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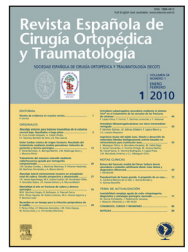

CLINICAL NOTE

Neurogenic heterotopic ossification of the hip. Presentation of two cases

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KEYWORDS
Heterotopic ossifications of the hip;
Neurogenic ossifications;
Traumatic brain injury;
Spinal cord injury

Abstract
Objective: To describe two cases of neurogenic heterotopic ossification (NHO) of the hip and to review the literature on this condition.
Material and methods: Two patients of 28 and 32 years old who spent some time in a coma due to a traumatic head injury and stroke respectively. Both developed NHO that required surgery.
Results: In the first case flexion improved 65 degrees and abduction 20 degrees. In the second, flexion improved 75 degrees, external rotation 15 degrees and abduction 30 degrees. Both patients could walk without pain and could tolerate a prolonged sitting position.
Discussion: The pathogenesis of these ossifications remains unknown. With CT we can see the exact location, the relationship of ossification to the femoral vascular bundle, the bone density and the hip joint condition. The removal of these lesions should be done when the ossification is mature enough, but before a significant lack of mobility of the hip is established.

PALABRAS CLAVE
Osificaciones heterotópicas de cadera;
Osificaciones neurogénicas;
Traumatismo craneoencefálico;
Lesión medular

Osificaciones heterotópicas neurogénicas de cadera. A propósito de 2 casos

Resumen
Objetivo: Describir 2 casos de osificaciones heterotópicas de cadera secundarias a una lesión neurológica (OHN) y revisión bibliográfica del tema.
Material y métodos: Pacientes de 28 y 32 años que pasaron un período de coma como consecuencia de un traumatismo craneoencefálico y un accidente cerebrovascular respectivamente. Ambos desarrollaron OHN que precisaron intervención quirúrgica. El seguimiento fue de 24 meses en el primer caso y de 12 meses en el segundo.

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Resultados: En el primer caso la flexión mejoró 65º y la abducción 20º; en el segundo la flexión mejoró 75º, la rotación externa 15º y la abducción 30º. Ambos pacientes caminan sin dolor y toleran una sedestación prolongada.
Discusión: La patogenia de estas osificaciones permanece desconocida. La TC nos permite precisar la localización, la relación de la osificación con el paquete vascular femoral, la densidad ósea y el estado de la articulación coxofemoral. El momento ideal para la exéresis de estas lesiones es aquel en que la osificación está suficientemente madura, pero antes de que se produzca un déficit significativo de la movilidad de la cadera.

Introduction

Neurogenic heterotopic ossification (NHO) of the hip means the ossification appearing in periarticular soft tissues following a central nervous system (CNS) injury, usually in association with prolonged coma. In this type of ossification, there is no direct or indirect injury or trauma to the joint–in contrast to that seen in the case of myositis ossificans, periprosthetic calcification, and the calcification associated with acetabular fracture. Although its true incidence is unknown, it appears to be related more to medullary neurological damage (with incidence ranging from 16% to 53% of patients) than to intracranial damage (10%-20%).

The objective of our study is to present 2 cases treated on our Service and describe the praxis for diagnosis and treatment of NHO.

Clinical cases

We present 2 clinical cases of NHO of the hip. In both cases, the intervention was performed under general anaesthesia using an anterior hip approach (Smith-Petersen) and widely exposing the osseous neoplasm. We believe it is crucial that a vascular surgeon be present in the operating room because these ossifications are often closely associated with the femoral vascular bundle. Chisels were used to resect the ossifications, with the assistance of an image intensifier. We recommend resecting the heterotopic bone progressively as improvement in hip mobility is being monitored, intraoperatively, because it is not absolutely necessary to resect the entire ossification. There must be meticulous haemostasis to prevent the appearance of third spaces that predispose to a post-operative infection.

