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ARTICLE

Pelvic MRI in spinal cord injury patients: incidence of muscle signal change and early heterotopic ossification

David McKean [1] · Sarim Ather[2] · Amar Gandhi[2] · Talia Hubble[2] · Maurizio Belci[3] · Simone Tiberti[3] · Joseph Papanikitas[1] · Sarah Yanny[1] · Deborah King[1] · Richard Hughes[1] · Thomas Meagher[1] · Luis Lopez de Heredria[3]

Abstract

Study design Prospective observational study.
Objective To evaluate pelvic MRI muscle signal changes and their association with early heterotopic ossification (HO) in patients with spinal cord injuries.
Setting National Spinal Injuries Unit, Stoke Mandeville, UK.
Methods Forty patients were imaged with at least two interval magnetic resonance (MR) studies of the pelvis in the first 6 months following a spinal cord injury. Scans were reviewed and scored for heterotopic ossification, muscle signal change and extent of muscle involvement.
Results Muscle signal change was present in 28 (70%) on the initial MRI and 31 (77%) by the second study. Six patients developed MR changes of prodromal or immature heterotopic ossification (15%). No restricted diffusion was demonstrated and no patient developed mature HO. Patients developing MR changes of early HO were more likely to have grade 3 muscle changes.
Conclusion Increased T2 muscle signal is common following cord injury, is frequently progressive in the subacute period and is associated with complete injury and early MR signs of heterotopic ossification.

Introduction

Heterotopic ossification (HO) refers to pathological bone formation in the soft tissues around joints in a wide range of conditions including spinal cord injury [1]. Incidence is variably reported ranging from 10 to 50% of spinal injury patients, though large more recent studies approximate this to 6–10% [1–5]. HO also affects non-traumatic cord injury with a similar incidence [6]. It typically presents between 4 and 6 weeks from initial injury and most commonly involves the hips; knee, shoulder and elbow joints may also be affected [7]. A genetic predisposition to developing HO has been suggested based on human lymphocyte antigen (HLA)-typing with some authors suggested a relationship between HLA B18 and HLA B27 [8–10] although other studies have not found a significant association [11]. Other risk factors associated with HO include thoracic trauma, tracheostomy, spasticity, pressure ulcers, pneumonia and urinary tract infections [12].

HO most commonly presents with swelling, mild erythema and skin induration. C-reactive protein and alkaline phosphatase may be suggestive of active HO but imaging confirmation is usually required for diagnosis as differential diagnosis includes deep venous thrombosis and infection [13, 14]. Triple phase bone scintigraphy has been the mainstay of imaging diagnosis though normal isotope scans do not exclude subsequent development of HO [15]. Ultrasound has been demonstrated to be effective in

✉ David McKean
David.McKean@nhs.net

1   Department of Radiology, Stoke Mandeville Hospital, Buckingahmshire Healthcare NHS Trust, Aylesbury, UK

2   Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, Oxford, UK

3   National Spinal Injuries Centre, Stoke Mandeville Hospital, Buckingahmshire Healthcare NHS Trust, Aylesbury, UK

identifying early changes which appear 3–4 weeks before radiographic signs are positive [16].

Complications of HO include ankylosis, pain, lymphoedema, decreased function and mobility that may impair rehabilitation. Localised mass effect from the oedema and bone formation may lead to peripheral nerve entrapment, vascular compression and lymphedema. These sequelae can also contribute to pressure ulcer formation [17].

MRI is sensitive for early changes of HO and demonstrates both early inflammatory change as well as mature osteoid. More recently it has been reported that widespread subcutaneous and muscle changes such as muscle, fascial and bone marrow oedema accompany many spinal cord injured patients with HO [18].

Medical treatments of HO have previously included bisphosphonates and non-steroidal anti-inflammatories [19]. Low dose radiotherapy has been advocated though has not gained widespread use in view of the relative youth of patients affected and concern regarding induction of tumours [20]. Surgical resection is reserved for late disease restricting joint movement [21].

As MRI is used increasingly frequently to assess a range of clinical problems in patients with cord injury including pelvic pressure sores [22, 23], we have noted that widespread increased T2 muscle signal is common in these patients and hypothesised a link with HO.

