ENCHONDROMATOSIS-OLLIER DISEASE-CASE REPORT

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Abstract

Enchondromas are common intraosseous, usually benign cartilaginous tumors, that develop in close proximity to the growth plate cartilage. When multiple enchondromas are present, the condition is called enchondromatosis also known as Ollier disease. Clinical manifestations often appear in the first decade of life. Ollier disease is characterized by an asymmetric distribution of cartilage lesions and these can be extremely variable.Clinical problems caused by enchondromas include skeletal deformities, limb length discrepancy and the potential risk for malignant change to chondrosarcoma. The condition in which multiple enchondromatosis is associated with soft tissue hemangiomas is known as Maffucci syndrome. The diagnosis is based on clinical and conventional radiological evaluations. Histological analysis has a limited role and is mainly used if malignancy is suspected.

Key words: Ollier disease, enchondromatosis, multiple enchondromatosis, dyschondroplasia

Definition

Enchondromas are common benign, usually asymptomatic cartilage tomors, which develop in the metaphyses and may become incorporated into the diaphyses of long tubular bones, in close proximity to the growth plate cartilage.

Enchondromatosis or Ollier disease is defined by the presence of multiple enchondromas and characterized by an asymmetric distribution of cartilage lesions that can be extremely variable in terms of size, number, location, evolution, age of onset and diagnosis and requirment for surgery.

The condition in which multiple enchondromatosis is associated with soft tissue hemangiomas is

known as Maffucci syndrome.

Epidemiology

The estimated prevalence of Ollier disease is 1/100.000.Maffucci syndrome has indeed a lower prevalence.

Solitary endochondromas are most commonly discovered between 20 and 40 years of age but Ollier disease tends to present before 10 years old.

Males are affected twice as often as females.

Etiology and pathogenesis

Endochondral bone ossification is a highly regulated process, which requires the progression of undifferentiated mesenchymal cells into hypertophic chondrocytes and the subsequent replacement of a cartilaginous matrix by mineralized bone.Enchondromas develop in the methaphysis of long tubular bones in close proximity to the growth plate.Consequently, it was proposed that they result from abnormalities in signaling pathways controlling the proliferation and differentiation of chondrocytes, leading to the development of intraosseous cartilaginous foci.

Genetics

Ollier disease and Maffucci syndrome are usually non-familial disorders and both disorders thus appear to occur spontaneously and are not inherited.The irregular distribution of the lesions in Ollier disease strongly suggests that it is a disorder of endochondral bone formation that occurs due to a post-zygotic somatic mutation that results in mosaicism.

Although an identical heterozygous mutation in the PTHR1 gene has been identified, other mutations involving this gene were identified.These studies suggest that the cause of Ollier disease is heterogenous and raise the possibility that two or more genetic mutations are required to develop the disease.

Additional mutational events may underly progression from enchondromas to tumors.

Histopathology

Macroscopic examination of enchondromas usually shows multiple oval shaped or round cartilaginous nodules in osseous portions of bone. The individual nodules are limited at their periphery by woven or lamellar bone and are separated from each other by intertrabecular marrow spaces.

The cartilaginous tumor matrix is usually solid, with myxoid changes, which manifest as frayings of the matrix.Enchondromas are characterized by the presence of a striking heterogeneity and diversity in the degree of cellularity and chondrocyte phenotype. This heterogeneity depends to some extent on factors such as localization and the patient's age.

In part, due to this important cellular heterogeneity the distinction between benign enchondromas and malignant chondrosarcomas by histochemical criteria is difficult.The histological criteria for malignancy that are used for conventional chondrosarcoma can not be used in Ollier disease because of the increased cellularity and therefore the distinction between enchondroma and grade I chondrosarcoma in the context of enchondromatosis is extremely difficult or even impossible.

Classification

There are six types of enchondromatosis but three are more common:

-In Ollier disease there are multiple enchondromas that are mostly unilateral or unevenly distributed throughout the metaphases of the long bones, sparing the cranium and spine.

-In Maffucci syndrome the enchondromas occur with multiple cutaneous hemangiomas that appear as soft tissue calcifications or phleboliths on x-ray.

-If there is symmetrical involvement throughout the body including the cranium, hands and feet the condition is known as generalised enchondromatosis.

Clinical description

Clinical manifestations in Ollier disease often appear in the first decade of life and usually start with the appearance of palpable bony masses on a finger or a toe, an asymmetric shortening of an extremity with a limping gait and osseous deformities eventually associated with pathologic fractures.Upon physical examination, enchondromas present on the extremities are usually visible as masses embedded within phalanges, metacarpal and metatarsal bones.The masses increase in size as the child grows along with asymmetrical shortening of a limb and either genu valgum or most commonly genu varum deformities. Enchondromas frequently affect the long tubular bones, particularly the tibia, the femur and/or the fibula. Flat bones, especially the pelvis, can also be affected.The lesions are usually asymmetrically distributed, exclusively or predominantly affecting one side of the body.

Affected bones are often shortened and deformed.