Case 1 was a 28-year-old male patient who presented with a traumatic brain injury with epidural haematoma. After being in a coma for 4 months, the patient, having left-sided hemiparesis as a neurological sequela and having received no prophylactic therapy in the hospital of origin to prevent NHO, gradually developed left-sided inguinal pain and limitation to passive mobility of the hip joint. A simple x-ray showed no changes (fig. 1A). Four months after the patient came out of the coma, a scan was done because of suspicion that he was developing NHO; the findings were suggestive of increased periarticular osteogenic activity. No prophylactic therapy was prescribed, and 6 months later–14 months after the neurological injury–there was clinical deterioration: on physical examination, patient had significant limitation of hip mobility (15º flexion, 0º extension, internal rotation blocked with an external position of 25º, 5º adduction, and 10º abduction. A simple x-ray showed anteromedial ossification in the left hip, about 20 cm in length, from the iliac wing to the proximal femur (fig. 1B). Computerised tomography (CT) showed how it was encompassing the psoas muscle, with medial displacement of the deep femoral artery and vein (fig. 1C). To determine the extent to which the vessels were involved and make the upcoming intervention safer, magnetic resonance angiography was done, which showed close association with the femoral bundle and how the lateral circumflex artery was surrounding the osseous neoplasm. After 4 months (18 months after the neurological injury), the decision was made to perform a conservative surgical excision of the ossification that would permit optimal range of motion. This patient experienced a significant improvement in symptoms, with the following range of motion in the hip: 80º flexion, 0º extension, 20º external rotation, 10º internal rotation, 10º adduction, and 30º abduction. Despite the neurological sequela of his hemiparesis, the patient was able to walk without canes. At the 2-year follow-up, no recurrence of the ossification was appreciated (fig. 1E).

Case 2 was a 32-year-old male patient who presented with ischaemic cerebrovascular accident (CVA) followed by 5 months in coma; no preventive measures were implemented with this patient, either. He was referred to our Service 7 months later, presenting with severely restricted mobility of the hip (15º flexion, -5º extension, 0º for both internal and external rotation, 5º adduction, and 15º abduction), moderate pain, and complete inability to sit in a chair. Simple x-ray showed periarticular anteromedial ossification of 24 centimetres (fig. 2A). On the CT that was done 5 months later (17 months after the CVA), involvement of the psoas muscle, the vastus intermedius, and the medial quadriceps was appreciated (fig. 2B). The external iliac artery and vein in the more proximal area and the femoral vascular bundle in the more distal area were medial to the ossification, and there was a fat plane of separation along the entire NHO trajectory. The surgery was performed at the end of 3 months (20 months after the CVA), confirming intraoperatively that the hip reached 90º flexion (fig. 2C). At the 1-year follow-up, patient had no signs of recurrence and experienced a significant improvement in symptoms: he was able to sit without difficulty, and the mobility in his hip had improved markedly (90º flexion, –10º extension, 15º external rotation, 5º internal rotation, 10º adduction, and 45º abduction).