Patients and methods

This prospective observational study was conducted according to the Declaration of Helsinki protocols and was approved by the local research and ethics committee (REC reference number: 11/LO/1432). Data collection took place between March 2012 and January 2014. Inclusion criteria were adult patients over 18 years of age, admitted to our institution with traumatic or non-traumatic spinal cord injury within 60 days of initial trauma. The initial magnetic resonance (MR) study was undertaken typically 6 weeks from acute insult and the second after a similar interval. Patients with two normal studies did not have a third scan, as per protocol.

MR studies were undertaken on a 1.5 T Symphony Tim system (Siemens, Erlangen) using a combination of spine coils and a phased-array body coil. Typically a FOV of 40 cm was used and 25–30 slice sections acquired with a 20% slice gap. Sequences included T1SE axial (TR 460, TE 11, NSA 2, 5 mm sl th, 512×256 matrix. Diffusion-weighted axial (B0, B500, B1000 TR 4000, TE 98, NSA 7, 6.5 mm sl th, 128×96 matrix), STIR coronal (TR 4030, TE 85, NSA 2, 5 mm sl th, FA 150°, TI 160 ms, 320×240 matrix) and 2D FLASH Gradient echo axial (TR 750, TE 9.5, NSA 1, 5 mm sl th, 448×270 matrix, FA 20°).

Fig. 1 Pelvic muscle signal grading. Coronal STIR image of Grade 1 pelvic muscle signal change with minimal muscle signal change.
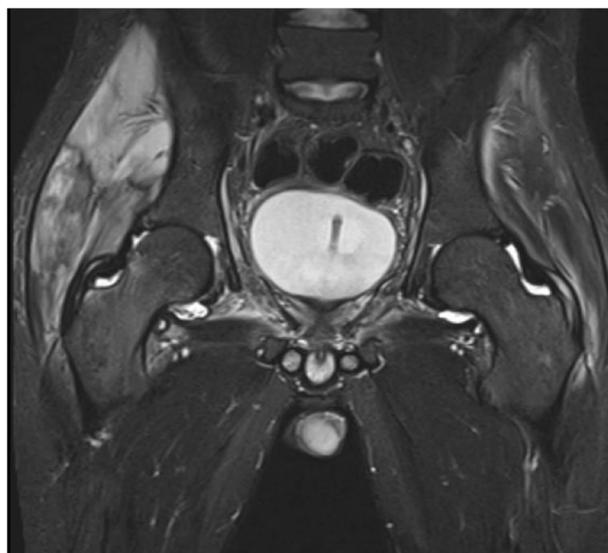

Fig. 2 Pelvic muscle signal grading. Coronal STIR image of Grade 2 pelvic muscle signal change with increased T2 muscle increased signal approaching fluid signal affecting <50% of the muscles of pelvis.

