An osteolytic lesion of the proximal ulna in a patient with Maffucci syndrome: a case report

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Maffucci syndrome is a rare, congenital, and nonhereditary syndrome characterized by the occurrence of multiple enchondromas and hemangiomas. According to previous studies, patients diagnosed with Maffucci syndrome have a higher risk of developing malignant tumors, such as ovarian cancer, pancreatic cancer, breast cancer, and central nervous system cancer, in addition to malignant transformations of enchondromas. The authors report a case of a 37-year-old male patient with Maffucci syndrome who presented with multiple enchondromas and hemangiomas. This patient’s presentation and management are discussed, along with a review of the literature. Maffucci syndrome should be expected when encountering a patient with multiple enchondromas and suspected hemangiomas in the limbs. Even if benign lesions such as enchondromas or hemangiomas are diagnosed, regular follow-up is required to monitor for malignant transformations and the development of malignant tumors in other organs.

Keywords: Maffucci syndrome, Enchondroma, Hemangioma

Introduction

Maffucci syndrome is a congenital and rare nonhereditary type of chondromatosis with multiple enchondromas near the growth plate and hemangiomas in the skin and subcutaneous tissues [1-3]. Enchondromas arising from Maffucci syndrome are known to occur due to abnormalities in the signaling pathways that control the differentiation and proliferation of chondrocytes. These lesions are generally benign cartilage tumors that have no symptoms and can occur in any area.

Enchondroma in Maffucci syndrome has been reported to cause fractures without trauma in 26% and to convert to chondrosarcoma, a malignant tumor in about 25% to 37% according to the literature [2]. In addition, patients with Maffucci syndrome are known to be more likely to develop malignant tumors such as ovarian cancer, pancreatic cancer, breast cancer, and central nervous system cancer [2,4,5]. Most of the hemangiomas in Maffucci syndrome are located in the dermis and subcutaneous fat adjacent to the area with enchondroma. They have a similar frequency on bilateral extremities. Hemangioma is a benign tumor and generally has no symptoms. However, there is a possibility of malignant transformation, requiring continuous follow-up.

The authors experienced a 37-year-old male patient with Maffucci syndrome. The patient had multiple subcutaneous hemangiomas in the hands and feet for more than 30 years, was diagnosed with intracranial enchondroma two years ago, and was transferred to our hospital with the suspicion of a pathological fracture caused by a tumor in the right proximal ulna. Therefore, we reported this case with a review of the literatures.
Case report

This report was approved from the Institutional Review Board of Dong-A University Hospital (No. DAUHIRB-23-209). Written informed consent was obtained from the patient for the publication of this report including all clinical images.

A 37-year-old male patient experienced discomfort in the right elbow for more than three weeks after a traffic accident. He visited a primary orthopedic clinic, where the X-ray examination showed a suspicious pathologic fracture of the proximal ulna with an osteolytic lesion. He visited our outpatient clinic for further evaluation of an osteolytic lesion in the right proximal ulna. At the time of the visit, he did not complain of any discomfort in other body parts. There were no other symptoms such as prominent tenderness or swelling except discomfort in the right elbow. The patient did not have an underlying disease. However, the patient visited another hospital due to headache 2 years ago. He underwent an MRI at that time, which revealed an intracranial mass. Subsequently, an excisional biopsy was performed on the intracranial mass and the final biopsy result confirmed it to be an enchondroma. The physical examination revealed multiple asymptomatic vascular lesions protruding from the skin on the left upper limb, right foot, and lower leg. The patient reported that these lesions have been present since childhood (Fig. 1). The patient was admitted for evaluating Maffucci syndrome, and a whole-body bone scan was performed to assess other possible lesions in different parts of the body. Active bone lesions were observed in both pelvic bones, femurs, and tibias. Simple radiographic examinations were conducted in both pelvic bones, femurs, and tibias, revealing intraosseous lesions in both iliac wings. In addition, soft tissue masses with calcifications were observed in the left hand, right foot, and ankle joints (Fig. 2). To ensure a comprehensive evaluation, consultation with the oncology department was performed. In addition to assessing intraosseous lesions, the patient was advised to undergo a series of imaging studies, including right upper extremity angiography, cervical computed tomography (CT) scan, chest CT scan, abdominal-pelvic CT scan, and pelvis magnetic resonance imaging (MRI), to investigate the presence of any other abnormalities. The imaging results did not reveal any masses in major organs such as the lungs and liver. However, on the pelvic MRI, multiple lobulated lesions were confirmed in both iliac wings in addition to well-defined mass in the right proximal ulna which is seen on the right elbow MRI (Fig. 3). Furthermore, in the right upper extremity angiography CT scan, in addition to the previously observed lesion in the proximal right ulna seen in the MRI, a nodular lesion with characteristics suggestive of venous malformation was observed on the outer aspect of the forearm.

