both consistencies and variations.

The clinical features in our case, including multiple subcutaneous, non-tender nodules, align with the classical findings of JHF. The patient's presentation with firm scalp nodules is consistent with the slow-growing, painless nature of the lesions described in the literature (Ribeiro et al., 2009; Krishnamurthy and Dalal, 2011) [1,2]. Interestingly, our patient did not present with gingival hypertrophy or joint contractures, common findings in severe cases, reflecting milder phenotypic expression.

Histopathological analyses corroborated the diagnosis, showing non-encapsulated hyalinized stroma with entrapped spindle cells. These findings are a hallmark of JHF and consistent with descriptions by Kitano et al. and subsequent studies (Lim et al., 2005; Tzellos et al., 2009) [3,4].

The identification of mutations in the CMG-2 gene on chromosome 4q21 has provided a clearer understanding of JHF's pathogenesis. Aberrant synthesis of glycosaminoglycans and disordered collagen metabolism have been proposed as underlying mechanisms (Lim et al., 2005; Yayli et al., 2006) [3,5]. Genetic testing in our case confirmed these mutations, aligning with findings in prior studies, and underscoring the importance of molecular diagnostics for accurate diagnosis and genetic counseling.

Management of JHF remains challenging due to the progressive nature of the disease and lack of a definitive cure. The surgical excision performed in our case aligns with literature advocating early removal of problematic lesions to improve esthetics and functional outcomes (Tehranchinia and Rahimi, 2010; Quintal and Jackson, 1985) [6,7].

However, recurrence is a well-documented complication, emphasizing the need for regular follow-up.

While our patient did not experience joint contractures, literature suggests intralesional steroids, physiotherapy, and capsulotomy for their management (Denadai et al., 2012) [8]. For cases involving severe gingival hyperplasia, gingivectomy combined with oral hygiene measures has been effective (El-Maaytah et al., 2010) [9]. Historically, severe cases of JHF often resulted in significant morbidity, including functional disability from joint contractures and poor nutrition due to gingival hypertrophy. In contrast, our patient presented with isolated scalp nodules, a less common and milder phenotype. Similar cases have been reported, demonstrating the variability in clinical severity and progression (Ribeiro et al., 2009) [1].

CONCLUSION

This case of Juvenile Hyaline Fibromatosis (JHF) underscores the critical role of integrating clinical, histopathological, and genetic investigations to achieve a definitive diagnosis and tailor management strategies effectively. The identification of characteristic histopathological features along with the confirmation of CMG-2 gene mutations provided conclusive evidence for JHF, guiding appropriate intervention and management. Surgical excision of the nodules offered symptomatic relief and improved the patient's quality of life, highlighting the importance of addressing physical manifestations of the disease.

Furthermore, the case emphasizes the necessity of genetic counseling in managing hereditary conditions like JHF, facilitating patient and family understanding of the disease's implications, its progression, and the genetic risks for future generations. Regular follow-ups and a multidisciplinary approach are paramount in managing the progression of JHF and mitigating complications, illustrating the complexities involved in treating rare genetic disorders. Ultimately, this report contributes to the limited but growing body of literature on JHF, aiming to enhance awareness and understanding of such rare conditions among clinicians. Increased recognition can lead to earlier diagnosis, improved management, and potentially, better outcomes for patients suffering from rare diseases like Juvenile Hyaline Fibromatosis.

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