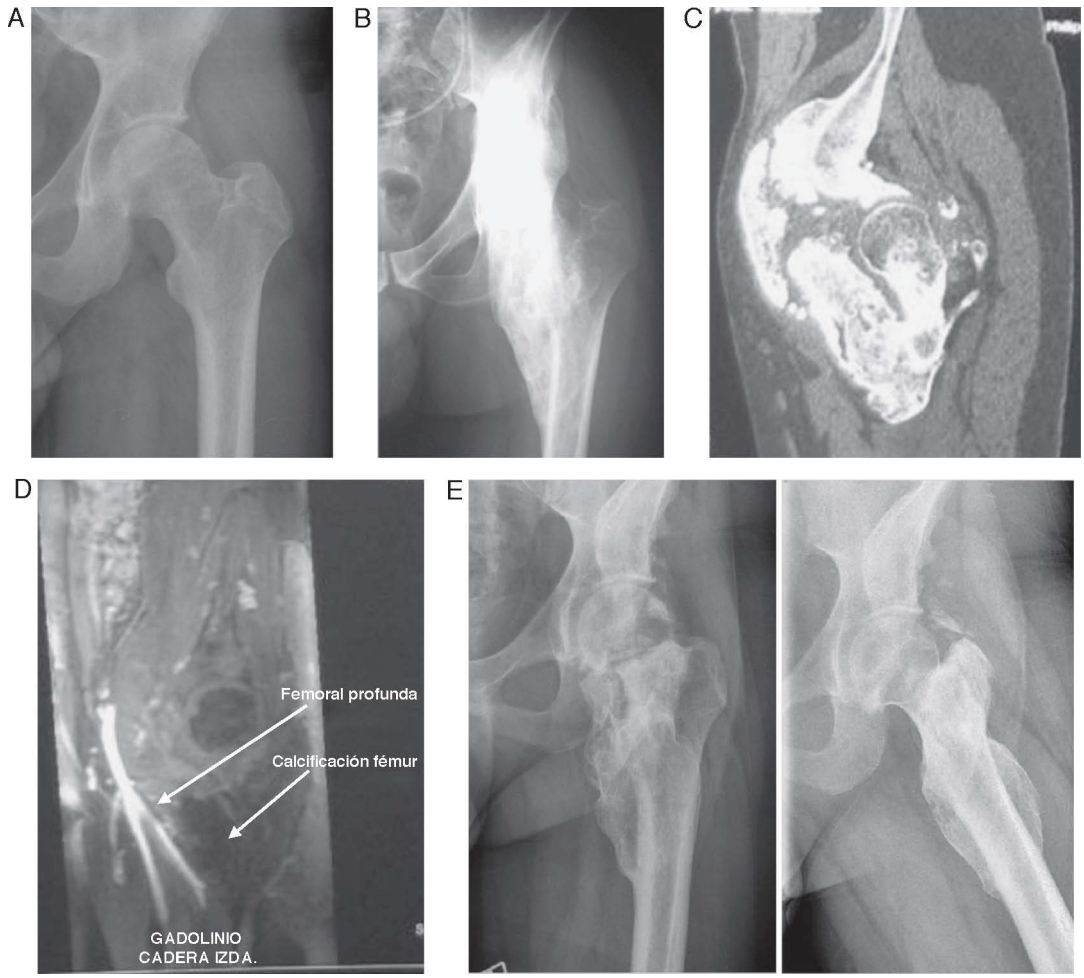

Figure 1 Images for case 1. A) X-ray of left hip 6 months after the trauma, with no visible ossification. B) Anteromedial ossification from iliac wing to proximal femur. C) CT of hip where heterotopic ossification is appreciated in the anteromedial aspect, encompassing the iliopsoas muscle. D) MR Angiography: displacement of the femoral artery and vein due to the ossification and association with the lateral circumflex artery. E) Anteroposterior and axial x-rays at 24 months after the surgery.

Although there are no Evidence Level I studies that give an explanation as to what prophylactic measures should be instituted post-operatively to prevent the recurrence of NHO, early rehabilitation, indomethacin, bisphosphonates, or radiation therapy were used. Both patients followed an intensive rehabilitation plan with 4 hours of passive range of motion exercises daily starting in the immediate post-operative period, and a regimen of indomethacin 25 mg every 8 hours for 15 days was used.

Discussion

NHO is a complication that should be remembered as a possibility in patients with neurological injury–generally coma and, to a lesser degree, medullary injury–because it can cause restricted mobility or joint ankylosis. NHO can develop in any joint, most commonly in the hip followed by the knee, the shoulder, and the elbow.

The aetiopathogenesis of NHO is an enigma. It is thought that neurological injury triggers the systemic release of a number of substances (bone morphogenetic proteins, prolactin, fibroblast growth factors, insulin-like growth factor 1, etc.) that stimulate pluripotential mesenchymal stem cells and that these, in the environment of metabolic alkalosis, tissue hypoxia, and changes in microvascularisation typical of multiple trauma patients, differentiate to osteoblasts. Spasticity, decerebrate posturing, diffuse axonal injury, prolonged immobilisation, and mechanical ventilation appear to be factors that facilitate osseous neoplasm in the soft tissues.[1]

The clinical symptoms are not very clear: joint swelling suggestive of an infection, with associated limitation of passive mobility in the hip, is a sign that may appear while the patient is still in a coma. As far as laboratory tests, there is a marked elevation in blood levels of alkaline phosphatase, which is an indicator of osteoblast activity.[2,3] However, even though this is a very sensitive marker, it is not very specific, for levels can also be elevated whenever there is a fracture or liver damage–circumstances commonly found in multiple trauma patients who are in coma. High urine levels of prostaglandin E2 have been