The patient was ultimately scheduled for curettage and biopsy of the right proximal ulna and right iliac wing. Although the lesion located in the right iliac wing was not the primary complaint at the time of admission, the patient reported chronic discomfort in that area during the detailed medical history assessment. Similar to the right proximal ulna lesion, it was also located on the right side, and both lesions could be addressed simultaneously through surgical draping. During the surgery, avascular wax-like masses were observed in the right proximal ulna.

Fig. 1. (A) Characteristic venous malformations on the patient’s left upper extremity. (B, C) Multiple hemangiomas are seen on the right foot.
Fig. 2. (A) Anteroposterior X-ray of the pelvis shows local uneven bone density (arrow) and multiple cystic lesions (arrow) with irregular sclerosis around them. (B, C) Bilateral feet and hands X-rays show multiple soft tissue masses (arrows) demonstrating calcifications on the left hand and right foot.

and iliac wing. Only a portion of the lesion in the iliac wing was removed because extensive excision of all visible pathologic lesions was not necessary for diagnosis, while all the visible masses in the proximal ulna were excised. In the area where the masses were removed from the proximal ulna, autologous bone grafting was deemed inappropriate due to the presence of multiple enchondromas. Therefore, an allogenic bone grafting procedure was performed using the demineralized bone matrix (Fig. 4). The patient was discharged without any significant postoperative complications. Histopathological examination of both masses revealed mature hyaline cartilage cells displaying lobular characteristics. Although cellularity was mildly increased, multinucleated cells were not observed, and there was no pronounced atypia in the nuclei of chondrocytes. Consequently, a final diagnosis of enchondroma was confirmed (Fig. 5). The period from operation to the last follow-up is 15 months, and considering the potential for malignant transformation of enchondromas and vascular malformations in Maffucci syndrome, as well as the risk of developing malignancies in other organs, it was decided to conduct ongoing outpatient follow-up and monitoring.

**Discussion**

Maffucci syndrome is a condition characterized by the coexistence of multiple enchondromas and hemangiomas primarily occurring more frequently on the hands, feet, and wrists, and its cause is not well understood. It typically manifests around the age of 4 to 5, and approximately 25% of cases are congenital [6]. It is associated with somatic mutations in the IDH1/IDH2 genes, and in 2021, a mutation in the ELKS/RAB6-interacting/CAST family member 2 (ERC2) gene, specifically the L309I mutation, was confirmed to be related to Maffucci syndrome [7,8].

