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Heterotopic ossification in burns: Our experience and literature reviews

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ABSTRACT

Purposes: Heterotopic ossification (HO) is an uncommon, but high profile complication of burns. In this paper, a retrospective study was undertaken to evaluate our treatment and results of HO. Relevant literature was also reviewed to search for new advances in prevention and management for patients with HO after burns.

Materials and methods: A retrospective study was undertaken in Chang Gung Memorial Hospital, Linkou. We collected 12 patients who suffered from HO after burn and received operation in our hospital between June 2000 and September 2007. The data was expressed as mean.

Results: Patients' gender distribution was 10 males and 2 females. The mean age was 43 years old (range, 30–59). Causes of burn were flame burn (75%), scald burn (8%), contact burn (8%), and high-voltage electrical burn (8%). Mean TBSA was 39% (range, 8–90%). Nine of 12 patients (75%) were admitted to intensive care unit (ICU) and 6 (50%) received mechanical ventilator support. The mean ICU stay was 82 days (range, 26–240 days). The elbow was the most commonly affected joint (92%). The outcome of surgery was acceptable in all elbows at the time of surgery. The mean ROMs before surgery were 31° (range, 0–75°). The mean ROMs after surgery were 99° (range, 70–115°); mean gain was 68° (range, 35–115°). One (8%) patients had recurrent HO after operation. The mean outpatient department follow-up time was 14.6 months (range, 1–40 months). The incidence of HO in our burn center is 0.15%.

Conclusion: Although HO after burn is uncommon, physicians should keep the complication in mind. When burn patients complain decreased ROM or "locking sign" in their joints, X-ray examination is indicated to rule out HO. Surgery is the treatment of choice when the diagnosis of HO is confirmed.

1. Introduction

The transformation of primitive mesenchymal cells in the surrounding soft tissue to mature lamellar bone is termed heterotopic ossification (HO). It was first described by Reidel in 1883 (cited in Dejerne and Ceilliar 1918 [1]). HO associated with burns was first described in the American literature in 1957 by Johnson [2,8]. It is an uncommon, but high profile complication of burns. The incidence of HO in a general burn population is reported to be between 1% and 3% [3–5]. HO after burn commonly occurs around major joints. Elbow, shoulder, and hip are the most commonly affected joints, in that order of frequency [6]. A retrospective study was undertaken to evaluate the treatment and results of HO in Chang Gung

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Table 1 – Patient number and incidence of HO in our burn center between 1999 and 2007.

	Male	Female	Total
Patient number	3514	1561	5075
HO	7	1[a]	8
Incidence (%)	0.2	0.06	0.15

[a] The female patient who suffered from HO over right knee after flamed burn in 1964 was excluded.

Memorial Hospital, Linkou. In this paper, the relevant literature was reviewed to search for new advances in prevention and management for patients with HO after burns.

2. Methods

A retrospective study was undertaken in Chang Gung Memorial Hospital, Linkou. We reviewed medical records and collected 12 patients who were diagnosed HO in our hospital between June 2000 and September 2007. All the patients suffered from HO after burn injury. Patients' gender, age, causes of burn, mean total body surface (TBSA), period in burn ICU, location of HO, time delay of diagnosis of HO, range of motion (ROM) before and after surgery are collected and expressed as mean ± S.D. (standard deviation).

3. Results

Twelve patients who were diagnosed with HO and received surgical excision were collected. Gender distribution was 10 males and 2 females. They suffered from burn injury between 1964 and 2007. Three of 12 received treatment of burn in other hospitals first, then visited our hospital for treatment of HO. Another nine patients received treatment of burn and HO in our hospital. We examined 5075 patients, including 3514 male patients and 1561 female patients admitted to our burn center between 1999 and 2007. The female patient who suffered from HO over right knee after flame burn in 1964 was excluded. Eight of 5075 patients (0.15%) developed HO. Seven of 3514 male patients (0.2%) and one of 1561 female patients (0.06%) developed HO, respectively (Table 1). There were 3006 patients with TBSA within 0–10%, 1692 patients with TBSA within 10–40% and 377 patients with TBSA >40%. One of 3006 patients (0.03%), 3 of 1692 patients (0.2%) and 3 of 377 patients (0.8%) developed HO, respectively (Table 2). The mean age of these 12 patients with HO was 43 ± 9 years old (range, 30–59). Causes of burn were flame burn (75%), scald burn (8%), contact burn (8%), and high-voltage electrical burn (8%). Mean TBSA was 39 ± 28% (range, 8–90%). Patients with major burn were admitted to burn intensive care unit (ICU). Nine of 12 patients (75%) were admitted to ICU after burn and 6 (50%) received mechanical ventilator support. The mean ICU stay was 82 ± 76 days (range, 26–240 days) (Table 3).