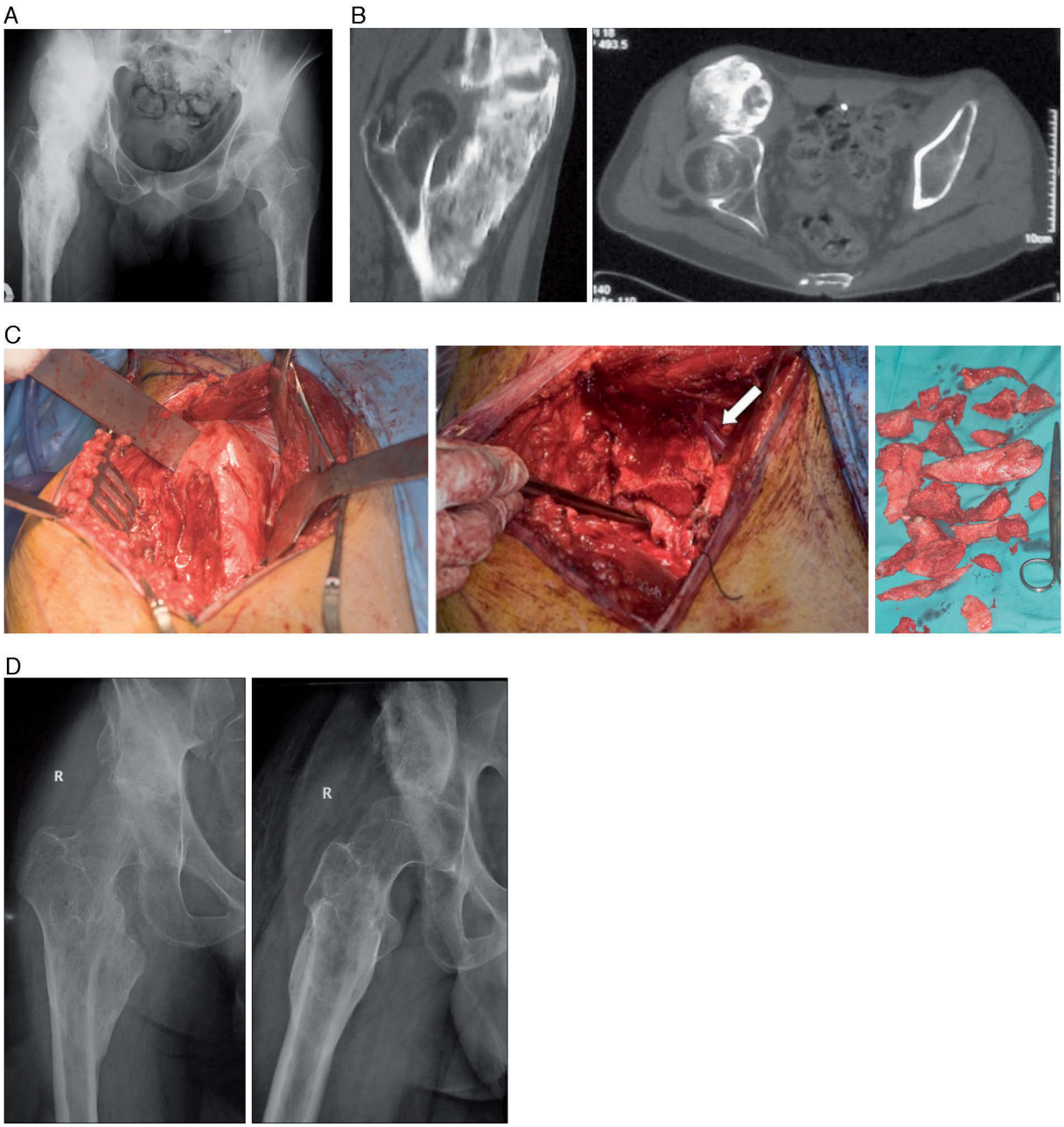

Figure 2 Images for case 2. A) X-ray of right hip at 12 months after the CVA. B) CT showing ossification involving the psoas, vastus intermedius and medialis. C) Images from the surgical procedure (left to right): exposure of the ossification via a Smith-Petersen approach; after most of the lesion was resected, its proximity to the deep femoral artery (arrow) was appreciated as well as the fact that it extended to the plane of the joint capsule (held by dissecting forceps); bony fragments removed. D) Anteroposterior and axial x-rays at 12 months after the surgery.

shown to be a useful marker in the early diagnosis of NHO.

The best diagnostic test is a simple x-ray of the pelvis, although the ossification may not be visible until several weeks or even months have passed.[3] A scan[2,3] allows for the earliest detection of NHO; however, as we will see below, routine use of it has been declining in recent years.

To prevent the formation of neurogenic ossification in the hip, passive range of motion for the joints can be started while the patient is still in the Intensive Care Unit because the ossification begins forming between 4 and 12 weeks after the neurological injury. To prevent the appearance of local microhaematomas that may, in turn, induce calcification or ossification of the soft tissues, this rehabilitation should not be too vigorous. Simonsen et al[4] suggest that the incidence of NHO could be lower if a rehabilitation plan is implemented early-on. Indomethacin has been shown to be effective as prophylactic treatment in patients who have suffered a medullary injury,[5] and it is considered a mainstay of prevention. The bisphosphonates

have also been used, but their efficacy has not been demonstrated. Radiation therapy, which is effective as prophylaxis against ossifications following hip replacement and acetabular fractures, is seldom used routinely in these patients because it is impossible to predict whether heterotopic bone will form and which joint it will appear in, if it does form.

