

Maffucci's Syndrome: A Rare Diagnosis

Ada Paloma Soto Brambila^{1,2}, Ingrid Patricia Dávalos Rodríguez^{1,2}, Rodrigo Santoscoy Valencia³

¹Division of Genetics, Center of Biomedical Research of the West, Mexican Institute of Social Security. Guadalajara, Mexico;

²University Center of Health Sciences, University of Guadalajara. Guadalajara, Mexico. ³Autonomous University of Guadalajara. Guadalajara, México.

Corresponding Author:

Dr. Rodrigo Santoscoy Valencia
Email: rodrigo_santoscoy@hotmail.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (creativecommons.org/licenses/by/3.0).

Received : October 11, 2017
Accepted : December 10, 2017
Published : December 30, 2017

Abstract

Background: Maffucci's syndrome is a rare genetic disorder that affects the skeletal and venous systems. It is also known as dyschondrodysplasia with hemangiomas, enchondromatosis with multiple cavernous hemangiomas, Kast syndrome, hemangiomatosis chondrodystrophica, and enchondromatosis Spranger type II. There have been only reported less than 200 cases in the world. **Case Report:** This case presents a 25-year-old male with malformations-deformations of the skeletal and venous systems: upper limbs with limbs asymmetry, shortening of the ulna with radius arching. Lower limbs examination showed, varus or valgus angulation of the knee and deformities of the ankle, adequate sensitivity, strength, trophic, without paresis, paresthesias, myalgias, normal preserved ROTS in 4 limbs. **Conclusion:** To diagnose Maffucci's syndrome it is essential to perform a thorough medical history, clinical and radiological examination. There are genetics analysis that help the diagnosis but are still under study. Management entails a very strict follow-up and careful examination and monitoring for malignant degenerations.

Keywords: Enchondromatosis, Hemangioma, Knee Joint, Myalgia, Paresis, Ulna.

Introduction

Maffucci's syndrome was first described in 1881 [1]. Maffucci's syndrome is a disorder that primarily affects skin and the skeletal systems. It is characterized by the presence of multiple enchondromas and hemangiomas. Maffucci's syndrome appears to be sporadically inherited, affects both male and female, and the first malformations are noted usually at the age of 4-5 years [2]. The vascular lesion (venous malformation) often protrudes as soft nodules or tumors, usually on the distal extremities, but they can appear anywhere. They can be unilateral or bilateral, but they usually are asymmetric. Enchondromas are benign cartilaginous tumors with the potential for malignant transformation into a chondrosarcoma (most common neoplasm) or any other malignant tumor. They can appear anywhere, but they usually

appear on the phalanges and long bones [3]. It is a very rare syndrome, and there have been less than 200 cases reported worldwide and fewer than 100 cases of Maffucci's syndrome have been reported in the United States [2]. We present this case of a Maffucci's syndrome which was diagnosed clinically and radiologically.

Case Report

We present a 25-year-old male with multiple skeletal malformations and deformities that is under the care of the departments of Orthopedics, Internal Medicine and Surgery. He was the product of a second pregnancy, born to non-consanguineous parents via an uncomplicated vaginal delivery at 38 weeks of gestation, following an uneventful pregnancy. Regarding his family history, his father also had multiple skeletal malformations and

deformities, however, a diagnosis was never made neither he received any kind of treatment. The patient has no perinatal pathological history and had a normal psychomotor development. He has had four surgeries, all of them were intervention to correct or minimize deformities; the first at the age of 7 he had a right femur; at age 10, the head of the right femur; and at the age of 13 right shoulder and left radius. The somatometry are: weight 120 kg (percentile >90), height 1.87 m (percentile >90), BMI 34.21 kg/m².

The physical examination revealed notable malformation in upper limbs, limbs asymmetry, shortening of the ulna with radius arching [Fig.1,2,3]. Lower limbs examination showed, varus or valgus angulation of the knee and deformities of the ankle, adequate sensitivity,



Fig.1-3: Limbs asymmetry, shortening of the ulna with radius arching.