MR scans were reviewed and scored for HO, muscle signal change and extent of muscle involvement. Muscle increased STIR signal was graded 1–3 depending on extent of muscle involvement (Figs. 1, 2, 3). HO was classified as prodromal, immature and established HO (Figs. 4, 5 and Supplementary File). These studies were graded by consultant radiologists experienced in musculoskeletal radiology and in spinal cord injuries imaging. All second MR studies were reported by two radiologists to assess interobserver agreement. The level of spinal cord injury,
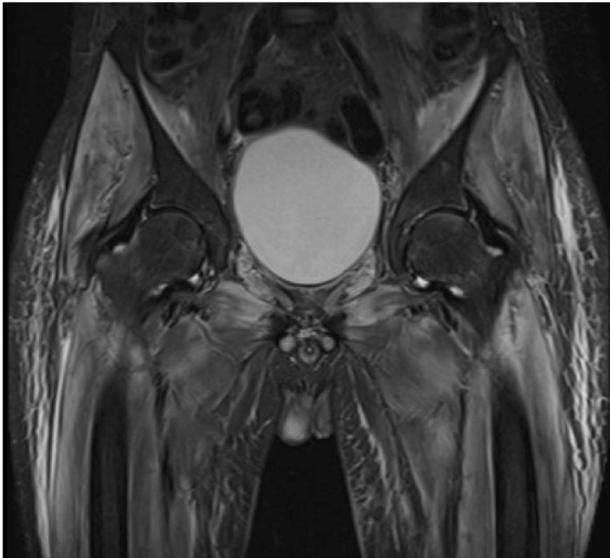
Fig. 3 Pelvic muscle signal grading. Coronal STIR image of Grade 3 pelvic muscle signal with extensive signal change affecting greater than half of the muscles of pelvis.
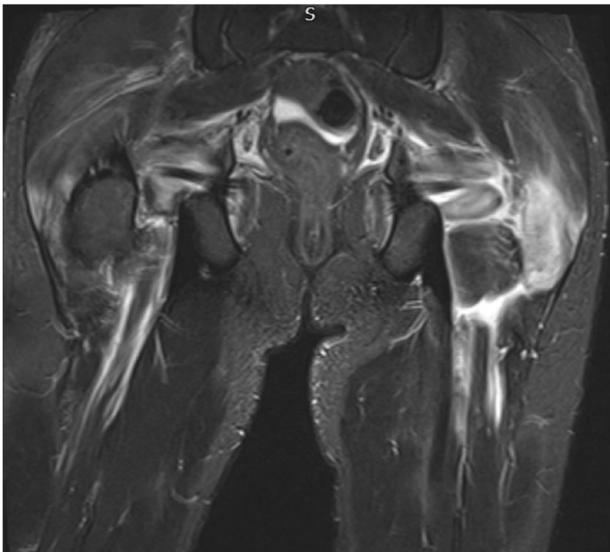

Fig. 4 Heterotopic ossification grading. Coronal STIR image demonstrating prodromal HO (Grade B) with marked enlargement of the left gluteus medius muscle and hyperintense intramuscular STIR signal.

American Spinal Injury Association Impairment Scale (AIS) [24] and date of cord injury were recorded.

Results

A total of 46 patients were consented but only 40 patients completed at least two MRI studies. Thirty-two patients were male and eight female. Average age was 41 years, median 49 years (range 21–87 years). Thirty-three patients (82%) had a traumatic cord injury and the seven had
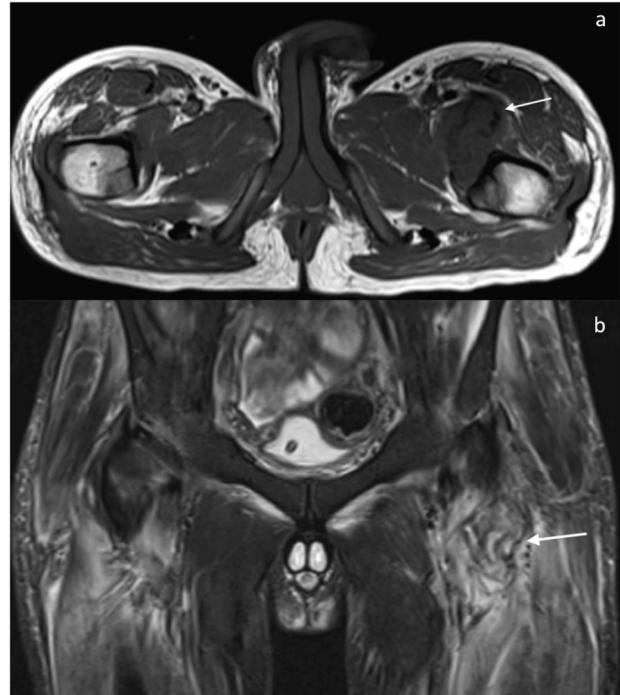

Fig. 5 Heterotopic ossification grading. Axial T1 (**a**) and coronal STIR (**b**) weighted images demonstrating immature heterotopic ossification (Grade C) with swelling and increased signal change in distal iliopsoas (**a**—white arrow) and flecks of curvilinear low signal on the corresponding coronal STIR sequence (**b**—white arrow).

non-traumatic cord injury, most commonly cord infarction (five patients). Mean time in days from initial injury to first MRI scan was 41 days (median 42, range 25–60 days) and to the second scan was 81.2 (median 82.5, range 55–122 days). Twenty-two patients had a third MR scan. Three patients had MR changes of prodromal HO and three had MR changes of immature HO (Fig. 5). All three patients with immature HO were AIS A ($P < 0.001$), Table 1.