Table 2 – Incidence of HO breaking it down by burn size in our burn center between 1999 and 2007.

	0–10% TBSA	10–40% TBSA	>40%TBSA
Total	3006	1692	377
HO	1	3	3
Incidence (%)	0.03	0.2	0.8

Eleven patients suffered from decreased ROM of HO-involved elbows. Diagnosis of HO was made by careful physical examination and X-rays (Fig. 1A and B). The mean delay between burn and diagnosis of HO was 10 ± 6 months (range, 3–24 months). Three-dimensional computed tomogra-

Table 3 – Details of 12 patients' age, injury mechanism, TBSA, period in burn ICU, location of HO, mean ± S.D., and ROM of elbows.

Case no.	Age (y/o)	Gender	Injury mechanism	TBSA (%)	Period in burn ICU (day)	Location of HO	Pre-op ROM of elbow (degree)	Post-op ROM of elbow (degree)	Gain (degree)
1	59	M	Scald burn	45	45	Left elbow, upper abdomen	75	110	35
2	37	M	Flame burn	25	0	Right elbow	35	100	65
3	37	M	Flame burn	90	240	Left elbow	70	110	40
4	45	M	Flame burn	50	90	Bilateral elbows	10	70	60
5	30	M	Electrical burn	17	30	Right elbow	35	105	70
6	35	M	Flame burn	43	30	Right elbow	60	100	40
7	39	M	Contact burn	8	60	Right elbow	20	95	75
8	45	M	Flame burn	90	180	Right elbow	30	105	75
9	50	M	Flame burn	*	0	Left elbow	5	70	65
10	37	M	Flame burn	12	26	Right elbow	0	105	105
11	43	F	Flame burn	30	40	Right elbow	0	115	115
12	55	F	Flame burn	22	0	Right knee			
Mean	43			39	82		31	99	68
S.D.	9			28	76		27	15	25

The 4th case suffered from HO in both elbows received surgical excision of right elbow in Thailand first and received surgical excision of left elbow in our hospital. The pre-op ROM of elbow of 4th case indicates his left elbow. The 12th case suffered from HO at her right knee. Abbreviations: M, male; F, female; TBSA, total body surface area; ICU, intensive care unit; HO, heterotopic ossification; pre-op, preoperative; post-op, postoperative; ROM, range of motion; S.D., standard deviation. *Data lost.

Fig. 1 – (A) Pre-operative lateral view X-ray of the right elbow of 11th case. HO extends from humerus to olecranon. (B) Post-operative lateral view X-ray of the right elbow of 11th case. HO was totally excised.

phy (3D CT) image study (Fig. 2A and B) was used preoperatively to confirm the exact anatomic location of HO. Serum levels of alkaline phosphatase (ALP), calcium and phosphorus were checked, but no significant higher level was noted.

When neuropathy or decreased ROM compromising daily activity in despite of physical therapy was noted, surgical resection of HO was indicated. There were totally 12 elbows and one knee that received surgically excision of HO. The elbow was the most commonly affected joint. Eleven of 12 patients (92%) suffered from HO in elbows, and one patient (8%) in knee. In these 11 patients suffered from HO in elbows, the right elbow was affected in 7 patients (63%), the left elbows in 3 patients (27%) and both elbows in 1 patient (9%). One patient who suffered from 45% TBSA scald burn then developed left elbow and abdominal subcutaneous HO. The subcutaneous abdominal HO was noted incidentally by kidney ureter bladder (KUB) X-ray and did not cause any discomfort. There was another female patient suffered from chronic unhealed wound after burn injury in right knee. HO was incidentally noticed in knee and was excised during wound debridement.

The patient who suffered from HO in both elbows after 50% TBSA burn injury received surgical excision of right elbow in hospital in Thailand first and received surgical excision of left elbow in our hospital 2 years later.

