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Chapter 11

Maffucci Syndrome

Miki Tanioka

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1. Introduction

Maffucci syndrome is characterized by the presence of multiple enchondromas associated with multiple hemangiomas (figure 1). Enchondromas are common benign cartilage tumors of bone. They can occur as solitary lesions or as multiple lesions in enchondromatosis (Schwartz 1987, Kaplan 1993). When hemangiomata are associated, the condition is known as Maffucci syndrome (figure 2). The patients are normal at birth and the syndrome manifests during childhood and puberty. The enchondromas affect the extremities and their distribution is asymmetrical. The most common sites of enchondromas are the metacarpal bones and phalanges of the hands. The feet are less commonly afflicted. Clinical problems caused by enchondromas include skeletal deformity and the potential for malignant change to osteosarcoma (figure 3). The risk for sarcomatous degeneration of enchondromas, hemangiomas, or lymphangiomas is 15-30%. Maffucci syndrome is also associated with a higher risk of CNS, pancreatic, and ovarian malignancies (Ono 2012) (figure 4).

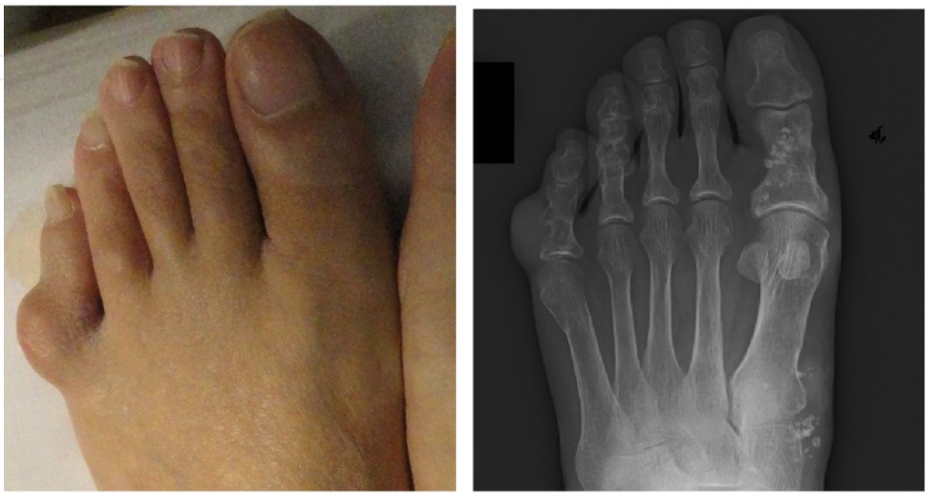


Figure 1. Multiple enchondromas

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Figure 2. Multiple hemangioma on the sole

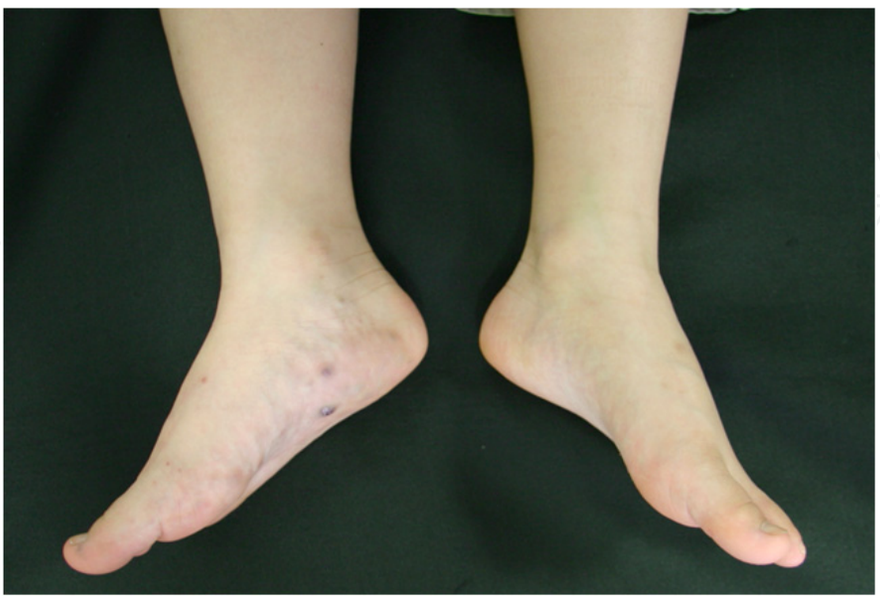


Figure 3. The differences of length and size of the legs are noted.

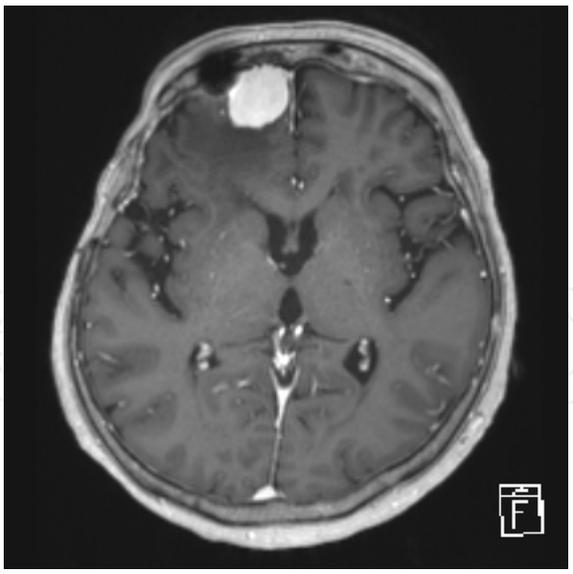


Figure 4. Brain tumor in a patient with Maffucci syndrome

2. Inheritance

Most cases of Maffucci syndrome have been sporadic and no specific hereditary form has been proven (Hakak and Azouz 1991).

It occurs in all races, and occurs in both sexes equally.

3. Cutaneous presentation of Maffucci syndrome

Multiple hemangiomas are presented as multiple nodules on the skin of the extremities, which looks like grapes (figure 2). However, the sites of hamangiomas are reported to be the colon and brain (Lee 1999). Multiple enchondromas present as a subcutaneous nodules fix to the underlining bones. Bleeding from the hemangiomas is clinically important and difficult to manage. Complete resection is usually impossible. Compression therapy is recommended.

4. Melecular genetics of Maffucci syndrome

The responsible genes for Maffucci syndrome have not been found. However, some studies were reported for multiple enchondromatosis.

In enchondromas and chondrosarcomas, mutations of the *PTHR1* gene was reported to be a candidate gene, however, subsequent studies could not confirm it (Hopyan 2002, Rozeman 2004).

Somatic heterozygous mutations in *IDH1* or *IDH2* were reported in enchondromas and spindle cell hemangiomas (Pansuriya 2011). Ten cases of 13 (77%) with Maffucci syndrome carried *IDH1* or *IDH2* mutations in their tumors. *IDH1* mutations in cartilage tumors were associated with hypermethylation and downregulated expression of several genes (Amary

2011). Mutations were absent in DNA isolated from the blood, muscle, or saliva of the subjects. Therefore, these mutations are believed to be somatic.

5. Management of Maffucci syndrome

Management entails careful examination and monitoring for malignant degenerations. Surgical interventions can correct or minimize deformities.

Compression therapy may be useful to control hemangiomas.

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