Fig.4: Varus or valgus angulation of the knee and deformities of the ankle.

strength, trophic, without paresis, paresthesias, myalgias, and preserved ROTS in 4 limbs [Fig.4].

The radiological skeletal findings include: exophytic and partially calcified over-growth with cartilaginous cap thickness; deformity of radius with carpal enchondroma; irregularity and discontinuity of the cortical bone [Fig.5-7]. Laboratory results were within normal limits. A bone biopsy from 2003, reported no signs of malignancy.

Discussion

Enchondromas are benign hyaline cartilage forming tumors in the medulla of metaphyseal bone. Enchondromatosis encompasses several different subtypes of which Ollier's disease and Maffucci's syndrome are most common, while the other



Fig.5,6: Exophytic and partially calcified over-growth with cartilaginous cap thickness.



Fig.7: Deformity of radius with carpal enchondroma, irregularity and discontinuity of the cortical bone.

subtypes (metachondromatosis, genochondromatosis, spondyloenchondrodysplasia, dyspondyloenchondromatosis and cheirospondyloenchondromatosis) are extremely rare. Most subtypes are non-hereditary, while some are autosomal dominant or recessive [3].

Maffucci's syndrome is a rare sporadic form of enchondromatosis, characterized by hemangiomas and multiple enchondromas. The tumors usually stop forming once the patient stop growing during early adulthood [1]. Maffucci's syndrome is a congenital non-hereditary condition that usually presents before the onset of puberty. The child is always normal at birth. It is not associated with mental retardation and intelligence is not affected. Maffucci's syndrome is sometimes confused with Ollier disease, which was described 19 years later and consists of multiple enchondromas without hemangiomas. Ollier's disease is a disorder characterized by multiple enchondromas, which are benign growths of cartilage that develop within the bones. These growths most commonly occur in the limb bones, especially in the bones of the hands and feet; however, they may also occur in the skull, ribs, and vertebrae. Ollier's disease is estimated to occur in 1 in 100,000 people.

To establish the diagnosis of Maffucci's syndrome we must base on the clinical findings of the skeletal deformations, hemangiomas; multiple enchondromas have a particular site predilection: the long bone of the legs and arms and the phalanges are most commonly affected [3,4]. Radiological investigations and biopsy are required to establish the diagnosis of the malignancy.

To establish a differential diagnosis between Ollier's and Maffucci's syndrome is difficult, due to their similarities, so it has been proposed that they are different degrees of expression of the same pathology. There can be another differential diagnosis; multiple familial enchondromatosis, which, unlike previous syndromes, has a pattern of

inheritance already known: autosomal dominant. Two tumor suppressor genes, involved in this disease, have been identified: EXT1 and EXT2, located on chromosomes 8q24 and 11p11-p12, respectively.

Its clinical picture is characterized by the development of two or more enchondromas in the epiphyses of the long bones, mainly in the femoro-tibial joint. It occurs during the first decade of life, with a mean age of diagnosis at 3 years of age. Unlike other enchondromatosis, once the growth cartilages are closed, the formation of new enchondromes stops [5]. Since these pathologies share many clinical characteristics, it is difficult to establish a differential diagnosis, the antecedent of affected relatives is oriented toward multiple familial enchondromatosis (MFE). In this case we could think that there may be a MFE; in so much the unilateral localization suggests Ollier's disease and the presence of bilateral enchondromas and hemangiomas orients towards the Maffucci's syndrome.

Genetic determination of the EXT1 and EXT2 genes by microarray is the most specific study for the diagnosis of MFE, however, not all hospitals can perform this study [5]. Identification of Maffucci's syndrome by surgical excision and pathological diagnosis can be life-saving due to its high malignant potential relative to other subtypes of enchondromatosis such as Ollier's disease [1,6].

