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Abdominal wall heterotopic ossification following damage control laparotomy: an unusual bone to pick

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Key words

damage control laparotomy, heterotopic bone formation, open abdomen, severe pancreatitis.

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Abstract

Background: Heterotopic ossification (HO) refers to the development of extra-skeletal bone in muscle and soft tissues, following tissue insult secondary to surgery or trauma. This pathological process is considered as the result of severe inflammatory cell cascade initiated after local trauma and subsequent attempt at tissue repair involving resident mesenchymal cells. We present a series of 12 cases of abdominal HO (AHO), over 8 years, following damage control laparotomies (DCLs).

Methods: Medical records of 50 patients who underwent DCLs at Alice Springs Hospital between 2010 and 2018 were retrospectively reviewed for AHO. Demographic data were extracted. Abdominal X-rays and computed tomography scans of 47 patients were reviewed for AHO.

Results: Twelve patients (25%) developed AHO of varying diversity ranging from small insignificant lesions to clinically palpable lesions in the abdominal wall. Data revealed relatively younger male preponderance. DCL for severe acute pancreatitis (SAP) was associated with AHO ($P < 0.1$, 90% CI). Longer periods of ventilation, intensive care unit stay and admission to hospital were strongly associated with AHO ($P < 0.01$, 95% CI). Occurrence of AHO with SAP was significantly higher compared to patients without SAP (relative risk 3.54, $P < 0.001$). Only two patients required surgical excision of HO prior to definitive closure of the abdomen.

Conclusion: The authors conclude that AHO occurred more frequently in younger males. DCL for SAP was a significant risk factor. Extended periods of ventilation, intensive care unit stay and hospital admission were strongly associated with the development of AHO. Preoperative detection of HO is essential prior to planning definitive closure of the abdomen.

Introduction

Heterotopic ossification (HO) is a condition when bone and cartilage develop in muscle and soft tissue where osseous elements normally do not exist.[1] Abdominal HO (AHO) in vertical abdominal incisions is well recognized but a rare phenomenon.[2] HO occurrence is common with certain predisposing conditions, including orthopaedic surgery such as hip arthroplasty,[3–5] and surgery for bone fracture,[6] head and spinal cord injury[7] and severe burns.[8] AHO is a less frequent and benign condition, usually secondary to previous abdominal surgery or trauma.[9] Literature search reveals that AHO develops in a higher proportion of cases following vertical abdominal incisions and damage control laparotomies (DCLs) even though exact incidence is unknown.[10,11] While most of the past literature on AHO are case reports, Wang *et al*. presented a series of 68 cases of HO after DCL.[11] We present a series of 12 cases of AHO following DCL with different aetiologies and their management.

Alice Springs Hospital is a level 2 trauma centre in Central Australia, covering an area of 1 million km^2, supporting a population of 55 000, of which one-third are indigenous Australians. The nearest tertiary centre is 1500 km away in Adelaide. Given these geographical challenges, DCLs have become an increasingly common strategy in Central Australia. This technique is deployed in a wide variety of critically ill patients including acute severe pancreatitis resulting in abdominal compartment syndrome, catastrophic abdominal sepsis, severe motor vehicle accidents and so on. Interestingly, on follow-up of these patients, some have demonstrated an uncommon entity, AHO.

While the complete pathogenesis of HO remains elusive, abdominal trauma and repeated surgeries appear to be the primary factors; other factors include severe inflammation, hollow viscus perforation, infection, ischaemia and prolonged immobilization. Currently, multiple case reports do exist on AHO; however, there are no epidemiological studies to report its true incidence. Preoperative recognition of AHO is essential prior to planning definitive closure of the abdomen.

Methods

A retrospective review of the medical records of all patients who underwent DCL at Alice Springs Hospital, for 8 years, from 2010 and 2018 was conducted. Data regarding aetiology, age, sex, number of days of intensive care unit (ICU) stay, ventilation support and hospital admission were extracted. Abdominal X-rays and computed tomography scans of these 47 patients were reviewed for AHO and confirmed by a consultant radiologist. All the patients had their open abdomen managed with negative pressure dressings. The primary aim of this study was to identify the occurrence of AHO in this patient group. Secondary objectives included assessment of patient demographics and associated risk factors for developing AHO. Severity of DCL was inferred based on the duration of open abdomen and ventilatory support, length of ICU and hospital stay. This study has been deemed a low-risk study and granted approval by CAHREC.

