European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2021

Review

MYOSITIS OSSIFICANS: A REVIEW ON A BIOLOGICAL BASIS

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ABSTRACT

Myositis ossificans (MO) is a rare benign ossifying disease that most frequently affects young people. It is characterised by the localised production of heterotopic bone with cartilage in extraskeletal soft tissue. In most situations, it is impossible to pinpoint a cause. The patient's trauma history, imaging appearance, histological investigation and clinical symptoms are often used to diagnose MO. This review was performed to search the biological basis of MO. The research studies were collected from PubMed, Science Direct and Google Scholar. After proper assessment and evaluation, 14 articles were included in the study. The study also covers the diagnosis, management and treatment interventions that will be helpful in the understanding of MO.

KEYWORDS: *myositis ossificans, MO, skeletal muscles, chondrocytes, osteoblasts*

INTRODUCTION

In myositis ossificans (MO), lamellar bone forms around soft tissues, particularly the major skeletal muscles in the arms and thighs. Neurogenic and non-neurogenic acquired MO can be distinguished from one another. The latter can be further broken down into idiopathic/pseudomalignant as well as post-traumatic restricted MO (60–75% of patients). Especially severe direct injuries and persistent minor trauma, including maltreatment, can lead to post-traumatic MO. Although the pathophysiology is still not fully established, the current theory is that an "endothelial-mesenchymal transition" occurs. Following injury, ischemia, or inflammation, mesenchymal stem cells undergo this transformation, which is regulated by a cytokine cascade, into chondrocytes and osteoblasts (1).

In the first four weeks of its life, MO has a rapid overgrowth. In the centre of the lesion, osteoblasts and chondrocytes are now producing a new osteoid matrix. Whenever the lesion ceases progressing, in between the fourth and tenth week, the characteristic peripheral calcifications can be seen. The so-called "zonal pattern organisation" can be seen radiographically and histologically once the lesion has matured. They have a growing core region of fibroblasts with the potential for necrosis and bleeding. An "intermediate zone of immature osteoid tissue" and cartilage follows this.

Received: 09 November 2021
Accepted: 16 December 2021

ISSN: 2038-4106

Enchondral ossification and a lamellar layer of mature bone promote this process (2, 3).

Clinically, the affected location swells painfully, and the surrounding joint's range of motion is limited. In most circumstances, a focused anamnesis enables a speedy diagnosis. However, the possibility of bone or soft tissue neoplasms must be considered when a tumour is developing without a history of trauma (4). The "centripetal calcifications" of the lesion can be identified via radiological imaging, bypassing the cortical bone; however, in the early weeks, these signs may not be present. The development of "pleomorphic osteoblasts" along with atypical nuclei and mitosis can be deceiving in ambiguous lesions if the biopsy is carried out too early or within the core lesion (5). As a result, MO might be difficult to distinguish from malignancies in the early stages. A review on MO is performed since this disease is not fully understood.

MATERIALS AND METHODS

The Science Direct and PubMed search engines and additional published articles from Google Scholar were used to conduct a database search. A specially created Performa was used to summarise the final publications.

RESULTS

Fourteen publications in all were taken into account for the systemic review and meta-analysis. Gender preference and age of engagement were incorporated in the forest mapping for demographics.

DISCUSSION

Pathophysiology

It is not fully understood how MO production occurs pathophysiologically. It is thought to happen due to fibroblasts diffusing improperly into osteogenic cells. Researchers have shown that the deregulated activity of local stem cells as a reaction to tissue injury with subsequent inflammation is the cause of the physiological response of heterotopic bone production. Recent research has shown that the "endothelial-mesenchymal transition" mechanism may be necessary for extraskeletal bone production. Injury to the skeletal muscles triggers a local inflammatory cascade. Cytokines are released as a result of this. These cytokines affect the vascular endothelial cells in skeletal muscle, causing them to undergo an "endothelial-mesenchymal transition". Whenever introduced to an "inflammatory-rich environment", these "endothelial-derived mesenchymal stem cells" may develop into chondrocytes or osteoblasts. The development of endochondral bone will then occur in extraskeletal tissue involving chondrocytes (6).

When a traumatic experience is evident, the term "traumatic MO" (TMO) is preferred. TMO makes up 60 to 75% of cases of MO and is the most prevalent kind (4). The diagnosis is relatively straightforward when a patient with TMO presents a typical history of trauma and an evident calcification on imaging. However, there have been several documented MO occurrences in individuals with no apparent history of trauma, which led some people to assume malignancy. As they mirror other benign or malignant lesions, such as abnormal parosteal osteochondromatous proliferation, melorheostosis, recurrent giant cell tumour, parosteal osteosarcoma, extraskeletal osteosarcoma, and soft tissue sarcoma, the imaging characteristics of MO are non-diagnostic (7).

Stages of myositis ossificans

Three distinct stages characterise MO. First, the proliferation comprises mesenchymal cells, secreting a myxoid matrix during the acute phase (i.e. first week). As fibroblasts undergo many mitoses at this stage, the mass appears pseudo-fibrosarcomatous. Histologically speaking, osteoblasts develop into fibroblasts during the subacute period (the next two weeks). They produce an osteoid matrix at the edge of the first myxoid zone. It seems pseudo-osteosarcomatous as a result. Finally, a precise histological diagnosis can be made during the maturation period (2–5 weeks) (8).

