

Short-term outcome after resection of neurogenic heterotopic ossification around the hips and elbow following encephalitis

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ABSTRACT Heterotopic ossification (HO) is a potential complication following brain or spinal cord injuries and diseases. Post-encephalitis HO is rare, and the number of affected joints is a prognostic predictor. A literature review revealed only a limited number of such cases, with one or two anatomical regions affected in each case. We report the case of a 21-year-old man who developed HO at the peri-articular regions of both hips and the right elbow post encephalitis. He had good functional outcome following excision of the ossific masses. There has not been any recurrence for up to two years from the first surgery. To the best of our knowledge, this is the first such case involving more than two anatomical regions, and the first reported case from Sri Lanka.

Keywords: encephalomyelitis, heterotopic ossification
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INTRODUCTION

Heterotopic ossification (HO) is a pathological process of lamellar bone formation in non-osseous tissues. It has been identified as a complication following brain or spinal cord injuries and diseases.⁽¹⁾ Post-encephalitis HO is rare. The literature has a limited number of such cases, where the condition affects one or two anatomical regions in the body.^(2–6) The aetiopathogenesis of HO is not clearly understood. Several bone morphogenetic proteins have been postulated to be involved in the process.⁽¹⁾ Thus, there is lack of consensus on treatment modalities and timing of interventions.⁽¹⁾ We report a rare case of post-encephalomyelitis HO around the bilateral hips and right elbow, and describe our management strategies and short-term outcomes.

CASE REPORT

A 21-year-old Sinhalese man presented to the orthopaedic clinic with difficulty in walking and restricted right elbow movement. He was recovering from motor weakness related to a brain infection. In December 2006, on his twentieth birthday, he was admitted to the neurology department with fever, headache, vomiting and altered consciousness. Magnetic resonance imaging confirmed acute disseminated encephalomyelitis. Cerebrospinal fluid culture did not show bacterial growth, and attempted viral isolation was negative. As clinical profile and imaging evidence were suggestive, the patient was treated with antiviral therapy and empirical antibiotics for two weeks. The patient's level of consciousness and respiratory functions deteriorated gradually over the first 24 hours after admission, leading to respiratory acidosis. He required endotracheal intubation and mechanical ventilation on the second day. During the initial 72 hours, he

was on controlled mechanical ventilation with muscle paralysis, followed by synchronised intermittent mandatory ventilation for 11 days. Adjustments to the mechanical ventilation process were made depending on the arterial blood gas values in order to avoid acidosis or alkalosis. The patient gained full consciousness after five weeks. He received passive range of movement limb physiotherapy 3–4 times a day during his hospital stay. At the time of discharge in March 2007, the patient was wheelchair-bound with spastic, grade 3–4 paretic limbs. HO was noted around the right elbow and both hips. As priority was given to the rehabilitation of the paretic limbs, orthopaedic referral was delayed. The following year, three episodes of pyrexia of unknown origin interrupted his rehabilitation. The patient had no family history of abnormal ossification.

At presentation to the orthopaedic unit in July 2008, the patient's cognitive functions were normal, and all his limbs had almost normal power and tone. His right elbow was ankylosed at 100° flexion with palpable ossific masses over the cubital fossa. Bilateral hip movements were restricted, with flexion of 0°–30°, extension of 0°–5° and abduction of 0°–15°. All other joints were normal, but the patient was dependent in ambulation. Plain radiography revealed Brookers' grade 4 HO around both hips and over the anterior aspect of the right elbow (Figs. 1 & 2). Computed tomography imaging confirmed the presence of ossific masses over the anterior, posterior and lateral aspects of both hips. The patient's serum alkaline phosphatase level and erythrocyte sedimentation rate were both normal.

Between August 2008 and July 2009, the patient underwent five operations, one joint at a time, for excision of the ossific masses. The patient and his family received pre-operative counselling, where the available management options, expected

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Fig. 1 Pre-operative anteroposterior radiograph of the pelvis shows heterotopic ossification (arrows).



