wjpmr, 2020,6(9), 19-22

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Case Report

ISSN 2455-3301

WJPMR

FIBROPLASIA OSSIFICANS PROGRESSIVA OR MUNCHMEYER'S DISEASE: PEDIATRIC CASE REPORT

Dr. L. Berrada*[1], H. Rhouda[1], M. Sahli[2], A. Sefiani[2] and Y. Kriouile[1]

[1]Pediatric Department II, Hopital D'enfants De Rabat BP 6527, Rue Lamfadel Cherkaoui, Rabat.
[2]Medical Genetic Department, Institut National D'hygiène, BP769 Agdal, 10090, Rabat.

***Corresponding Author: Dr. L. Berrada**

Pediatric Department II, Hopital D'enfants De Rabat BP 6527, Rue Lamfadel Cherkaoui, Rabat.

Article Received on 12/07/2020 **Article Revised on 02/08/2020** **Article Accepted on 23/08/2020**

ABSTRACT

Myositis or Fibroplasia Ossificans Progressiva (MOP or FOP) or Munchmeyer's disease is a rare genetic disease. Its diagnosis is easy at an advanced stage where standard radiography shows a true ectopic skeleton associated with bilateral malformations of the feet and hands. Its evolution is fatal with the risk of rootedness, petrification and death by restrictive respiratory failure. We report a case of FOP diagnosed in a 9-year-old child. The genetic study confirmed the diagnosis. The aim of this article is to recall the circumstances of discovery, the radiological diagnosis with the importance of the association of characteristic congenital malformations and finally to highlight the difficulties of management and treatment.

KEYWORDS: Fibroplasia Ossificans Progressiva; Munchmeyer's disease; genetic disorder.

INTRODUCTION

Myositis or Fibroplasia Ossificans Progressiva (MOP or FOP) or Munchmeyer's disease is a rare genetic disease transmitted in the autosomal dominant mode with variable penetration.

It corresponds to an abnormality of mesenchymal differentiation with lamellar bone development in connective tissue and muscle. Its diagnosis is easy at an advanced stage where standard radiography shows a true ectopic skeleton associated with bilateral malformations of the feet and hands. Its evolution is fatal with the risk of rootedness, petrification and death by restrictive respiratory failure.

The aim of this article is to recall the circumstances of discovery, the radiological diagnosis with the importance of the association of characteristic congenital malformations and finally to highlight the difficulties of management and treatment.

OBSERVATION

We report a case of diagnosed in a 9-year-old child with no specific history, including no trauma. The patient was seen in consultation for progressive rooting of the trunk with decreased dorsal mobility.

The clinical examination finds a child in good general condition, whose weight and height are normal in relation to age, with reduced mobility of the neck, right and left shoulder, cervical rectitude, two small induced swelling at the lateral edges of the sternum, a stiffness of the left knee, a deformation: dorsal scoliosis (Figure 1), a hallux valgus in the 2 feet and an exostosis on the back of the right hand (Figure 2). In addition, it shows hypoplasia of the distal phalanges of the two auricular ones.

The biological assessment carried out was without anomalies, especially the level of alkaline phosphatases which was normal.

A cervico-thoracic computed tomography was performed, objecting a voluminous ossification of the superficial and deep soft tissues spread on the sagittal plane along the axial skeleton, from the occiput to the coccyx, following the path of the para-vertebral cervical-thoracic and lumbar muscles, measuring approximately 50 mm in length and 15 mm in thickness. It has bilateral and asymmetric branches reaching the anterior thoracic wall passing under the scapular regions engacing the thoracic wall. These calcifications show connections with the occiput, the 3rd cervical vertebra, the inner side of the left scapula and are welded with the left arm. (Figure 3)

Radiography of the feet showed that the 1st phalange was short triangular, and welded with the 2nd phalange of the big toes with a synchondrosis appearance of the first metatarso-phalangian.

The genetic study carried out objectified the presence of the recurrent mutation c.617G>A (p.Arg 206His), at the exon 6 of the ACVR1 gene, thus confirming the diagnosis of Fibroplasia Ossificans Progressiva.

Management included regular mild physiotherapy sessions, combined with corticosteroid therapy during flare-ups. No curative treatment can be offered to our patient.