Statistical analysis

Variables recorded from AHO and nil groups were compared to each other. Continuous variables were examined for normally distributed by Kolmogorov–Smirnov–Lilliefors test. Comparisons between two groups was made using Student's *t*-test or the Mann–Whitney *U*-test when appropriate for continuous variables. Categorical variables were given as absolute number and percentages. Testing for association was performed applying the chi-squared test for the variable sex, and testing differences in proportions from aetiologies was performed applying the binomial exact test. Relative risk (RR) for the aetiologies was performed using the Wald's test. Logistic regression analysis was performed using Student's *t*-test. All calculations were performed using the software R (Robert Gentleman and Ross Ihaka, Department of the University of Auckland, Auckland, New Zealand). Statistical significance was considered when $P < 0.1$ for means and proportions, and for $P < 0.05$ for RR.

Results

Analysis of the data revealed that of the 50 patients who had undergone DCL during this period, 12 patients (24%) developed AHO of varying diversity from small insignificant lesions to clinically palpable lesions in the abdominal wall. Of the total 12 patients who developed AHO, seven (58%) had severe acute pancreatitis (SAP); five had SAP with acute compartment syndrome and two had SAP with early infected pancreatitis. The other four (33%) patients had blunt trauma to the abdomen with bowel injuries and one (8%) had catastrophic sepsis of the abdomen with perforated gall bladder and duodenum.

Table 1 Demographics and clinical outcome associations with AHO on univariate analysis

Variable	AHO	Nil AHO	*P*-value ($P < 0.1$)
Age (mean, years)	40.75	50.73	**0.086**
Sex			0.109
Females	2 (11%)	16 (89%)	
Males	10 (31%)	22 (69%)	
Ventilation (days)	13.25	7.89	**0.001**
ICU days	24.08	14.92	**0.001**
Stay in hospital (days)	50	26.97	**<0.001**

AHO, abdominal heterotopic ossification; ICU, intensive care unit.

Table 1 describes patient demographics, clinical outcomes and the ensuing AHO.

Age

The average age of patients who developed AHO was 40.75 years after DCL compared to patients who did not develop AHO, with an average age of 50.75 years. Relatively younger age (mean 40.75 years) was associated with HO ($P < 0.1$, 90% CI).

Sex

There were 32 (64%) men and 18 (36%) women in the study group. Of the 12 patients with AHO, a male preponderance was noted. AHO occurred in 10 (31%) men compared to two (11%) women.

Ventilation, ICU stay and duration of hospital admission

Longer periods of ventilation (mean 13 days), days of ICU stay (mean 24 days) and length of hospital admission (mean 50 days) were all strongly associated with AHO with 95% CI ($P = 0.001$).

Aetiology

Table 2 demonstrates the association between different aetiologies and AHO using binomial exact test. Aetiologies included SAP, blunt injury, bowel perforation, trauma, ischemic bowel, gynaecological-related procedures and miscellaneous procedures.

AHO occurred in seven (77.7%) patients with SAP and four (33.3%) with blunt injury; five (20.8%) patients with bowel perforation developed AHO. No AHO was seen in two (22.2%) patients with SAP, eight (66.7%) with blunt injury and 19 (79.2%) with bowel perforation. No patients with ischaemic bowel and gynaecological-related procedures developed AHO. Multivariate analysis revealed SAP was associated with HO with $P < 0.1$ (90% CI).

RR assessment

Table 3 displays RR assessment using Wald's test for the different aetiologies. The probability of getting AHO from SAP was significantly higher compared to patients without SAP (RR 3.54, $P < 0.01$). All other aetiologies were less frequent in the AHO group compared to the non-AHO group.

Table 2 Association between different aetiologies and AHO using binomial exact test

Aetiology	HO: total, %	NIL: total, %	90% CI	*P*-value ($P < 0.1$)
SAP	7, 77.7	2, 22.3	0.5, 1	**0.08984**
Blunt injury	4, 33.3	8, 66.7	0.15, 1	0.927
Bowel perforation	5, 20.8	19, 79.2	0.1, 1	0.99
Ischaemic bowel	0, 0	6, 100	0, 1	1
Gynaecological-related procedures	0, 0	5, 100	0, 1	1
Miscellaneous and unknown	0, 0	4, 100	0, 1	1

AHO, abdominal HO; HO, heterotopic ossification; SAP, severe acute pancreatitis.