Increased T2 muscle signal change (Grade 2 and above) was present in 28 (70%) of patients on the initial MR study and this increased to 31 (77%) by the second study. Of 23 patients who had a third study 6 (26%) improved, 1 (4%) deteriorated and 16 (70%) were unchanged, Table 2.

Patients who were AIS A (sensory and motor complete SCI) were significantly less likely to have normal muscle signal (Grade 1): 1/18 AISA (5%) compared with 8/22 AISB–D (36%), Table 3.

At the initial MR study 15 (37%) had normal muscle signal and this decreased to 11 (27%) by the second study and correspondingly Grades 2 and 3 increased. Abnormal increased T2 signal was most commonly seen in the gluteal and quadriceps muscles and less commonly identified in the adductor and iliopsoas muscles, Table 4.

The incidence of Grade 3 muscle signal change was 60% in those patients with early changes of HO and in the patients who did not develop early changes was 31%.

Table 1 Summary of injury level, AIS score and MR findings.

Case	Level	AIS	1st MR Grade	HO status	2nd MR Grade	HO status	3rd MR Grade	HO status
1	C4	D	1	A	2	A	2	A
2	C5	C	2	A	2	A		
3	C4	C	2	A	2	A		
4	C4	D	1	A	1	A		
5	C5	D	1	A	1	A		
6	C3	D	3	A	3	A	2	A
7	T4	A	3	B	3	A	2	C
8	C6	A	2	A	2	A		
9	T6	A	2	B	3	A	2	A
10	T12	A	3	B	3	A		
11	C4	C	3	A	3	A		
12	C3	D	1	A	1	A		
13	T11	B	1	A	2	A	2	A
14	C4	A	3	B	3	B	2	A
15	T11	A	3	B	3	A	3	A
16	C5	A	3	A	3	B	3	C
17	T12	A	3	A	2	A	2	
18	C4	B	3	A	2	A	2	A
19	C4	A	3	A	3	A		C
20	C3	D	1	A	1	B	3	B
21	T9	A	3	A	3	A	3	A
22	L1	A	2	A	2	B		
23	T3	A	1	A	3	B	2	B
24	C5	B	1	A	2	B		
25	T4	A	2	A	2	A	2	
26	T3	A	3	A	1	A		
27	C5	B	3	A	3	B	2	B
28	C7	D	1	A	1	A	2	
29	L1	C	1	A	2	A	3	A
30	T3	A	2	A	2	A	2	A
31	C2	C	3	A	3	A		A
32	C3	A	2	A	2	A		A
33	L1	A	1	A	1	A	3	
34	C4	C	1	A	1	A	2	
35	T3	C	2	A	3	A	2	A
36	C4	D	1	A	1	A	1	A
37	T10	A	2	A	2	A		A
38	T8	C	1	A	1	A	1	A
39	C4	C	3	A	3	A		
40	C4	D	1	A	1	A		A

Muscle STIR signal was graded 1–3 depending on extent of muscle involvement (Figs. 1, 2, 3 and Supplementary File). The presence of HO as: A—no evidence of heterotopic ossification (HO); B—prodromal HO; C—immature HO; D—established heterotopic ossification (Figs. 4, 5 and Supplementary File).

Interobserver agreement

The calculations above only consider exact matches between observers. The number of observed agreements were 23 (82% of the observations) a Kappa of 0.73 (SE 0.104). The number of agreements expected by chance: 9.4 (34% of the observations), a 95% confidence interval from 0.528 to 0.935. The strength of agreement is considered to be 'good'.

Table 2 Increased muscle signal.

	Grade 1	Grade 2	Grade 3
Baseline MRI ($N = 40$)	12	23	5
First follow-up MRI ($N = 40$)	9	18	13
Second follow-up MRI ($N = 23$)	2	15	6

Table 3 Increased muscle signal and AIS score on second MR.

