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Case Report

Unforeseen consequence: heterotopic ossification following traumatic brain injury and acetabulum fracture-a case report

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ABSTRACT

Heterotopic ossification (HO) is a rare pathological condition characterized by the formation of bone in soft tissues outside the normal skeletal system. HO can result in restricted joint mobility, nerve compression, and pain. We present a case report of a 34-year-old male who developed HO. There is a history of neurological injury and fracture acetabulum (left). Imaging studies revealed extensive HO with complete bony bridging of the hip joint, leading to severe functional impairment and chronic pain. The patient had previously undergone multiple medical treatments with non-steroidal anti-inflammatory drugs, and physiotherapy with limited success. Ultimately, he underwent a complex surgical intervention involving resection of HO, release of joint contractures, resulting in significant improvement in joint mobility and pain control. Here we discuss a rare and debilitating presentation of HO and the treatment options available for such patients. Clinicians should be aware of this challenging condition and manage patients through a multidisciplinary approach.

Keywords: HO, Neurological injury, Acetabulum fracture

INTRODUCTION

Heterotopic ossification (HO) is a pathological process in which bone formation occurs in soft tissues such as muscles, tendons, and ligaments. This can result in the formation of bone outside the normal skeletal system, leading to complications such as range of motion, neurovascular compression, and pain. Three possible causes: progressive myositis ossificans: genetic cause, traumatic myositis ossificans: through direct/surgical trauma and most common cause, neurogenic cause of HO described by Dejerine and Ceilier in 1918 as para-osteoarthropathy in patients with medullary lesions.[1]

HO can occur after a variety of injuries, including fractures, joint dislocations, burns, and spinal cord injuries. In some cases, it may also occur after elective surgeries, such as joint replacements. The exact cause of HO is not fully understood, but it is thought to involve the abnormal proliferation of mesenchymal stem cells, which differentiate into bone cells inappropriately. Also, it is proposed that excessive local mechanical stimulus results in periosteal activity promoting new bone formation.

Clinical presentation of HO may vary depending on location and severity of condition. However, some of the common symptoms associated with HO include: Restricted range of motion in the affected joint, swelling and tenderness, stiffness and pain in affected joint, difficulty in weight-bearing activities, warmth and redness around the affected joint and formation of bony bridges between adjacent bones.

It is important to note that the above symptoms are not specific to HO and can also be associated with other joint disorders. Therefore, imaging tests such as X-rays, CT

scans, and MRI can help in establishing the diagnosis of HO even at early stage.[2] A biopsy may also be necessary to confirm the diagnosis and rule out other conditions.

CASE REPORT

The patient, aged 34, involved in a road traffic accident in 2019, was admitted in hospital with head injury and fracture left acetabulum. The patient was operated for head injury in 2019 under neurosurgery department at SMS hospital, Jaipur and managed fracture acetabulum (left) conservatively. After 18 months, X-ray hip revealed left hip heterotrophic ossification signs (Figure 1).

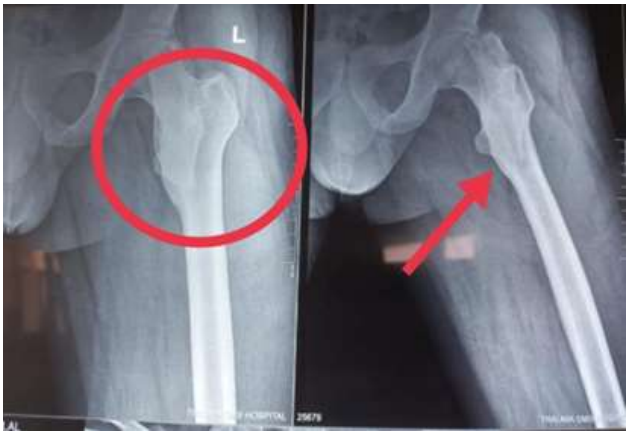

Figure 1: Pre-operatory x-ray.

The patient was transferred in a physical medicine and rehabilitation and neurosurgery for further management. no drugs prescribed for heterotrophic Ossification, only symptomatic management and physiotherapy was started. Hence, the passive motion in the left hip joint was gradually impaired and after 2 years from the accident a massive 20 cm HO was identified. The patient was admitted in SMS hospital Jaipur, with complain of pain and restriction in range of motion of left hip joint. On examination there is restriction in abduction and flexion at hip joint (left) with internal rotation (Figure 2).

Figure 5: Pre-operative restriction in abduction and flexion at hip joint with internal rotation.

For surgical management, a simple X-ray (Figure 1), CT scan and CT arteriography with 3D reconstruction (Figure 3), were performed to establish the exact dimensions and vascular-nervous relation and routine investigations was done.