Table 3 RR assessment for different aetiologies associated with HO using Wald's test

Aetiology	*X*	*Y*	*m*1	*m*2	RR ($P < 0.05$)	95% CI	*P*-value ($P < 0.1$)
SAP	7	9	9	41	3.54	1.8, 6.96	**0.001289**
Blunt injury	4	8	12	38	1.583	0.58, 4.35	0.39
Bowel perforation	5	7	24	26	0.77	0.3, 2.11	0.618
Ischaemic bowel	0				0		
Gynaecological-related procedures	0				0		
Miscellaneous/unknown	0				0		

HO, heterotopic ossification; RR, relative risk; SAP, severe acute pancreatitis.

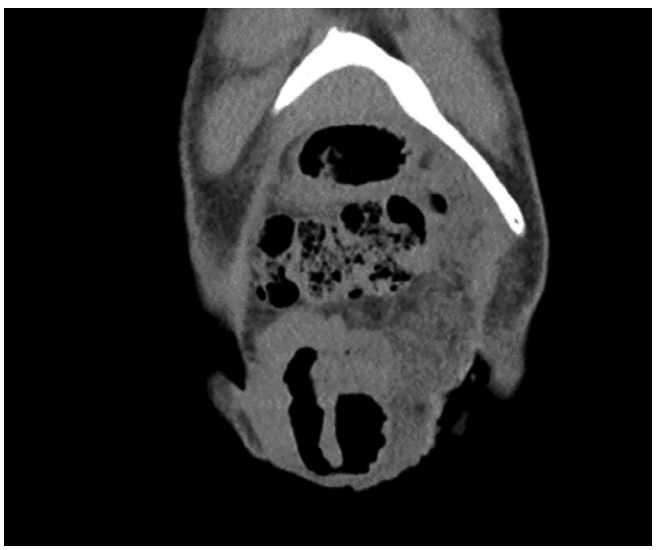

Fig. 1. Abdominal computed tomography showing abdominal heterotopic ossification in the anterior abdominal wall.

None of the 12 patients with AHO complained of any symptoms related to the lesion. This is unusual as most patients with early HO report localized pain, tenderness and oedema.[1] In our patients, HO was picked up on post-operative imaging prior to planning definitive surgical procedures (Figs 1,2). All AHO deposits were found in the sub-fascial and intramuscular plane with no intraperitoneal deposits. All patients initially had their abdomen temporarily closed with a negative pressure dressing prior to definitive closure. Only two (16%) patients had significant bone formation in the abdominal wall, which required surgical excision prior to definitive closure. Ossification was confirmed on histopathology (Fig. 3). There were no procedure-related mortalities in this series.

Discussion

HO refers to the development of extra-skeletal bone in muscle and soft tissues, following tissue insult secondary to surgery or trauma. This pathological process is considered as the result of severe inflammatory cell cascade and attempt at tissue repair involving resident mesenchymal cells, which has gone aberrant.[1] Literature review reveals that several intermediary steps are required for HO to occur. An inciting event, inflammatory signal from the site of injury, osteogenic transformation of resident multipotent mesenchymal cells and finally a conducive tissue environment are required for HO to occur.[9] While HO is frequently seen associated with bone fractures, orthopaedic surgery, following head trauma, spinal cord injuries and burns, AHO is relatively uncommon.[1,9] The true incidence of AHO after DCL is not known. Wang *et al*. conducted a retrospective study of 68 patients after DCL, from 2009 to 2015 at a Canadian level 1 trauma centre, in which 36 (53%) patients developed AHO.[11] In most of the cases, AHO occurred within the first year of surgery. In our series, AHO was observed from 4 to 7 months onwards and there was considerable variability of the size of HO. SAP was the main aetiology of our cases of AHO, this could possibly be explained by a more elaborate and enhanced inflammatory response which persists longer, increased time on ventilation and possibly saponification as an inciting event. Even when they are of considerable size, our patients did not complain of significant pain or discomfort. AHO need not be removed unless it interferes with closure of the abdomen or the patient is symptomatic, as it is a benign condition. Bisphosphonates and non-steroidal anti-inflammatory drugs have been used for prophylaxis of HO but there is no consensus on this.[1] They may be considered in critically ill patients with midline laparotomy and open abdomen who are expected to have prolonged ICU stay. Cox-2 selective inhibitors are also being tried but their efficacy does not appear to be to better then non-steroidal anti-inflammatory drugs.[12]