Fig. 2 Pre-operative anteroposterior and lateral radiographs of the right elbow show heterotopic ossification (arrows).



Fig. 3 Anteroposterior radiograph of the pelvis 21 and 15 months post right and left hip surgeries, respectively, shows absence of recurrence (arrows).



Fig. 4 Anteroposterior and lateral radiographs of the right elbow 26 months post surgery show the absence of recurrence (arrows).

outcome and possible complications were explained. The patient's right elbow was operated on first, as the restricted movement was affecting his writing and feeding. It was approached antero-medially. Subsequently, each of the hips was approached in two stages, anteriorly and posterolaterally. Surgery included elevation of the periosteum and excision of the bone masses with osteotomies in order to free the joints. The extent of excision was determined by the adequacy of joint movements achieved by manipulation during surgery. During the process, joint cavities were not opened and capsulotomies were not performed, as ossific mass excision and operative manipulation provided adequate joint movements. Soft tissue releases or elongations were also not required. All the masses consisted of mature bone. Upper limb splinting and lower limb traction immobilisation were not done during the immediate postoperative period.

Surgery of the right hip (anterior approach) was complicated with deep wound infection. 25 mg indomethacin prophylaxis thrice a day was continued for three weeks from postoperative Day 1 after each surgery. Active joint movements were commenced within the pain-free range from postoperative Days 3–4.

Physiotherapy was commenced as 10–15 minutes short sessions of supervised, active, pain-free range of movements four times a day for about one week after each resection. This was gradually increased up to one-hour sessions by the third postoperative week. The patient was allowed to bear weight on the operated lower limbs by the fourth postoperative week. Histopathology confirmed mature lamellar bone formation.

At the last follow-up visit, which was 26 months after the elbow surgery and 15 months after the last hip surgery, the patient was found to have acceptable range of movements at the affected joints. Bilaterally, the range of hip movements was as follows: flexion 0°–90°; extension 0°–10°; and abduction 0°–30°. The range of elbow movements was 0°–120°. The patient could ambulate independently without walking aids and was able to put on his socks and tie shoelaces by himself. His activities of daily living and at the university were unaffected. No recurrence was observed on radiography (Figs. 3 & 4).

DISCUSSION

HO may occur following surgery, trauma, neurological diseases or injuries, or due to hereditary disease.⁽¹⁾ Surgery- or trauma-

related and neurogenic HO occurs as a localised disease. Hereditary HO is a rare progressive disease that usually manifests in childhood. The mechanism and pathophysiology leading to HO is still not fully understood. It is thought that primitive mesenchymal cells differentiate into osteoblasts, leading to HO. The origin of these mesenchymal cells and the stimulus that results in their differentiation are poorly understood. Distinct types of bone morphogenetic proteins and growth factors are believed to play a role in the process.⁽¹⁾

Neurogenic HO is a known complication following spinal cord or brain injuries, and to a lesser degree, following encephalitis, poliomyelitis, tetanus and anoxic encephalopathy.^(1,7) Prolonged coma, mechanical ventilation, spasticity and limited extremity movements are postulated as initiators of neurogenic HO.⁽⁷⁾ Our patient had all the risk factors; he was in a prolonged coma following encephalitis, requiring mechanical ventilation, and had prolonged immobilisation. Newman et al studied the accelerated fracture healing in head injury patients and suggested that respiratory alkalosis associated with severe head injury or its treatment, including ventilation, affects the rate of deposition of the callus by modifying the pH at the fracture site.⁽⁸⁾ A similar process is thought to affect the formation of HO in ventilated patients, but the exact mechanism is not clearly understood. However, the index patient did not experience prolonged respiratory alkalosis during mechanical ventilation. Passive and active-assisted movements, especially beyond the pain-free range, have been shown to increase HO and joint ankylosis in burn patients.⁽⁹⁾ The same study also showed that postoperative patients with excised ossific masses, as well as burn patients who followed a programme of active exercise within the pain-free range, gained excellent range of motion without developing HO.⁽⁹⁾

