Hong Kong Journal of Orthopaedic Research
(An Open Access Journal for Orthopedics and Trauma Research)

Research Article

Hong Kong J Orthop Res
2021; 4(3): 86-88
ISSN (e): 2663-8231
ISSN (p): 2663-8223
Received: 19-11-2021
Accepted: 02-12-2021

www.hkorthopaedicjournal.com
DOI: 10.37515/ortho.8231.4307

Fibrodysplasia Ossificans Progressiva- A case report of exceedingly rare cause of heterotropic ossification

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Abstract

Fibrodysplasia ossificans progressiva is an exceedingly rare genetic disorder that causes the formation of the second skeleton after birth by the heterotopic bone. It is commonly misdiagnosed and treated inappropriately. Although there is no cure for the disease, early and correct diagnosis may slow the disease progress, avoid unnecessary intervention and in turn improve the quality of life. We report a 13 years old girl with fibrodysplasia ossificans progressiva who presented with progressive stiffness of the bilateral hips after a trivial fall. Further history has found progressive joint stiffness involving multiple joints. She had not been diagnosed even though multiple encounters with the health facility for similar complaints. This has highlighted the importance of awareness of the disease among healthcare personnel.

Keywords: Rare genetic disorder, Fibrodysplasia ossificans progressiva, Heterotopic ossification.

INTRODUCTION

Heterotopic ossification (HO) is an abnormal form of bone formation in extraskeletal tissues. It can occur either spontaneously, following trauma or neurologic injury. Fibrodysplasia ossificans progressiva (FOP) is an exceedingly rare genetic disorder mostly caused by sporadic mutation but inheritance can occur by autosomal dominant transmission. The patient can be presented since birth with abnormal skeletal formation over the neck, femoral neck and great toes. Minor trauma causing progressive HO formation since the first decade of life which can be disabling. There are only 834 living individuals with FOP globally according to a report by IFOPA in 2016 [1].

CASE REPORT

A 13 years old girl presented to the orthopaedic clinic with a two years history of stiffness over the bilateral hips, bilateral shoulder and jaws. The hips pain was preceded by the incidence of trivial fall in sitting position. While the hips pain gradually reduced, the hips were getting stiffer and then fixed in position. Otherwise, the shoulders and jaws stiffness were unprovoked. Further history from parents revealed that she was having bony prominent over the base of bilateral great toe noticed since infant period (Fig. 1). The patient was also not able to turn her head toward the sound and extend her head just like other children when she was put in a prone position during the infant period. Parents and other siblings are all normal. Parents had sought treatment from a general practitioner, orthopaedic surgeon, dental surgeon as well as physician, however, she was never being diagnosed and treated.

On examination, the patient had multiple bony prominent over the neck, hips region and around the knee. Non tender and no signs of inflammation over the bony swellings. Neck movement markedly reduced in all directions. Mouth opening was restricted to less than one finger breath (Fig. 2). The shoulders range of movement is largely maintained except internal and external rotation. Pelvis tilts up at the right side with limb length discrepancy of 5cm. Right hip in internal rotation position with fixed adduction at 10 degree. Left hip in external rotation position with fixed abduction at 15 degree. No lymphadenopathy and no organomegaly can be appreciated.

Inflammatory markers and other laboratory results were normal for her age. X-ray study showed abnormal cervical spine, abnormal neck of femur formation with HO formation and malformation of great toes

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(Fig. 3a, 3b, 3c). Genetic study was not done because of the classical presentation of history and imaging study. Co-management with rheumatologist aims to provide symptomatic treatment and disease progression prevention. Counselling was provided and the patient was educated on the nature of FOP.

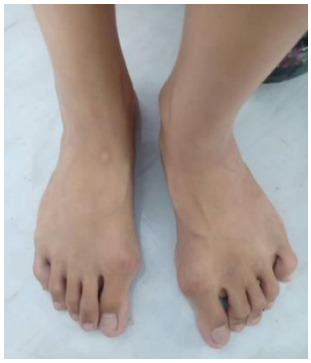

Figure 1: Bilateral Hallux Valgus

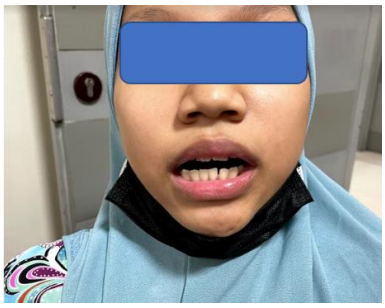

Figure 2: Maximum width of mouth opening

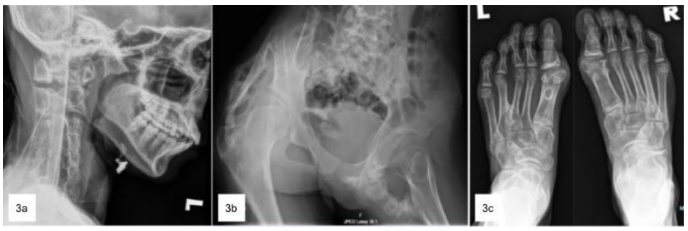

Figure 3: Plain X-ray. **(a)** Abnormal cervical spine formation with multiple fused vertebral bodies. **(b)** Extensive HO formation at bilateral hips. **(c)** Malformation of bilateral great toes.

