

Acquired Heterotopic Ossification following Encephalitis and Intractable Seizures

Dear Editor,

Heterotopic ossification (HO) is the abnormal formation of bone in soft tissue outside of the skeleton. The incidence of HO has been known to occur after spinal cord injury, traumatic brain injury and after hip and knee arthroplasty. HO associated with encephalitis is rare. We report the case of a 26-year-old female who developed HO after encephalitis and intractable seizures.

Case History

The subject is a 26-year-old female with no past medical history, who was admitted for seizures and concurrent febrile illness. A magnetic resonance imaging (MRI) of the brain was unremarkable, and cerebrospinal fluid cultures were negative. She was treated for presumed viral encephalitis, which was complicated by status epilepticus. She was placed under phenobarbitone-induced coma followed by thiopentone-induced coma and required intubation for 28 days. She was subsequently treated with a combination of oral lamotrigine, phenytoin and valproate and developed cholestatic hepatitis secondary to the anti-epileptic medication.

When the patient was transferred out to the general ward, she continued having several seizures a day. There were apparent cognitive deficits, namely disorientation, short attention span, short-term memory loss, inappropriateness and deficiency in executive functioning. Six weeks after admission, she complained of acute thigh pain. It was noted that there was difficulty in performing range of motion therapy 3 days before this complaint. X-ray of the pelvis and lower limbs did not reveal any fracture but there was vague haziness in the soft tissues. A computed tomographic (CT) scan of the lower extremities was then performed, which revealed ossification mainly in the adductor muscles as well as the vastus medialis bilaterally (Fig. 1). The diagnosis of HO was also confirmed with a triphasic bone scan.

She was transferred to Rehabilitation Medicine, and was treated with diclofenac and etidronate for 6 and 12 weeks respectively. Gentle range-of-motion exercises were started albeit with difficulty due to severe pain, and there was difficulty getting the patient into a functional position due to her hips being in a position of external rotation. With further therapy, pain was reduced with improved range of motion.

She was eventually able to ambulate with elbow crutches with the hips abducted, externally rotated, and slightly



Fig. 1. CT lower extremities – coronal view, calcified masses within medial aspect of upper thighs.

flexed. The subject underwent surgical excision of the HO on the left hip 7 months later and on the right a year later. She developed complications of extensive blood loss, fracture of the left femur shaft and deep vein thrombosis. She had radiotherapy post-surgery. There was no recurrence of HO and moderate gain in the range of motion.

Case Discussion and Literature Review

The underlying mechanism for formation of HO is still elusive. There may be an association with human leukocyte antigens such as HLA-B18, HLA B27 and HLA-DW7, the forcible mobilisation of an immobilised joint and the release of certain factors causing HO in trauma or neurologic injuries. The presence of limb spasticity, complete spinal cord lesions and pressure sores are risk factors for formation of HO in spinal cord injury patients.

This subject had intractable seizures that may have led to trauma and also predispose her to hypoxia. She also had prolonged intubation and was in a drug-induced coma. These were the associated factors described in the formation of HO.¹⁻³

It was difficult to accurately ascertain when the HO began, as the subject was cognitively impaired and could not complain of pain. There was difficulty in using biochemical markers to help determine onset of HO in this subject. A study done to assess the predictive value of creatinine phosphokinase (CK) and alkaline phosphatase in patients after spinal cord injury suggested a correlation between elevated CK levels and subsequent development of HO.⁴ Her case was however confounded by liver dysfunction, ischaemic hepatitis and seizures.

Etidronate disodium has commonly been used for the prevention and treatment of HO. A recent Cochrane systemic review suggested that there is insufficient data on the long-term outcome with treatment using etidronate although one of the studies suggested greater likelihood of preventing the progression of radiographic HO grade.⁵

Medications such as non-steroidal anti-inflammatory drugs (NSAIDS), etidronate and radiation have been used prophylactically after traumatic brain injury, spinal cord injury and after joint replacement. Established HO has been traditionally treated with NSAIDS and etidronate. Surgery is usually postponed till 1 to 2 years later when the ossification matures. Surgery within 1 year of injury or 6 months of formation of HO could result in a return of ectopic bone. Indications for surgery include limitation of range of motion minimising function or for the prevention of secondary complications such as pressure ulcers and compression of neurovascular structures due to ankylosis. Late surgery, 5 years or more after injury is not recommended due to increased fracture risk due to local osteoporosis. Some motor control is desirable to achieve significant improvement of quality of life.

Nevertheless, there have been cases whereby early excision was successful despite increased risk of intra-operative haemorrhage, infection and prolonged immobility. There was improvement in range of motion of the hips, better seating posture and improvement in mobility and self care, with no recurrence of HO at the excised sites. Studies have investigated the role of radiation therapy on prevention of HO, especially after surgery and it has proved to be helpful.

Conclusion

In patients with cognitive deficits, the early diagnosis of HO may be difficult. It should be considered as a differential diagnosis when such a patient develops decreased joint range of motion. The use of biochemical markers may be useful in some cases. Earlier treatment may prevent progression of the condition and reduce the amount of

functional limitation. In the event that the patient has severe pain or functional limitation due to joint immobility, or difficulty in maintaining personal hygiene, earlier excision may be considered after careful evaluation, with medical therapy or radiation therapy continued after the surgery. Further studies for the early diagnosis and optimal management of HO are required, especially in patients with conditions other than those commonly associated with its development.

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