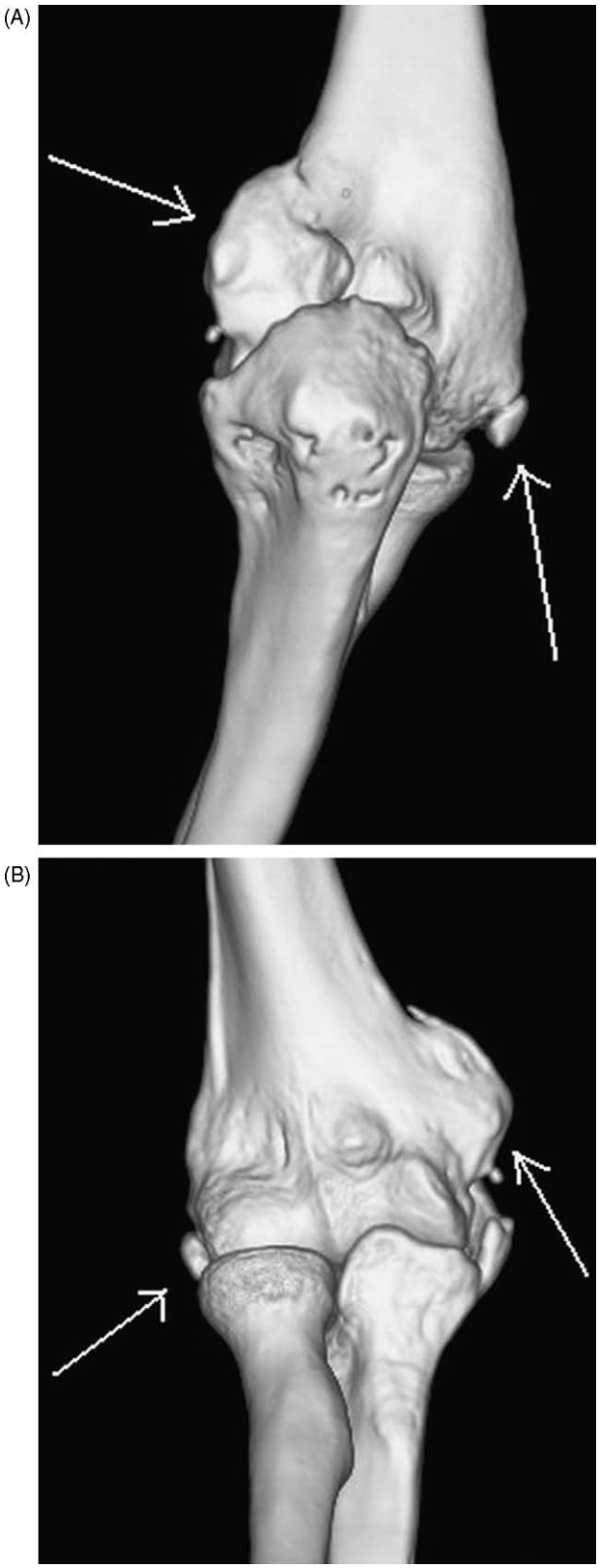

Fig. 2 – (A) Pre-operative 3-D CT posterior and anterior (P-A) view of the left elbow of the 4th case. HO was noted at the lateral and medial side of elbow. The medial HO separated from the medial humeral epicondyle. The lateral HO extends from humerus to olecranon. (B) Pre-operative 3-D CT A-P view of the left elbow of the 4th case.

Surgical excision of the elbow was performed by two orthopedic surgeons in our hospital. The surgical technique included posterior approach, dissection and resection of HO, anterior transposition of ulnar nerve if there was neuropathy, and postoperative wound drainage. All patients received early gentle passive physical therapy or use of an assisted continuous passive motion (CPM) machine and active exercise within the pain-free ROM on the first postoperative day if the wound was stable after surgery. Nonsteroidal anti-inflammatory drugs (NSAIDs) were given postoperatively for pain relief. Radiotherapy was not used in these patients.