Only two out of 12 patients required surgical removal of the HO to facilitate definite closure of the abdomen. Both patients presented with

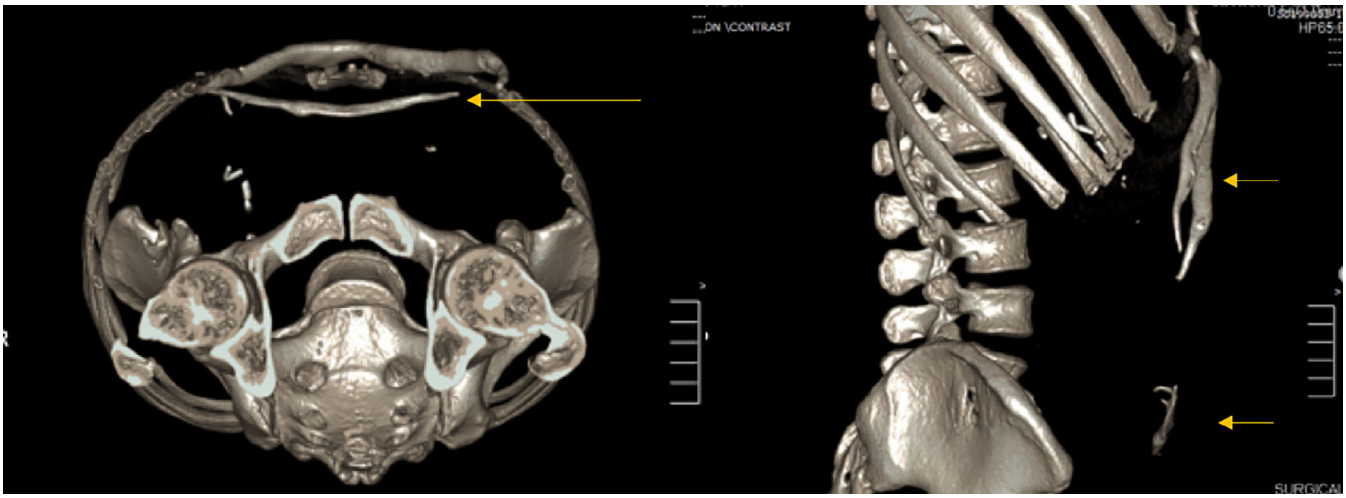

Fig. 2. Bone view reconstructed images showing extensive anterior abdominal wall heterotopic ossification (HO). Prominent upper abdominal formation and subtle curvilinear lower abdominal HO (arrows).

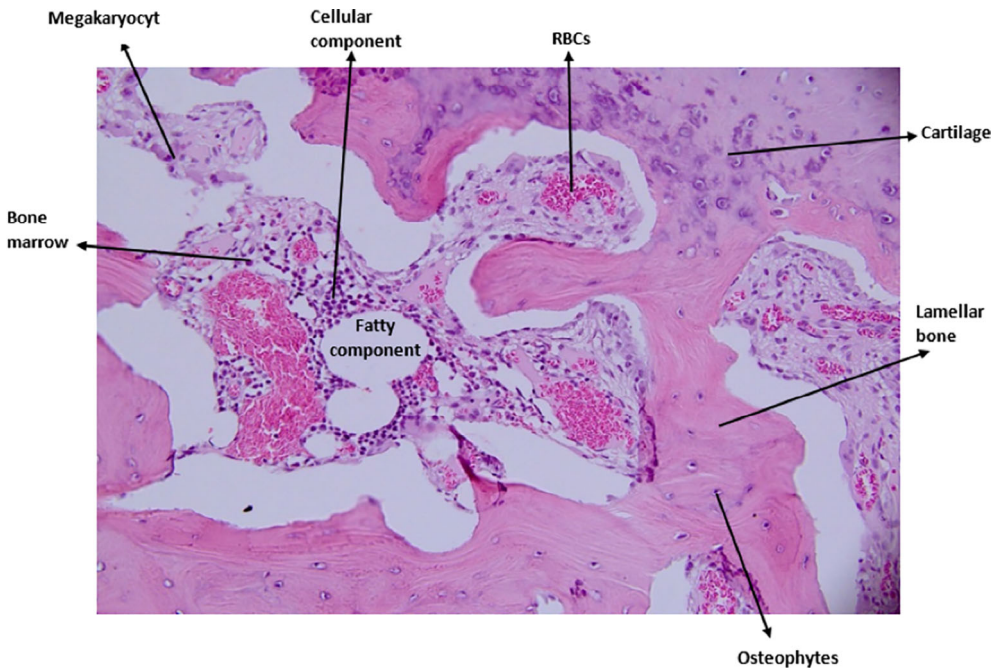

Fig. 3. Photomicrograph showing histological evidence of osseous, cartilaginous and myelogenous elements, which distinguishes this entity from dystrophic calcifications.