Bone shortening may be the only clinical sign of the disease and these bone shortenings are often associated with bone bending and curving and may lead to limitation in articular movement.

Forearm deformities are frequently encountered and these are similar to those observed in hereditary multiple exostosis (HME).Ulnar shortening is usually more relevant than shortening of the radius.

The trunk is usually not affected except for costal enchondromas and secondary scoliosis resulting from pelvic imbalance.

During childhood, the lesions are subjected to pathologic fractures.

Diagnostic methods

The diagnosis of Ollier disease is based on clinical and conventional radiological evaluations.

Histological analysis has a limited role and is mainly used if malignancy is supected.

Additional investigations such as scintigraphy,

Ultrasound, magnetic resonance imaging (MRI) are not useful for establishing the diagnosis and they are indicated for the evaluation and surveillance of lesions that become symptomatic (pain, increase in size).

Biopsy of suspicious lesions may be required.

Radiography

Enchondromas are rarely observed at birh,although the lesions are most likely already present. X-ray show multiple, radiolucent, homogenous lesions which run parallel with long bone axis. The lesions usually calcify with time and become diffusely punctated or stippled, a light trabeculation may be visible. Enchondromas are frequently assembled as clusters, thus resulting in the metaphyseal widening.When localized at the bone border, the enchondromas produce a typical notch-like image.

The lesions are almost exclusively localized in the metaphysis of long bones and in the small bones of the hands and feet. They are initially localized close to growth plate cartilage and then migrate progressively towards the diaphysis.The epiphyseal region next to an affected metaphysis may show irregularities.In the hands, the lesions almost never affect all metacarpal bones and phalanges.

Signs of malignant transformation should be looked for, as it is a major complication of enchondromatosis. These signs includes cortical erosion, extension of the tumor into soft tissues and irregularity or indistinctness of the surface of the tumor.

Enchondromas tend to be well circumscribed and to show a uniform pattern of mineralization, whereas chondrosarcomas show poor demarcation and the presence of unmineralized parts.

Differential diagnosis

The differential diagnosis may include:

-Hereditary multiple exostosis –HME is an autosomal dominant disorder characterized by multiple bone tumors capped by cartilage, that occur mostly in the metaphyses of long bones.

-Other rare forms of chondromatosis which include metachondromatosis, spondyloenchondrosia and genochondromatosis type I and II

-Polyostotic fibrous dysplasia

-Diaphyseal aclasis

-Kaposi sarcoma

-Klippel-Trenaunay syndrome

-Weber –Parks syndrome

Treatment

There is no medical treatment for Ollier disease.

Surgery is indicated in enchondromatosis complicated by pathological fractures, growth defect or malignant transformation.

Complications

Besides asymmetrical growth, the condition might be complicated by pathological fractures and malignant change as chondrosarcoma and osteosarcoma.

In Ollier disease, about 25% of cases will undergo malignant change by the age of 40.

Prognosis

The prognosis for Ollier disease is difficult to assess. Early onset disease seems to have a more severe course. Research has shown that patient with numerous lesions may

have a better prognosis than patients with localized cartilaginous lesions since the latter may induce major shortening of a lower extremity and thus limb asymmetry.

After puberty, the enchondromas typically stabilize as cartilage is replaced by bone.

The reported incidence of malignant transformation is variable and estimated to occur in 5-50%.

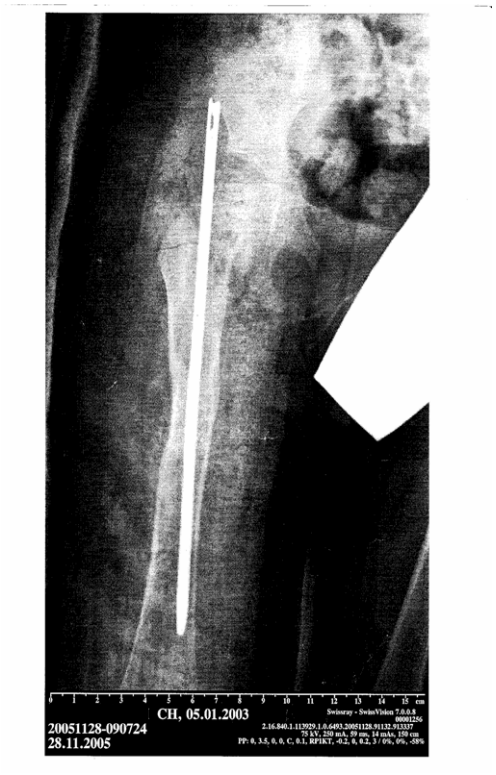
Case report

We present a case of a six year old boy that was admitted in our department four years ago for pain involving the right lower limb and a limping gait.

After an x-ray examination, the diagnosis of bone cyst of the proximal right femur was established.

A biopsy of the suspicious lesions was performed and the histopathological diagnosis was mistakenly established as aneurysmal bone cyst.