In Maffucci syndrome, enchondromas typically about or have continuity with the growth plate, suggesting a potential origin from improper regulation of adjacent growth plate chondrocyte proliferation and final differentiation. Furthermore, the condition is often associated with vascular malformation, such as cavernous hemangiomas and venous dilatation. Unlike typical venous malformation, which is compressible and tends to collapse upon pressure, the venous malformation in Maffucci syndrome typically manifests as firm and nodular cutaneous lesions [9]. Maffucci syndrome can typically be diagnosed relatively easily based on clinical criteria alone, although further studies including radiographs and arteriography, may be required at times. In particular, when hemangiomas are large, arteriography can be used to determine the need for arterial embolization. Clinical issues related to enchondromas in Maffucci syndrome include skeletal deformities and the potential for malignancy. While the likelihood of malignancy in patients with simple enchondromas is generally less than 1%, malignant transformation has been reported in approximately 25% to 37% of documented cases of Maffucci syndrome worldwide. Additionally, there is an increased risk of developing malignancies such as pancreatic cancer, breast cancer, and malignant tumors of the central nervous system [2,4,5]. Therefore, in cases where Maffucci syndrome is suspected, it is essential to conduct periodic monitoring to detect malignant transformations early. This involves assessing the
Fig. 3. (A, B) A well-defined lobulated intramedullary metaphyseal lesion (arrow) occupying the proximal ulna and displaying a low signal on T1-weighted imaging (A) and a bright signal on T2-weighted imaging (B). (C, D) The size of the lesion is about 2.8×2.1×1.8 cm. Pelvic magnetic resonance imaging shows multiple lobulated mass lesions with extrasosseous extension and cortical bone destruction in both pelvic bones, which have T1 low signal intensity (C) and T2 heterogeneous high signal intensity (D). Arrows, osteolytic mass in the proximal ulna.

progression of multiple lesions and, when necessary, performing biopsies and making pathological diagnoses.

Maffucci syndrome shares some similarities with Ollier disease, which is characterized by multiple enchondromas. However, Ollier disease has a higher prevalence, with an incidence of approximately 1 in 100,000 individuals, making it more common than Maffucci syndrome. Ollier disease is distinguished by unilateral multiple enchondromas and does not exhibit venous vascular abnormalities or hemangiomas, in contrast to Maffucci syndrome. Importantly, Maffucci syndrome carries a significantly higher risk of malignant transformation compared to Ollier disease, emphasizing the need for early differentiation [4,10].

Maffucci syndrome does not require specific treatment when there are no symptoms, and surgery may be considered in cases with complications such as pathological fractures, growth disturbances, or malignant transformations. The primary goal of surgery is to alleviate symptoms by removing the lesions and obtaining an accurate diagnosis through biopsy. If malignancies like chondrosarcoma are confirmed later on, additional treatments may be necessary, including sclerotherapy, radiation therapy, and laser therapy.
Fig. 4. During surgery, erosion and abnormal bony lesions were found. (A) Intraosseous masses found at the right iliac wing. (B) An intraosseous mass found at the right proximal ulna. (C) Specimen taken from the right iliac wing and right proximal ulna for biopsy. Arrows, avascular wax-like masses in the right iliac wing.

Fig. 5. Histopathologic findings of the proximal ulna (A, B) and iliac wing (C, D). (A, C) Both tumors were composed of mature hyaline cartilage and showed multinodular architecture (hematoxylin-eosin, ×40 magnification). (B, D) Both tumors showed slightly increased cellularity, with chondrocytes lying in the lacunae and having small round nuclei without marked cytologic atypia (hematoxylin-eosin, ×100 magnification).
The patient had a history of brain tumor diagnosis with confirmed enchondroma in the past and presented with suspected enchondromas in the right upper limb, bilateral pelvis, and bilateral lower limbs. Biopsies conducted in the right upper limb and right pelvis ultimately confirmed enchondroma. Additionally, venous malformations were observed in both upper limbs and suspected vascular lesions in the right lower limb, along with calcifications. There was discomfort in the right elbow and iliac wing, and imaging findings indicated suspected enchondromas in these areas, leading to the decision for removal and biopsy through surgery. Furthermore, considering the suspected multiple vascular lesions observed in the right foot, surgical treatment for cosmetic reasons could have been an option. However, the patient chose not to undergo lesion removal for cosmetic reasons. In this case, even though the biopsy resulted in an enchondroma which is benign, it is essential to maintain ongoing surveillance due to the reported approximately 30% malignant transformation rate in Maffucci syndrome.

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**Conflicts of interest**

The authors have nothing to disclose.

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