HO may occur within two weeks of the initial insult, and ectopic bone would take 6–9 months to mature. None of the available prophylactic measures would influence the outcome of HO once the process has begun.⁽¹⁰⁾ Therefore, surgical excision is the mainstay of treatment. Garland et al recommended an 18-month delay before surgical excision in order to allow the bone to mature and the patient to recover from the insult.⁽¹¹⁾ However, McAuliffe and Wolfson demonstrated positive outcomes when surgery was performed within seven months of the insult.⁽¹⁰⁾ Delayed neurological recovery and subsequent illnesses were the limiting factors for early surgery in our patient.

As recurrence is a known complication, excision surgery of ossific masses must be accompanied by pharmacological prophylaxis or irradiation.⁽¹⁾ Pharmacological prophylaxis is usually achieved with indomethacin, selective COX-2 inhibitors, and less frequently, with etidronate. These modalities to prevent HO following total hip arthroplasty (THA) or acetabular fixation are considered in most studies. Moore et al compared the use of indomethacin 25 mg thrice a day for six weeks with irradiation with 800 cGy following acetabular fixation,⁽¹²⁾ and showed that both modalities were equally effective; however, radiation therapy was 200 times more expensive than indomethacin therapy.

Banovac et al, in a randomised, prospective, double-blinded, placebo-controlled clinical trial, showed that 25 mg indomethacin thrice a day for three weeks could prevent HO in patients with spinal cord injuries.⁽¹³⁾ Vasileiadis et al, who studied the use of etidronate 20 mg/kg/day for 12 weeks vs. indomethacin 75 mg/day for two weeks for the prevention of HO after THA,⁽¹⁴⁾ concluded that both modalities were equally effective, but etidronate therapy was six times more expensive than indomethacin. Pakos et al showed that a combined regimen with a single radiation dose of 7 Gy followed by indomethacin 75 mg/day for 15 days was effective in preventing HO following THA.⁽¹⁵⁾

The potential risks of irradiation include malignancy, impaired healing, infertility and genetic alteration. However, these symptoms have not been reported with modern dosage levels. The potential complications of indomethacin include decreased fracture healing, gastrointestinal irritation and/or ulceration, decreased platelet aggregation and renal toxicity.⁽¹²⁾ The desirability of radiotherapy for benign diseases needs to be weighed against the potential risk of radiation-induced sarcoma in patients with a long life expectancy.⁽¹⁰⁾ For this reason, we preferred indomethacin prophylaxis over irradiation. As our patient had staged operations, we considered three weeks of prophylaxis as an appropriate duration so as to minimise possible adverse effects. Most studies conducted on prevention of HO by prophylaxis therapy have reported the efficacy of this method at around one year.^(12–15) However, as there is a possibility that HO would persist after one year, Vasileiadis et al suggested a three-monthly follow-up for up to one year, and annual follow-up thereafter in patients with THA.⁽¹⁴⁾ Garland et al found that the risk of recurrent HO was high if three or more joints were involved, but the level of neural residua was still considered the main determinant of recurrence.⁽¹¹⁾ Although three of our patient's joints were involved, he belonged to Garland et al's category I,⁽¹¹⁾ with minimal neurological deficits, thus indicating a good prognosis. He had no recurrence of HO for up to 15 months after the last surgery, with an acceptable range of movements and showed good short-term outcome.

In conclusion, in the absence of specific guidelines, treatment and prevention of HO is still at the discretion of the attending physician or surgeon. Each patient should be managed with an appropriate protocol based on the institutional experiences. Counselling of the patient regarding the risk of recurrences following surgery as well as the possible adverse effects of other therapeutic options is a mandatory aspect of management.

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