	Grade 1	Grade 2	Grade 3
AIS A ($N = 18$)	1	9	8
AIS B ($N = 3$)	0	2	1
AIS C ($N = 9$)	1	5	3
AIS D ($N = 10$)	7	2	0

Table 4 Muscles affected with increased signal on second study.

	Muscle involvement
Gluteus medius	27
Gluteus maximus	23
Quadriceps	20
Adductors	15
Iliopsoas	14

Discussion

Immature HO is well described, presenting clinically and appreciable on isotope scintigraphy and ultrasound [13, 14, 16, 25]. Early ossification may be visible on plain radiographs and CT but these are frequently normal up to 4 weeks after a patient develops symptoms [25, 26]. However, imaging is also known to demonstrate foci of HO which are subclinical and it is also established that foci of immature HO may reverse [13, 25].

We had noted many patients with extensive increased T2 muscle signal in the rehabilitation phase and the genesis of this study was trying to ascertain if this was linked to early HO. The cause of HO remains uncertain [12]. Suggested theories include whether the mass and swelling associated with HO might be related to ischaemia, so we also evaluated whether diffusion-weighted imaging might prove useful. None of 26 patients evaluated with DWI demonstrated restricted diffusion including all patients with prodromal HO ($n = 3$) and immature HO ($n = 3$). This suggests there is no evident benefit from using this sequence in evaluating patients with suspected HO.

Wick et al. demonstrated that abnormal muscle signal is associated with established HO. In their review of 14 patients, all had widely increased T2 muscle increased signal, most commonly affecting quadriceps [18]. Our series supports this finding in patients with HO, all of whom had bilateral extensive muscle signal change. The most commonly affected muscles in our cohort were gluteus medius in 28 (67%), gluteus maximus 24 (57%), quadriceps 20 (48%), adductors 15 (36%) and iliopsoas 14 (33%). This is consistant with previous studies of HO localisation [27, 28]. A potential limitation may have been assessment in the coronal plane which limits the assessment of the quadriceps and iliopsoas compared with other muscles. Wick also highlighted the use of gradient echo sequence (GE) in identifying early ossification [18]. This was used in 16 of our patients but did not significantly alter diagnoses.

The MR imaging appearances described by Ledermann et al. are of more established neurogenic HO with progressive and mature ossification seen in a patient cohort consisting of thirty-one patients with traumatic spinal cord injury, two patients with spinal cord infarctions, and three patients were with multiple sclerosis (MS), ischemic brain damage, and spina bifida [29]. MRI also depicted high signal change in the Grade 1 classification of this group (gradation established by CT appearance) and increased MR signal in muscle and para-articular tissues is similarly described. The patient group included MS and head injury.

Results from our cohort indicate progressive muscle signal change with time between 40 and 80 days, the average time between scans, but more patients improved by the third scan than deteriorated. This accords with the observation that the most common onset of symptomatic HO is around 6–8 weeks from acute injury. Increased muscle signal was also more prevalent in AIS A and of a higher grade (Tables 1, 3) compared with incomplete grades. This is also in keeping with known association of HO incidence.

There are many limitations to this study. Numbers are small, sequences did not include contrast which can be helpful in depicting HO and GE series was not used on all patients. There was no comparison with other modalities including CT to correlate with early calcinosis. Despite these limitations, the data suggests a significant link between incremental muscle signal change and the development of HO. Pelvic MRI 40 days following injury may be helpful to detect these changes and identify those at risk of HO. Further studies are required to determine whether early medical intervention is associated with less severe disease and associated complications.

Conclusion

The incidence of HO in this study of patients with SCI is 7%, and approximates to previously published rates. MRI using STIR and T1 weighted sequences is useful in

depicting HO but diffusion-weighted sequences were unhelpful. Increased muscle signal is common and progressive in the initial months following cord injury and is associated with AIS A injury and development of immature HO. Imaging with MRI ~40 days following injury may help identify those at risk of early HO.

Data availability

Compliance with ethical standards

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