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 tumors, 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 requirement 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 hypertrophic chondrocytes and the subsequent replacement of a cartilaginous matrix by mineralized bone. Enchondromas develop in the metaphysis 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.
in the first decade of life and usually start with the
Clinical description
known as generalised enchondromatosis.
body including the cranium, hands and feet the condition is
-If there is symmetrical involvement throughout the
calcifications or phleboliths on x-ray.
-multiple cutaneous hemangiomas that appear as soft tissue
-In Maffucci syndrome the enchondromas occur with
spine.
metaphases of the long bones, sparing the cranium and
More common:
-hereditory multiple exostosis (HME).Ulnar shortening is usually more relevant
These signs includes cortical erosion, extension of the tumor
into soft tissues and irregularity or indistinctness of the
surface of the tumor.
Enchondromas tends 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

Classification
There are six types of enchondromatosis but three are
more common:
-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.
-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.

Radiography
Enchondromas are rarely observed at birth, 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.
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 an intramedullary 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.

A biopsy of the 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 enchondromatosis 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 monitored every two months.

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 enchondromatosis and ruled out a malignization process. The postoperative period was uneventful.

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

[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.
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, nonetheless around 25% of lesions will undergo malignant transformation by the age of 40.

We recommended clinical follow-up once a year until 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.

References

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