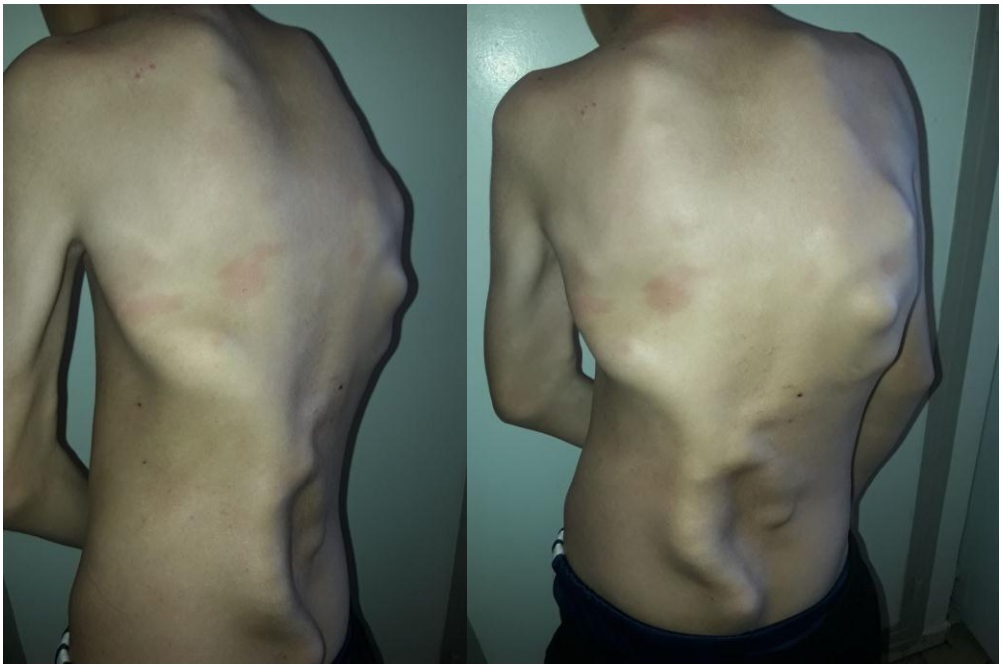

Figure 1: Ectopic ossification clinically appearing.

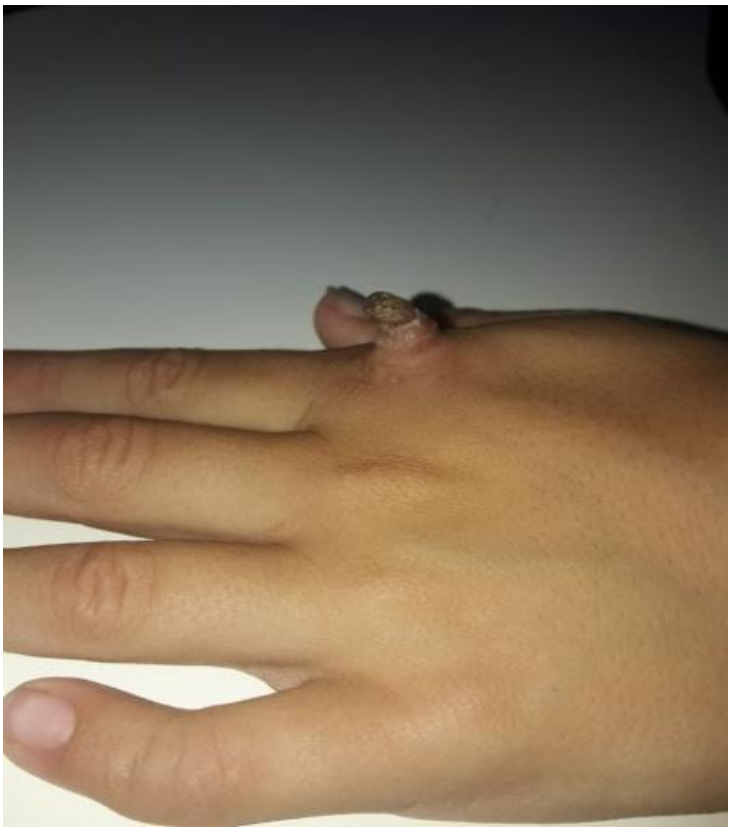

Figure 2: Exostosis and bone finger deformation.