The outcome of surgery was acceptable in all elbows at the time of surgery. The mean ROMs before surgery were $31 \pm 27^\circ$ (range, 0–75°). The mean ROMs after surgery were $99 \pm 15^\circ$ (range, 70–115°). Mean gain of ROM was $68 \pm 25^\circ$ (range, 35–115°). The mean outpatient department follow-up time was 14.6 ± 12 months (range, 1–40 months). One of 12 patients (8%) received surgically excision of HO had recurrent HO 3 months later after operation. This patient suffered from 17% TBSA of electrical burn then developed right elbow HO. Complications of decreased ROM and non-healing wound was noted after right elbow surgery. He had received totally three operations, and the ROM of elbow after last surgery was 105°. The patient is still in a rehabilitation program in our outpatient department now.

4. Discussion

The true pathogenesis of HO after burn is still unclear. A posited theory is that HO results from the presence of osteoprogenitor cells pathologically induced by an imbalance in local or systemic factors, such as trauma or burn injury [7]. Many factors are considered to relate to the genesis of HO, such as percentage of burn, location of burn, period of immobilization, forceful passive manipulation, extended time to wound closure [8] and genetic predisposition. Vrbicky reported that a 7% human leukocyte antigen B27 (HLA-B27) distribution in the normal population compared with 70% in a population with HO [9]. Based on our retrospective study, some interesting findings are brought up here:

1. Patients who have greater TBSA burn are more likely to develop HO. Tsionos and Rochet [10] and Hunt et al. [11] reported HO affected patients with mean TBSA of 49% and 55%, respectively. The mean TBSA of 12 affected patients in our study was 39%. However, one patient in our study who had only 8% TBSA developed HO. He suffered from mechanical crushing and contact burn injuries over right upper limb by high temperature machine, which was then complicated with right arm compartment syndrome. No fracture was detected from right upper limb X-ray. He received fasciotomy immediately and was admitted to our burn ICU. Wound debridement and repeat fasciotomy were performed in ICU. He was admitted in ICU for total of 60 days for wound care and physical therapy. We assumed that burn combined with compartment syndrome and prolonged wound closure may predispose to the genesis of HO in this patient.
2. HO usually develops in joints with overlying burn. All of our patients developed HO in burned joints. However, some literatures described HO occurring a distance from any third-degree burn involvement [12].
3. Patients who suffer from burn necessitating long-term immobilization are more likely to develop HO. Evans and Smith reported that the length of bed confinement was perhaps the most important factor in the development of HO [12]. Patients with major burn are admitted to burn ICU and may be kept in bed for several weeks due to ventilator support or skin graft transplantation. Hunt et al. [11] reported 86% of affected patients were admitted to ICU and 81% received ventilator support. Patients with major burn were admitted to our burn ICU and all received physical therapy once their wound was stable. In our study, 9 of 12 affected patients (75%) were admitted to ICU and 6 (50%) received ventilator support. Patients were sedated during mechanical ventilator support in our ICU. The mean ICU stay was 82 days.

The incidence of HO in our burn center is 0.15%, which is much lower than other reviews (1–3%). The possible reasons are: cultural difference, racial difference, and ignorance of HO. We noticed that it was unique of oriental culture for burn patients to tolerate the disability of decreased ROM of a joint and not seek medical help till their condition become severe. Most burn patients in our hospital were asian who may have a lower incidence of HO as compared to those of European descent in other reviews. HO is uncommon and can easily be ignored in asians and thus could be for lower incidence of HO in our study. Three patients received treatment of burn in another hospital first then visited our hospital for treatment of HO. We assume that there may be some patients received treatment of burn injury in our hospital then visited other hospital for treatment of HO, so the incidence of HO in our burn center may be more than 0.15%.

Clinical symptoms and signs of elbow HO include decreased ROM, a painful joint, localized swelling, and ulnar nerve palsy with intrinsic muscle weakness. Sometimes, it is difficult to differentiate HO from scar contracture by clinical symptoms and signs. We noticed that most patients suffering from elbow HO had locking sensation when they reached the extension-flexion limit of the elbow joint. We call it ''locking sign''. Patients with elbow scar contracture do not have such sign.

Physicians should keep the diagnosis of HO in mind when burn patients complain of decreased ROM in their elbow joints. X-ray is a fast and economical tool for diagnosis of HO. Other diagnostic tools include CT, magnetic resonance imaging (MRI), bone scan and ultrasound. MRI may have implications for early intervention in the development of HO [13]. 3D CT reconstruction can show the exact anatomic location of HO, and it is helpful for preoperative evaluation.