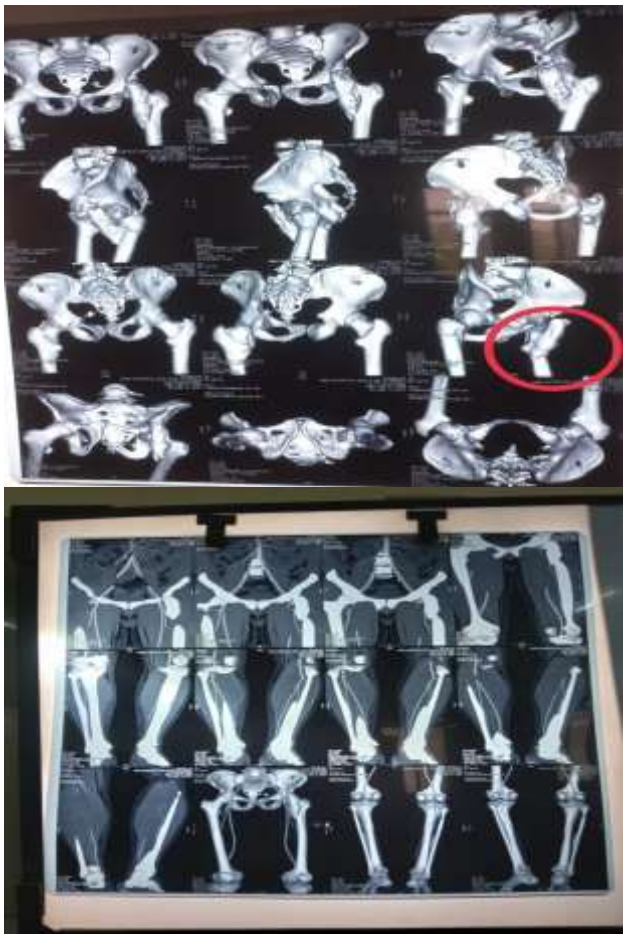

Figure 3: Pre-operatory CT.

Brooker classification is one of the oldest and most widely used systems for grading HO-grade 1: islands of bone within the soft tissues around the hip, grade 2: bone spurs arising from the proximal femur or pelvis with at least 1 cm of bone between the opposing bony surfaces, grade 3: bone spurs arising from the proximal femur or pelvis with less than 1 cm of bone between the opposing bony surfaces and grade 4: ankylosis of the hip joint.

The severity of heterotrophic bone formation post trauma has been graded based on "Brooker classification" is grade 3. The ossification affects iliopsoas muscle and related structures, localized antero-medial, from the left iliac crest and up to the lesser trochanter excluding major nerves and vessels.

The patient was operated in supine position with smith Petersen approach, reflecting the sartorius and right rectus femoris muscles. After ossified bone was identified, demarcated along with its pedicle and extracted in single segment (Figure 4).

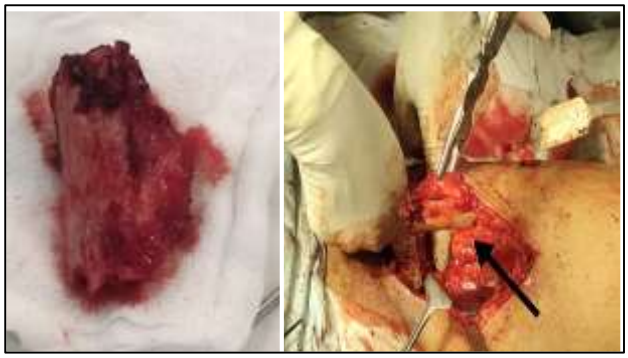

Figure 4: Intra-operative picture.

Blood losses were important: 900-1000 ml intra-operatory and 500-600 ml post-operatory, 1-unit prbc 1-unit FFP was transfused during surgery. After surgery the antibiotic, prophylaxis treatment, anticoagulant and NSAID was started.

Figure 5: Post-operative X-ray and post-operatory.

DISCUSSION

HO is characterized by the formation of mature lamellar bone in tissues outside the joint capsule and periosteum. While it can remain asymptomatic, it typically presents with symptoms such as pain and swelling, causing functional impairment that is identifiable through limited range of motion near a joint.[3.]

Formation of bone within soft tissue who's pathogenesis is different from metastatic and dystrophic calcification. Transformation of mesenchymal originated primitive cells present in connective tissue within muscle into osteogenic cells is pathogenic cause of HO.[4]

By Chalmers et al 3 conditions needed for HO: osteogenic precursor cells, inducing agents and permissive environment.[5]

Pathology

Wang et al according to the research findings, it was observed that introducing recombinant human BMP-2A through implantation led to cartilage formation by day 7 and bone formation by day 14.[6] Multiple studies have demonstrated that BMP2 and BMP4, when combined with other factors such as VEGF and TGF-b, can significantly enhance the process of endochondral bone formation.[7] Moreover, the expression of BMP and its receptor, along with the upregulation of its mRNA, have all been found to increase post-brain injury.