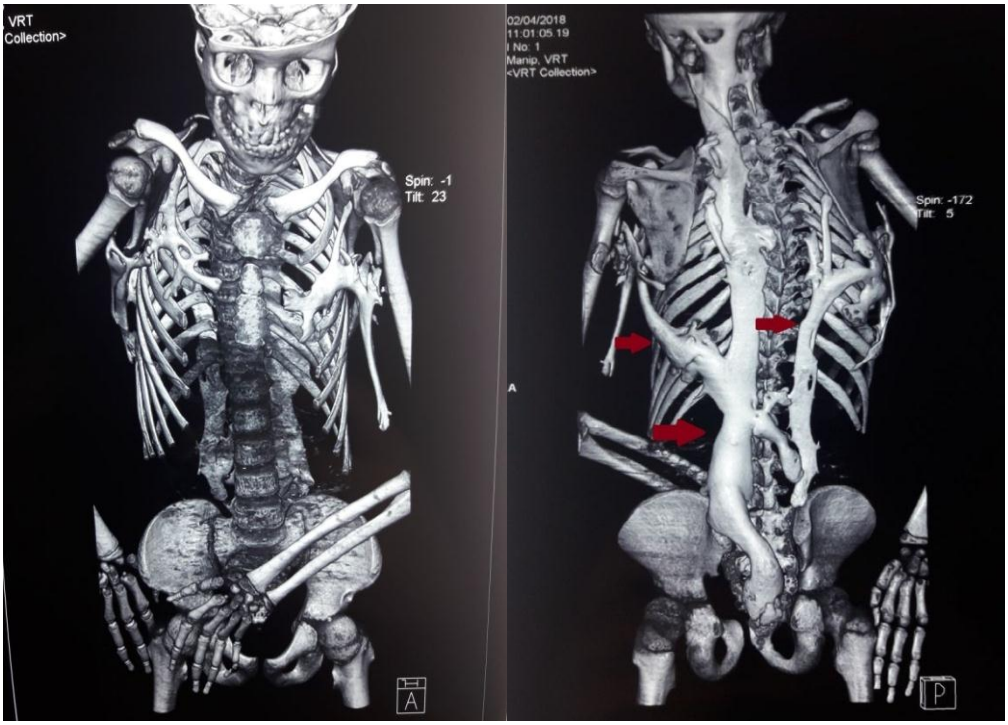

Figure 3: Ectopic ossification on CT scan.

DISCUSSION

1- The first description of the FOP was made by the French doctor Guy Patin in 1692, repeated in 1736 by the English surgeon Freke.[1] The more recent work of F. Kaplan has enabled the precise description of the lesions and the variability of this condition, the physiopathology, the molecular bases and the principles of management.[2]

2- The diagnosis of FOP is based on the coexistence of abnormalities in the first radii of the feet, and ossification flares, the evolution of which is slowly progressive in the craniocaudal and proximodistal direction.

3- The prevalence of the disease is estimated at about 1 in 2 million.[3] There is no preference for sex, race or ethnicity. This disease usually appears before the age of 10.[5] The current estimated number of patients is 2500, of which 600 are known (data from the international association of the FOP).

FOP is an autosomal-dominant disease. Sporadic cases as in our case are the most common.[6,7]

4-This pathology is still idiopathic.
Some suggest an abnormality of the morphogenetic proteins of the bone, in particular the protein-4 morphogenetic bone whose high production would be involved in the inflammatory pre-bony process, with dysregulation of the production of cells and mediators of inflammation in the connective and muscular tissue.

5- The main mutation found is that of ACVR1. Most of these mutations appear de novo. Some family cases of dominant autosomal transmission have been described with often minor extremity abnormalities in the ascendants. The main heterozygous mutation c.617G > A, (p.Arg206his) objectified in our genetic study, gives the classical form. In 2009, atypical forms, called FOP "variant" and FOP "plus", were described.[1,2] The "variant" FOP is characterized by the normality of large toes or, on the contrary, severe finger damage. "Plus" forms are defined by the combination of a classic FOP and other signs (marfanoid appearance, central nervous system malformations, craniopharyngioma and brain stem gliomas, endocrine disorders, ophthalmological, dental, urogenital, and aregenerative anemia).

Ossification surges often start between 2 and 4 years, in the muscles of the back, neck or shoulders [8,9] in the form of possibly painful, inflammatory swellings, of supple consistency, which evolve in a few weeks towards regression giving way to a deep ossified induration and a limitation of joint mobility.[15]

6- The clinical examination reveals these malformations, which interest the feet and hands: brevity, shortening, fusion and hypoplasia. The most important characteristic of these malformations are those of the first metatarsal and the phalanges, of the first toe which deformation simulates a hallux valgus. The phalanges of the thumb can be reached in the same way as those of the toes.[10,11] Our patient had an ear defect (Fig.). Other abnormalities may be encountered during the disease such as scoliosis, osteoporosis, deafness and baldness.[10,12]

Progression of ossifications leads to loss of mobility, predisposing patients to dramatic complications (lungs linked to intercostal bridges, restriction of joint mobility,

interference with food when they occur in the vicinity of temporomandibular joints, etc.).