This patient presents the distinctive features of the Maffucci's syndrome such as enchondromas and hemangiomas in the long bones such as the radius, ulna, tibia and fibula; also has the distinctive radiological signs such as the exophytic enchondroma, the overgrowth of the cartilaginous cap, and the irregularity and discontinues on the cortical bone, that's why we based more on Maffucci's syndrome. Something interesting with this case, is his father and sister history of skeletal deformations in his father and sister, and these malformations were not diagnosed or treated

and this might makes us think over a multiple familial enchondromatosis, but we would need to proceed with a genetic determination of genes EXT1 and 2 in microarray. There is a tendency for malignant transformation of enchondromas into chondrosarcomas or of hemangiomas into vascular sarcomas, and that is the reason we should make and early diagnosis, treatment, follow-up and careful surveillance of these masses. Previous studies demonstrate that individuals diagnosed with Maffucci's syndrome have approximately 100% lifetime risk of malignant transformation [1,6].

Management of Maffucci's syndrome aims at relief of symptoms and early detection of malignancies. No medical care is needed in Maffucci's syndrome patients who are asymptomatic, but they need follow-up care to evaluate changes in lesions. Surgical interventions can correct or minimize deformities; and for the control of hemangiomas the management can be more conservative or more aggressive depending on the individual's symptoms and the severity of the lesion [7]. Symptomatic patients may benefit from anticoagulation, compression therapy, sclerotherapy or surgical excision when the more conservative approaches have failed [4,7]. Maffucci's syndrome patients usually have a normal life depending on the malignant transformation of the enchondromas.

Conclusion

The diagnosis of Maffucci's syndrome is based on the clinical and radiological features. The differential diagnosis in Maffucci's syndrome and Ollier's syndrome is generally based on the presence or absence of hemangiomas or any soft

tissue venous malformation, and the difference with multiple familial enchondromatosis is in the genetic determination of EXT1 and EXT2. Management entails a very strict follow-up and careful examination and monitoring for malignant degenerations. Surgical interventions can correct or minimize deformities, and hemangiomas management needs to be the more conservative therapy possible.

Contributors: APSB: manuscript writing, literature review; IPDR: manuscript editing, literature review; RSV: critical inputs into the manuscript, and literature review. APSB will act as guarantor. All authors approved the final version of this manuscript.

Funding: None; *Competing interests:* None stated.

References

1. Prokopchuk O, Andres S, Becker K, Holzapfel K, Hartmann D, Friess H. Maffucci syndrome and neoplasms: a case report and review of the literature. *BMC Res Notes*. 2016;9:126.
2. Amary MF, Damato S, Halai D, Eskandarpour M, Berisha F, Bonar F, *et al.* Ollier disease and Maffucci syndrome are caused by somatic mosaic mutations of IDH1 and IDH2. *Nat Genet*. 2011;43(12):1262-1265.
3. Pansuriya TC, Kroon HM, Bovée JVMG. Enchondromatosis: Insights on the different subtypes. *Int J Clin Exp Pathol*. 2010;3:557-569.
4. Maione V, Stinco G, Errichetti E. Multiple enchondromas and skin angiomas: Maffucci syndrome. *Lancet (London, England)*. 2016;388:905.
5. Zwenneke Flach H, Ginai AZ, Wolter Oosterhuis J. Best cases from the AFIP: Maffucci syndrome: radiologic and pathologic findings. *Radiographics*. 2001;21:1311-1316.
6. Verdegaal SHM, Bovée JVMG, Pansuriya TC, Grimer RJ, Ozger H, Jutte PC, *et al.* Incidence, predictive factors, and prognosis of chondrosarcoma in patients with Ollier disease and Maffucci syndrome: An international multicenter study of 161 patients. *Oncologist*. 2011;16:1771-1779.
7. Gupta N, Kabra M. Maffucci syndrome. *Indian Pediatr*. 2007;44:149-150.