DISCUSSION

FOP, Albright hereditary osteodystrophy and progressive osseous heteroplasia are among the three distinct genetic illnesses that cause the heterotopic bone in soft tissue [2]. FOP deserves special attention as it can be diagnosed via clinical presentation together with radiological findings. FOP is the only one among these three genetic illnesses that have a course of soft tissue flare up following injury, spare the skin and with great toes malformation [3]. It is commonly misdiagnosed as myositis ossificans and underwent surgical interventions. The diagnosis of FOP is based on three criteria: congenital malformation of the great toes, progressive heterotopic endochondral ossification, and progression of the disease in well-defined anatomical and temporal patterns [4].

The total registered population of the global FOP community in the year 2016 was 834 living individuals based on the database of International Fibrodysplasia Ossificans Progressiva Association (IFOPA) [1]. The prevalence varies from 0.04 per million to 0.65 per million across the world [1]. The high variability in apparent prevalence is likely associated with lack of awareness of FOP, delay in achieving the correct FOP diagnosis and the inability of individuals with FOP to reach the FOP association [1]. There is no gender, racial or ethnic predilection for FOP [1]. Most cases of FOP are sporadic, but inheritance can occur by autosomal dominant transmission. Heterozygous missense mutations in activin receptor A, type I (ACVR1), a bone morphogenetic protein (BMP) type I receptor, were identified in all affected individuals [5]. Hence genetic analysis for ACVR1 gene mutation used as a confirmatory test.

FOP is progressively disabling due to the formation of a second skeleton of heterotopic bone after birth beside the primary normotopic skeleton that formed during embryogenesis. The normotopic skeleton is normal except for malformation of the great toes (95% of the affected individual), femoral neck and cervical spine [2]. The patient is usually presented in the first decade of life with episodic flare up of painful soft tissue swelling leading to progressive HO. Minor trauma such as fall, intramuscular injection, biopsy and operation or Influenza like viral illness can trigger new flare up [3]. The ossification can occur in tendon, ligaments, aponeuroses, fascia and connective tissue of skeletal muscle render compromise the function of such structures [2]. Smooth muscles are generally spared.

The progression pattern of HO in FOP is typically from axial to appendicular, cranial to caudal and proximal to distal [2]. As the disease progresses, the sufferer will become progressively disabled due to extra articular ankylosis in joints throughout the body render restricted or no movement [5]. The jaw region usually is the last to be involved, however, the submandibular area flare up is particularly important as it can lead to difficulty in breathing which can be life threatening [4]. Other complications are deep vein thrombosis, deafness and the most worrisome lung infection. Lung infection by far is the main cause of mortality in FOP patients due to severely restricted chest wall movement [2]. There is no specific treatment for FOP, thus the treatment aims for symptomatic relief and prevention of complications. Corticosteroids can be used for initial phases of acute flare up to inhibit the acute and bulk inflammatory infiltration of skeletal muscle and mast cells stabilizers can be used to reduce the symptoms of acute flare up [2]. Surgical removal of the heterotopic ossification often followed by significantly more severe recurrent hence is not recommended. Physiotherapy which aims to maintain joint function may be harmful as well by causing flare up.

CONCLUSION

Although FOP is rare, however, it can be easily identified via its typical presentation and radiological findings. Awareness among health care workers is important in order not to miss the disease. Early correct diagnosis of FOP is essential to avoid unnecessary intervention that causes iatrogenic aggravation of the disease.

Conflicts of Interest

No conflict of interest related to this article.

Authors' Contribution

Ng YH, Ng CR and Ibrahim S involved in the management of patient. Ng YH and Ng CR are involved in the acquisition of information. Chai YC and Ng YH wrote the manuscript with input from all authors. Chai YC was involved in revising and editing the manuscript critically. All authors read and approved the final manuscript.

Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article.

We would like to record our appreciation to the patient's parents who provided the written consent to authors for publication of this case report.

Funding

The authors received no specific grants from any funding agencies.

Consent for Publication

The patient's parents provided the authors written consent for the publication of this case report.

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