7- CT initially shows an oedema of soft tissue that remains non-specific to the disease. Secondarily, the corticalised ossification of the fascias appears in strips of bone, flattened extending partially or totally around the muscle. This one, encircled, hypertrophies and presents within itself multiple points of ossification that will form between them bone bridges constituting a real fabric manufacturing of the marrow and composed of adipocytes and haematopoietic cells. This results in a thickening of the soft tissue and an early central hypodensity of the muscle, which will fully ossify over time.

8- Clinical development is achieved through indeterminate surges and remissions. Each push may involve a new muscle and/or aggravate the damage to muscles already damaged during previous pushes.[10]

9- The average survival is about 45 years.[14] but the majority of patients become bedridden around the age of 30.

Fatal evolution may be due either to respiratory failure by restricting the movements of the thoracic cage or to mandibular ankylosis cachexia.[16]

10- The knowledge of the diagnosis allows an early management in functional physiotherapy, but especially for the prevention of outbreaks by avoiding risk situations (surgeries, intramuscular injections, infectious episodes). Bone swelling surgery may result in explosive ossification flares. Dental care and general anesthesia require special care. Hearing monitoring and restrictive respiratory syndrome searching should be regular. The drug treatment, which is not curative, is based on corticosteroid therapy during flares. In the future, innovative treatments such as palovarotene (gamma retinoic acid agonist) in human trials could improve the prognosis of this disease.[17]

CONSCLUSION

Being an extremely rare but disabling condition, FOP should be mentioned in front of any unexplained torticolis occurring at any age; associated with congenital bone abnormalities of the big toes. The discovery of the ACVR1 gene brings hope to develop therapies for this disease, which was previously incurable.

ACKNOWLDEGMENT

Conflict of interest: None.

REFERENCES

1. Huning I, Gillessen-Kaesbach G. Fibrodysplasia ossificans progressiva: clinical course, genetic mutations and genotype-phenotype correlation. Mol Syndromol 2014; 5: 201–11.
2. Kaplan FS, Xu M, Seemann P, et al. Classic and atypical FOP phenotypes are caused by mutations in the BMP Type I Recep-tor ACVR1. Hum Mutat 2009; 30: 379–90.
3. van der Meij EH, Becking AG, van der Waal I. Fibrodysplasia ossificans progressiva. An unusual cause of restricted mandibular movement. Oral Dis, 2006; 12: 204-7.
4. Herford AS, Boyne PJ. Ankylosis of the jaw in a patient with fibrodysplasia ossificans progressiva. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2003; 96: 680-4.
5. Mahboubi S, Glaser DL, Shore EM, et al. Fibrodysplasia ossificans progressiva. Pediatr Radiol, 2001; 31: 307-14.
6. Altschuler EL. Consideration of Rituximab for fibrodysplasia ossificans progressiva. Med Hypotheses, 2004; 63: 407-8.
7. Dhamangaonkar AC, Tawari AA, Goregaonkar AB. Fibrodyspla- sia ossificans progressiva: a case report. J Orthop Surg Hong Kong, 2013; 21: 383–6.
8. Pignolo RJ, Shore EM, Kaplan FS. Fibrodysplasia ossificans progressiva: diagnosis, management, and therapeutic horizons. Pediatr Endocrinol Rev 2013;10:437–48.
9. Lucotte G. Bathelier C. Mercier G. Actualités. Fibrodysplasie ossifiante progressive : étude de 20 cas. J Pediatr Puericulture, 2000; 2: 115-9.
10. Lasry F, Touki A, Abkari A, et al. A rare cause of painful cervical swelling: myositis ossificans progressiva in childhood. Report of a case. Joint Bone Spine, 2005; 72: 335-7.
11. Mahboubi S, Glaser DL, Shore EM, et al. Fibrodysplasia ossificans progressiva. Pediatr Radiol, 2001; 31: 307-14.
12. Kaplan FS, Glaser DL, Shore EM, et al. The phenotype of fibrodysplasia ossificans progressiva. Clin Rev Bone Min Metabol, 2005; 183–8: 356
13. J.-L. Devoize, G. Sztark et al. Fibrodysplasia ossificans progressiva: A case report. Revue neurologique, 2013; 169: 911-919.
14. J. Paysal, C. Sarret et al. Anomalie réductionnelle transverse et fibrodysplasie ossifiante progressive atypique, à propos d'un cas de diagnostic tardif. Archives de Pédiatrie, 2017; 24: 547-551.