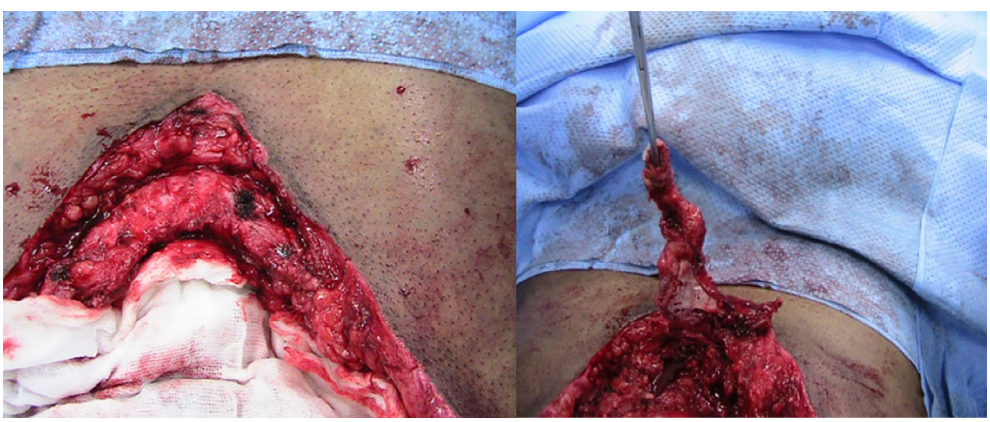

Fig. 4. Intraoperative image of abdominal heterotopic ossification and its removal, without which definite closure of the abdomen would not be possible.

fulminating acute pancreatitis with acute compartment syndrome and severe organ dysfunction requiring DCL. The first patient was a 45-year-old man who was critically ill. In spite of all medical management to control abdominal compartment syndrome, he continued to deteriorate and required decompressive laparotomy. He made a gradual and steady recovery at the cost of an open abdomen. His abdomen remained frozen at day 20 and therefore, split-skin grafting was employed over the viscera, accepting a subsequent ventral hernia. At 9 months follow-up, the patient developed palpable hard lumps in the abdominal wall, without any symptoms. Imaging by computed tomography scan confirmed AHO (Figs 1,2). It was important to wait for the skin graft to mature because during this process of maturation, the skin graft along with omentum separate from the viscera and can be easily separated from the bowel. The mature skin graft was dissected from the bowel and HO was removed as it interfered with the repair (Fig. 4). The abdomen was closed directly following component separation.

The second patient was a 39-year-old male with severe haemorrhagic pancreatitis and ACS. Decompressive laparotomy was done and the resultant frozen abdomen was covered with skin graft. Follow-up at 8 months showed extensive HO of the abdominal wall with no intraperitoneal ossifications. The patient underwent removal of the mature skin graft, removal of large AHO and the abdomen was closed with a bridging mesh.

Both the patients had an uneventful post-operative recovery.

Conclusion

Our data AHO showed a male predominance, although the exact cause of this is unclear; a possible theory is that young males may mount an increased inflammatory response. Extended periods of ventilation, ICU stay and hospital admission were strongly associated with the development of AHO (all $P < 0.01$). SAP emerged as a significant risk factor for AHO in our series ($P < 0.01$, 90% CI). None of our patients presented with any symptoms attributable to AHO. Only a minority of AHO patients develop larger lesions which require surgical excision as seen in our series. Preoperative assessment and diagnosis of AHO are important prior to planning definitive closure of the abdomen, as these may interfere with surgery and healing.

Conflicts of interest

None declared.

Author Contributions

Jacob Jacob: Conceptualization; data curation; investigation; methodology; project administration; supervision; writing-original draft. **Jonathan Reddipogu:** Formal analysis; investigation; methodology; project administration; resources; supervision; validation; writing-review and editing. **Mathew Jacob:** Conceptualization; data curation; investigation; methodology; project administration; writing-original draft; writing-review and editing.

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