Surgical excision of the ossifications is the only treatment that has been shown to be effective. This intervention is indicated when a significant reduction in joint range of motion causes the patient difficulty with walking, sitting, or personal hygiene or limitations in daily living due to neurovascular compression or pain.[6] Prior to taking the patient to surgery, it is important to be certain, from a neurological standpoint, that the patient cannot improve any further and that the patient's deficit is due to mechanical limitations imposed by the ossification.

The greatest difficulty lies in determining the best time for surgical intervention. The classical thinking was to wait until the ossification was as mature as possible[2,7]–that is, until it had reached a radiological density similar to that of healthy cortical bone–for the purpose of preventing its recurrence; serial scans were done with the expectation that uptake would gradually become colder. Monitoring alkaline phosphatase was also useful because levels start dropping when osteoblast activity decreases.[3,7] Garland[3] came to believe that the ideal time for surgical intervention would be 6 months, if it was a traumatic ossification; 12 months, if it was after a medullary injury; and 18 months, if it was a cerebral injury.

There has been a change of "philosophy" lately because recent articles have shown that delaying surgery creates 2 problems. The first would be a steady loss of mobility that could progress even to ankylosis of the hip–and ankylosis is directly related to the appearance of a degenerative-type deterioration of the joint space. The second of these problems is severe osteopenia arising in the head and neck of the femur, which dramatically increases the risk of fracture. In this regard, Genet[8] related severe osteoporosis to cases where there was a greater loss of mobility, and fractures were detected only in those patients who had ankylosis; the non-ankylosed hips showed no articular damage. Carlier et al,[9] by comparing bone density in the head of the femur with that in the ipsilateral iliac wing, developed a classification and established 4 degrees of osteopenia: normal (M1), moderate demineralisation (M2), significant demineralisation with fracture risk (M3), and bone density similar to fatty tissue with chance of imminent fracture (M4). This author encountered neither severe osteoporosis nor intra-operative fractures when the intervention took place within 24 months of the CNS injury. The presence of osteoporosis means an increased risk of fracture, of course, but we should always be mindful of this possible complication and be prepared to address it.

Surgical intervention occurred relatively early-on in our patients. Case 1 underwent surgery 18 months after the neurological injury, once we had been informed by the Neurology Service that the left-sided hemiparesis was irreversible and not amenable to improvement, and in view of the painful limitations the patient was experiencing. Case 2 underwent surgery 20 months after the CVA, when the options for rehabilitation had been exhausted and the patient was completely unable to sit.

A CT had been done on both patients pre-operatively. This test is crucial to proper pre-operative planning in that it permits the exact location and size to be known. On the other hand, scans appear to be losing popularity, given that it can take months or even years until they "cool", which may result in surgery being seriously delayed and risking development of the much-feared ankylosis.

While maturity of the ossification must be taken into account prior to its surgical excision, based on the literature reviewed, it appears that the loss of mobility preceding ankylosis is a more important factor than the maturity in deciding when to perform the operation; doing it early-on facilitates the patient's rehabilitation because the risk of joint injury and intra-operative fracture is reduced, and the risk of recurrence does not appear to be increased.[8-10]

Depending on the anatomical location of the ossification, more serious complications may arise due to nerve or vascular injury, apart from bleeding of the resected bone surface, which can be profuse. Recurrences are related to inadequate intra-operative haemostasis and to operating on very immature ossifications. Despite the lack of clear evidence, early rehabilitation is recommended, whether manually or with a continuous passive motion machine, and drugs such as the non-steroidal anti-inflammatories or indomethacin should be used. Some authors recommend radiation therapy at a dosage of 600 cGy within the first 72 hours after surgery, but there is no evidence of its effectiveness. Another possible complication is intraoperative fracture of the neck of the femur, for which treatment is not very satisfactory: the osteosynthesis is usually unstable, given the poor bone quality, and total hip replacement may pose additional risks of infection (lengthy surgical procedures, urinary infections from the patient's ongoing catheterisation, immunosuppression, etc.) or dislocation of the prosthesis due to the lack of proper neuromuscular control. Neurovascular injuries are not uncommon, so it is recommended that a vascular surgeon be available to assist.

Protection of human and animal subjects

The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data

The authors will declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent

The authors must have obtained the informed consent of the patients and / or subjects mentioned in the article. The

author for correspondence must be in possession of this document.

Evidence level

Evidence level V.

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