Commentary

Heterotopic ossification – a long-term consequence of prolonged immobility

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See related research by Argyropoulou *et al.*, http://ccforum.com/content/10/5/R152

Abstract

Heterotopic ossification is a condition affecting an appreciable minority of critical care patients; it can have long-lasting effects on recovery and return to functional status. Ectopic bone forms in soft tissues near the large joints, causing pain, swelling, limitation of movement and ultimate disability. X-ray changes may be delayed for several weeks after the diagnosis is clinically suspected. Magnetic resonance imaging may be more sensitive for detecting early changes, yielding positive results several weeks before X-rays. However it is not clear that diagnosing the process early will influence long-term patient outcome, because no effective treatments are available.

Currently only a small minority of long-stay intensive care patients are followed up by the critical care service, and thus there is no 'bridge' between the critical and rehabilitation phases of illness. Recent studies have demonstrated that survivors suffer long-term consequences that can have a marked impact on their recovery and quality of life for years after discharge, and a current paper highlights a specific physical issue: heterotopic ossification (HO) [1].

Return to normal functional status is often slow, with different rates of physical and psychological improvement [2-4]. Lack of understanding and experience of possible long-term sequelae of critical illness may hinder patient recovery further because access to the full range of services required in the rehabilitative phase may not be provided.

HO is a recognised condition in critical care patients, causing significant long-term morbidity in up to 5% patients after a prolonged stay [5]. The condition is not widely recognised and may evade diagnosis, yet it may be a major cause of impaired mobility and pain in the months after discharge [5]. The condition has been described in patients with head or spinal cord injury, pancreatitis and acute respiratory distress syndrome (ARDS), although any sedated patient is vulnerable [6,7].

The presentation is non-specific, with pain, swelling, fever and decreased joint mobility – common signs that may be frequently overlooked. Furthermore, presentation may be obscured by sedation or muscle relaxants.

Argyropoulou and colleagues [1] describe a series of 11 patients who developed HO of the knee during prolonged critical care stay; head injury was the cause for admission in most cases. They report early 'lacy' changes in the vastus medialis and lateralis muscles on magnetic resonance imaging (MRI) (T1-weighted and short TI inversion recovery (STIR) images) and homogeneous high signal changes in the medial portion of the vastus medialis. The authors report that MRI changes occurred very rapidly after clinical suspicion of the diagnosis, but X-ray changes were delayed for a further 23 days. On follow-up MRI scanning, the medial portion of the vastus medialis had developed heterogeneous changes suggestive of HO in all cases. X-rays at this time showed calcification in the same position. This delay in X-ray presentation is plausible, because substantial calcification of the area needs to occur for X-ray changes to be evident. This occurs at a relatively late phase of the disease. Histologically the first changes are infiltration of the muscle by immature connective tissue, fibroblasts and collagen fibres, and this may be what the MRI changes are representing [8]. The authors therefore suggest that MRI scanning should be employed early to confirm the diagnosis, rather than waiting for the delayed X-ray changes.

What causes muscle to calcify and turn to bone is still poorly understood. Argyropoulou and colleagues give an account of the hypothesised pathogenesis: dormant osteoprogenitor

ARDS = acute respiratory distress syndrome; HO = heterotopic ossification; MRI = magnetic resonance imaging.

stem cells in soft tissue seem to be activated by bone morphogenetic protein, the release of which is triggered by a variety of stimuli (such as head injury) [9]. This results in differentiation of these stem cells into osteoblasts, which go on to form bone. The knee is commonly affected, in particular the vastus medialis. The reason for this is not yet clear; muscle atrophy after disuse predisposes to HO and this is exaggerated in muscle rich in slow-twitch fibres, such as the medial aspect of the vastus medialis.

Functional limitation resulting from HO and other factors (such as muscle wasting and entrapment neuropathy) has been shown to be significant even 1 year after discharge from intensive care: ARDS survivors are only able to walk 66% of predicted distance in 6 minutes, and only 49% return to work in the first year [5]. It is therefore important to avoid and treat HO where possible. During the acute inflammatory phase the joint should be rested but passive exercising should begin as soon as possible. Treatment modalities of established HO are limited; non-steroidal anti-inflammatory drugs and irradiation of the affected area have been suggested as options in HO after hip replacement [10]. Surgical removal of excess bone is an option, but only after full maturation has occurred or else recurrence is inevitable [11]. After surgery, bisphosphates may be used to prevent further recurrence [12]. However, no therapies have been proven to be of benefit in avoiding or halting the disease in critical care patients.

This leads us to ask whether early diagnosis by MRI scanning is actually of any benefit. MRI scanning of the critically ill is fraught with challenges, such as the need to use equipment incorporating only non-ferrous metals. Many MRI scanners are poorly equipped with invasive monitoring facilities, meaning that only the most stable patients can be scanned safely. In the above study, out of 670 patients screened for HO, 31 were identified (clinically); only 11 were included and deemed stable enough to be transferred to the MRI scanner. Cost implications must also be considered.

If a clear therapeutic intervention could be employed to halt the progression of HO, then, logically, early MRI scanning would only be of benefit if a resultant therapeutic intervention could halt the progression of HO. Currently no treatment can claim to do this. Instead, the focus should probably be on effective physiotherapy and joint exercise during the period of immobility to try to prevent the condition from developing. A well-formulated rehabilitation programme after discharge is the best that can currently be offered to affected patients; this may lead to accelerated physical and psychological recovery [3]. Until the condition is better understood and effective treatment is available, this should be the target of our resources.

Competing interests

The authors declare that they have no competing interests.

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