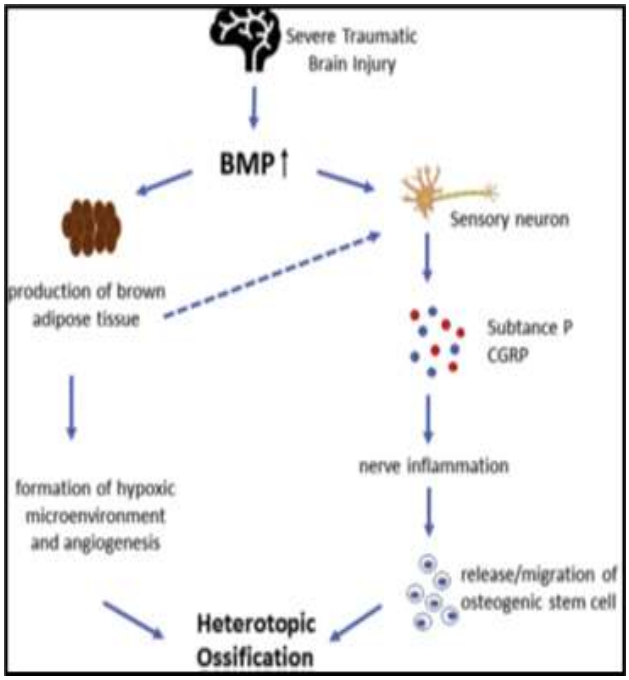

Figure 6: Overview of the function of BMP on TBI in HO. After a traumatic brain injury (TBI), the expression of BMP and its receptor is increased. This leads to activation of sensory neurons and the release of inflammatory cytokines, substance P, and CGRP. Nerve inflammation occurs, which promotes nerve regeneration and the migration or release of stem cells. Elevated BMP levels also stimulate the production of BAT, which creates a hypoxic environment and promotes angiogenesis. This process generates heat and further stimulates sensory neurons to release substance P and CGRP. BMP=bone morphogenetic protein; BAT=brown adipose tissue; CGRP=calcitonin gene related protein; HO=heterotopic ossification; SP=substance P; TBI=traumatic brain injury.)

Some studies emphasize that prostaglandin E2 (PGE2) is mediator of the progenitor cells.[8]

SP is produced by various cells in the central and peripheral nervous system and can bind to three different receptors, with a stronger preference for NK1r.[9] NK1r is expressed on skeletal cells and has been linked to chondrocytic and osteoblastic differentiation, as well as osteoclastic activity.[10]

Inflammation plays a crucial role in HO development, for instance, IL-6 promotes mesenchymal stem cell differentiation into bone cells, lowers osteoblast apoptosis, and boosts angiogenesis.[11]

In terms of biology, monitoring of alkaline phosphatase-PA levels that indicate increased osteoblastic activity. Elevation of urinary PGE2 (prostaglandin E2) level; however, due to its high costs, this test was not conducted. Simple radiography still remains the primary method for detecting HO as it is efficient and cost-effective, although it does take around 6-8 months to confirm the diagnosis. The 3-phase scintigraphy can detect HO much earlier, within a week, but it is not as commonly used. Even though MRI can detect HO in its early stages.[12]

According to clinical and radiological assessments, differential diagnosis for HO should include conditions such as myositis ossificans circumscripta, myositis ossificans progressive, osteoma, nodular fasciitis, osteosarcoma, and chondrosarcoma. Furthermore, slowly calcifying lesions such as synovial sarcoma, rhabdomyosarcoma, and malignant fibrous histiocytoma should also be considered.[13] It is crucial to exclude osteosarcoma as it is the most critical pathology to be ruled out. Presence of mature lamellar bone on histopathologic examination confirms the diagnosis of HO.

After total hip replacement surgery, HO is most commonly observed, and various strategies have been explored in the literature to prevent this condition. Administration of diphosphonates and nonsteroidal anti-inflammatory drugs (NSAIDs) such as indomethacin and naproxen are some of the preventive modalities used. Radiotherapy is another option to reduce HO incidence in orthopedic management. Apart from these, researchers are currently evaluating three novel preventive methods, which include Noggin, a BMP inhibitor, pulsed electromagnetic fields (PEMF), and free radical scavengers like allopurinol and N-acetylcysteine.[14]

Casavant et al, the study found that it is safe to perform passive range of motion (PROM) and early mobilization in patients with TBI and HO, which is widely accepted in the clinical field as a means of not only treating but also preventing HO.[15]

As previously mentioned, patients may present with a range of symptoms associated with heterotopic ossification (HO). In cases where radiographic examination and bone scanning confirm the presence of HO in its formative stage, it is advisable to initiate symptomatic treatment and allow for complete bone maturation before considering surgical excision. Studies have reported varying outcomes of the condition, with some cases showing regression while others remain stable after excision.

CONCLUSION

Patients who have suffered polytrauma are at a higher risk of developing neurological heterotopic ossification (NHO), and the surgical management of post-traumatic NHO requires coordinated efforts from a multidisciplinary team in a specialized medical facility. Favorable clinical outcomes and reduced risk of recurrence can be achieved with optimal medical and surgical management in this patient population.

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