We report an intraoperative pathological fracture of the right femur at the level of the enchondromatous lesions and a intramedually rod was inserted followed by casting [Figure-1]. The patient presented an uneventful postoperative period. Initially, the patient was followed up clinically and radiologically every 2 months for the first 6 months and subsequently once a year.The rod was retrieved after 6 months without visible shortening of the right lower limb, but with a persistent mild limping gait. Consequently, the patient experienced pain in the right lower limb.The patient also had associated pain involving the right upper limb and right podalgia.

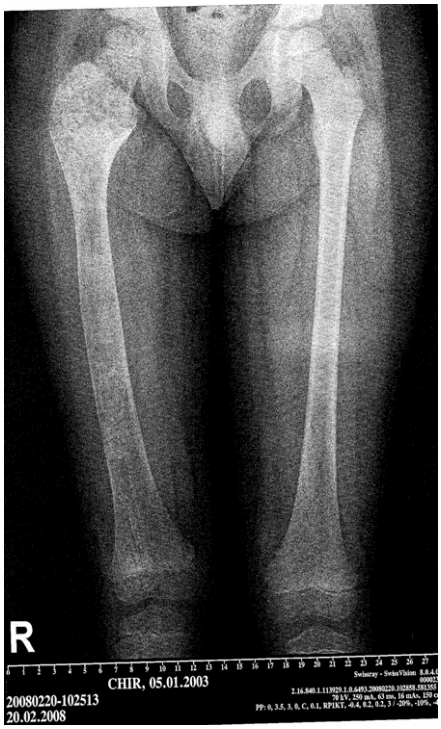


[Figure-1] Postoperative X-ray illustrating bone fixation using an intramedullary rod.

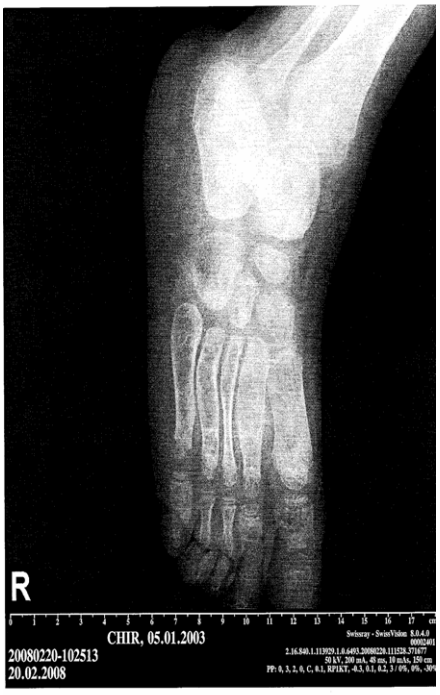
At the age of four, x-rays of the skull, superior and inferior limbs were performed and revealed multiple radiolucent homogenous oval shaped lesions with a well defined slightly thickened bony margin-enchondromas like-localized at the superior metaphyseal and diaphyseal regions of the right femur, right distal tibia, metatarsal bones and proximal falanges [Figures 2 and 3]. Cliches of the skull and superior limbs were normal. A biopsy of suspicious lesions from the right tibia was undertaken. Comparative histopathological studies conducted by the histopathology departement affiliated with our clinic and Le Centre de Pathologie from Montpellier - France confirmed the initial diagnosis of enchodromatosis and ruled out a malignization process. The postoperative period was uneventful.

Two years later (on April 24th 2009), under a perseverant clinical and radiological monitoring, the patient was readmitted in our department with a pathological fracture of the right femur following a minor injury caused by a fall. Open reduction and internal fixation using an intramedullary rod were performed and an additional biopsy was undertaken only to ascertain the benign histology of the enchondromatous lesions.

At the present time, the patient is immobilized and monitorized every two months.



[Figure-2] Roentgenogram illustrating enchondromas involving the superior metaphyseal and diaphyseal segments of the right femur.



[Figure-3] Roentgenogram revealing enchondromatous involvement of right distal tibia, metatarsal bones and proximal falanges.

Prevention

Despite the universal acceptance that Ollier disease carries a high risk of malignant change the data from the literature about systematic screening for early diagnosis are scarce. One such paper advised periodic surveillance of the brain and abdomen for occult malignant lesions in patients with enchondromatosis (12), but failed to be more specific the optimal screening frequency.

Another article emphasized the association with an increased risk of malignancy including intracranial chondrosarcomas, and labelled early diagnosis and screening patients with Ollier disease as being of a crucial relevance (13). But then again, the optimal screening frequency is a subject that has been conspicuously omitted. It did state that the treatment of choice for intracranial cartilaginous tumors is complete surgical excision, but this is fraught with technical difficulties. An alternative therapeutic option to be considered would be proton-beam therapy.

Conclusions

Ollier disease is an extremely rare, non-hereditary skeletal condition. There is no medical treatment for this disease, with surgical treatment only intervening in the unfortunate instance of a complicated enchondromatosis. The evolution of most enchondromas enters a steady state after puberty as cartilage is replaced by bone, nontheless around 25% of lesions will undergo malignant transformation by the age of 40.

We recommended clinical follow-up once a year untill puberty, a deadline by which ossification is completed

Thereafter a long term follow up until the age of 40, once a year or every 2 years for early detection of a malignant change.

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