The treatment of HO includes surgery in combination with rehabilitation. Surgical procedure for the elbow includes making a long posterior midline longitudinal incision through the most durable dorsal skin to gain access to the elbow, medial and lateral exposure done to facilitate more complete release [14], resection of HO, removal of bone dust or demineralized bone powder, ulnar nerve anterior transposi-

tion after neurolysis if there is neuropathy and postoperative wound drainage. The former concepts suggested that surgical removal of HO in patients with burns should be delayed until bone scans returned to normal, because some authors considered that the recurrence rate of HO was high if it was excised without maturation. However, some most recent papers suggest early excision of HO can also obtain good results [10,15–17]. Based on our experience, patients who received early HO excision due to decreased ROM compromised their daily activity or neuropathy despite undergoing aggressive physical therapy. The results of our patient after early HO excision were satisfactory.

Postoperative physical therapy is necessary and can begin within 24–72 h once wound is stable after surgery [15,18]. Exercise program beyond the range of pain-free movements should be avoided makes [19]. Most patients in this series used CPM machine to do pain-free active exercise on the first postoperative day.

NSAIDs are commonly used to prevent HO after spinal cord injury and hip surgery. They are believed to prevent the formation of HO by inhibiting cyclooxygenase (COX). Indomethacin is the most popular NSAID used for prophylaxis of HO in orthopedic procedures. Indomethacin 75 mg orally twice a day or 25 mg orally three times a day for 3–6 weeks postoperatively is suggested by some authors, though the optimal timing, dose and duration of treatment is still controversial. Schmidt et al. reported that indomethacin was superior to a placebo in preventing HO recurrence after hip surgery in 1988 [20]. However, some authors do not recommend the routine use of NSAIDs for prophylaxis against HO because there is a significantly increased risk of major bleeding complications [21,22].

In the last decade, a new class of drug, the COX-2 selective NSAIDs, has been developed. Several studies reported that COX-2 selective NSAIDs had similar or greater effects in preventing HO and have less risk of bleeding complications than NSAIDs. Rofecoxib was reported effective in prevention of HO after spinal cord injury in a randomized, prospective, double-blind, placebo-controlled clinical trial [23]. It was also reported to have similar effects as indomethacin on the incidence of HO after hip arthroplasty [24]. Celecoxib was reported more effective than ibuprofen in preventing HO formation after total hip replacement in a randomized, prospective clinical trial [25]. COX-2 inhibitors may be another choice for prevention of HO if the bleeding complication of NSAIDs is considered.

There is no trial about NSAIDs and COX-2 inhibitors in prevention of HO in burn patients. We do not routinely use NSAIDs for our burn patients, but use them for postoperative analgesia. Physicians should judge the benefits and side effects of these medications carefully before prescribing them to burn patients.

External beam radiation therapy (RT) is reported to provide prophylatic effect for HO in orthopedic procedures [26,27]. RT has no effect on existing HO because the cells have already differentiated and have formed bone [28]. RT decreases incidence of HO if administered within 24 h preoperatively or within 72 h postoperatively [15,29,30]. A single dose of 700–800 rad is recommended. We did not apply RT to our patients for HO prevention in this study.

Pakos and Ioannidis conducted a meta-analysis of seven randomized studies in 2004 comparing RT with NSAIDs [31]. They concluded that postoperative RT is more effective than NSAIDs in preventing HO after major hip procedures, and its efficacy is dose dependent. However, the absolute differences were small. Pakos et al. presented another study of combined radiotherapy and indomethacin for HO prophylaxis in 2006 [32]. The combined therapy was effective in preventing HO after total hip arthroplasty in this study.

5. Conclusion

Although HO after burn is uncommon, clinical physicians should keep the diagnosis in mind. When Burn patients complain decreased ROM or ‘‘locking sign’’ in their joints, X-ray examination is indicated to rule out HO. Surgery is the treatment of choice when the diagnosis of HO is confirmed. Recent reports suggested early excision of HO is better than delayed surgery. The treatment result of early excision combined with gentle physical therapy is satisfactory. Medication therapy and RT are reported to be effective in HO prophylaxis after orthopedic procedures.

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