Osteosarcoma must be ruled out due to bone growth and similar epidemiology. Imaging is crucial for detecting MO in its early stages. Radiographs, however, are frequently negative early in the disease. An incorrect diagnosis of sarcoma may result from a biopsy performed early in MO. Conversely, a real sarcoma could go unnoticed if the biopsy is postponed.

The characteristic features of this condition, such as the detachment of the mass from the nearby cortex and the reduced attenuation of the mass's core, are best detected with computerised axial tomography (9).

Laboratory testing

Numerous writers have examined the usefulness of laboratory tests on serum. There is presently no diagnostic test, but a number of correlations have been found. Initial levels of "serum alkaline phosphatase (SAP)" remain normal. But after three weeks, it acutely elevates concurrently with bone growth. Particularly in people with clinically severe MO, this happens. During the initial phases of MO, acute phase reactants such as the prostagandin-E2 serum level, erythrocyte sedimentation rate, and C-reactive protein level are raised. Just before spike in SAP, the serum calcium value normally drops for a brief time before returning to normal. If muscle is involved, the amount of creatine phosphokinase is usually increased. And, unlike SAP, it might be able to forecast how severe and how soon MO will develop (10).

Imaging studies

Imaging investigations are a crucial component of the MO diagnosis procedure. In many circumstances, radiographic evidence are adequate to make the diagnosis. To make a definitive diagnosis, though, more advanced imaging techniques such a CT scan, MRI, or bone scintigraphy may be required (6). In order to accurately characterise the lesion prior to surgery and to better define the pattern of calcification, CT scans are preferred to radiographs. If requested quickly and early in the disease's progression, a bone scan can show higher uptake in the affected area and is thought to be particularly sensitive. However, there isn't enough support in the literature to prove how useful bone scintigraphy is in deciding when to perform surgery. Previously, it has been hypothesised that levels of SAP may peak 3 weeks after the primary injury in the context of traumatic MO. At around 10 weeks, it can take on any value that is more than 10 times the upper limit. By 18 weeks, it will have returned to normal levels. However, because the SAP level might remain normal even in active lesions, it cannot accurately assess the maturity as well as activity of a lesion. As a result, it's important to interpret SAP values in both the clinical as well as radiographic settings (11).

Diagnosis and treatment methods

Histopathological analysis is usually used to get a diagnosis. It could be challenging to distinguish a MO from a sarcoma based only on histology data. The clinical as well as radiological data' correlation is crucial in these situations. Once the confirmation of MO has been made by excision, additional treatment is not required. Understanding the aetiology and pathophysiology of MO, an uncommon clinical condition, helps spare the patient the concern of having a suspected neoplasm (9).

Surgical treatment

Surgery is not always the first course of treatment for MO ossificans because it is typically a self-limiting condition. The development of intractable pain, decreased range of motion compromising quality of life, neurovascular deterioration brought on by compressive impact, and failure of non-surgical approaches to treat the symptoms are all valid criteria for surgical care of MO. When surgery is necessary, the lesion is removed after it has fully developed. The laboratory (i.e., SAP level), clinical, plus radiographic elements should all be considered when making this choice (11).

Symptomatic MO lesions are typically the only ones that require surgical excision. It is advised to do an excision with precise resection margins because recurrence has been recorded. The diagnosis of MO is difficult when symptoms are not linked to trauma. The MRI results might point to a malignant fibrous histiocytoma-like mesenchymal tumour (12).

Non-surgical treatment

Nonsurgical intervention aims to reduce symptoms while maintaining function. Because MO is typically a self-limiting and self-resolving phase, nonsurgical therapy is frequently effective. Even though evidence is lacking, the finding that individuals with bleeding problems are more likely to have MO supports the idea that MO is linked to hematoma development, whether or not there is concurrent periosteal trauma. Therefore, it makes sense to treat muscle damage as soon as possible in order to prevent hematoma growth and preserve function.

It has been advise a brief period of relative immobilisation for 3 to 7 days together with rest, ice, compression, and

elevation for the first therapy of muscle damage. Crutches may help to reduce hematoma development by allowing the injured region to rest. Cryotherapy, which involves applying cold for 15 to 20 minutes every 30 to 60 minutes, can reduce intramuscular blood circulation by 50%. In the very earlier phases, aggressive physical treatment should be avoided to prevent symptom worsening (6).

Within a "pain-free arc of motion", supported range-of-motion activities can start as soon as 48 to 72 hours after surgery. An exercise programme that progresses gradually starts with isometric training, then moves on to isotonic training, isokinetic activities, and dynamic exercises. Aspiration could help large fluctuant hematomas that are symptomatic. Active range-of-motion as well as resistive strengthening activities are crucial to preserving and enhancing joint range of motion and functionality in more advanced lesions (13).

There is little pharmacological usage in the prevention of MO following injury. It was mostly inferred from research looking at the growth of heterotopic bone following hip surgery with pelvic trauma. Nevertheless, two doses of pamidronate were linked to recovery in both the clinical and radiographic symptoms reported in a case study of traumatic MO development in an athlete (14).

CONCLUSION

Although the cause of myositis ossificans is unknown, the clinical appearance is often marked by an ossifying soft-tissue tumour. Advanced cross-sectional imaging by itself can be vague and may resemble more nefarious causes. In order to provide an appropriate diagnosis, the study of a suspected soft-tissue tumour frequently requires the use of various imaging modalities. A biopsy may be necessary in cases where imaging is unable to provide a histologic diagnosis. On the other hand, histopathology differs according on evolutionary stage. Since a precise diagnosis is essential to a good outcome, myositis ossificans therapy is complicated and frequently undertaken in a multidisciplinary manner.

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