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Review Paper
TMJ Disorders

Acquired heterotopic ossification of the temporomandibular joint

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Abstract. Although the risk factors and diagnosis of heterotopic ossification (HO) are discussed in the orthopedics literature, the etiology of HO, as well as its prevention and management, remain theoretical. Furthermore, there is a lack of information in the literature regarding HO in temporomandibular joint replacement (TMJR). This article provides a qualitative review of information relative to the etiology, diagnosis, and management of HO to inform and encourage further investigation in TMJR. The orthopedic HO literature considered for this qualitative review was drawn from a comprehensive examination of the subject published previously by one of the authors. Using the key words ''heterotopic ossification'' or ''heterotopic bone'', citations in the PubMed database from both the dental and oral and maxillofacial surgery literature were reviewed. Based on this, it appears that the etiology, diagnosis, imaging, laboratory testing, risk factors, prophylaxis, and non-surgical and surgical options available for the management of TMJR-related HO are similar to those for orthopedic HO, but further elucidation is required for TMJR. There is a lack of published information in the literature on TMJR. Therefore, using the literature from this review as a foundation, studies should be developed and reported so that alloplastic TMJ surgeons have evidence-based protocols that will lead to the early detection and potential prevention of HO.

Key words: heterotopic ossification; temporomandibular joint; joint replacement.

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Heterotopic ossification (HO) (also known as heterotopic bone, or ankylosis) involves the formation of ectopic lamellar bone in soft tissues such as muscle, tendon, ligament, and joint capsule[1–3]. This can lead to immobility of the joints and/or their alloplastic replacements. In orthopedics, HO can occur as a result of soft tissue trauma, amputations, brain and spinal cord injuries, tumors, vasculopathies, and joint replacement[4].

There are two types of HO. The more common is the acquired form, which is typically the result of localized trauma (e.g. fracture, or as a complication of alloplastic joint replacement), or because of neurogenic insult (spinal cord or central nervous system injury). Traumatic HO – myositis ossificans traumatica – can occur after musculoskeletal trauma, surgical intervention, or soft tissue injury and involves ectopic bone formation in muscle that is inflamed. Myositis ossificans traumatica has been reported in the maxillofacial skeleton, often associated with trauma to the masticatory muscles after the injection of local anesthetics[5–11].

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The second, rarer form of HO is a hereditary, autosomal dominant form called fibrodysplasia ossificans progressiva[12]. Fibrodysplasia ossificans progressiva involving the maxillofacial region resulting in temporomandibular joint (TMJ) ankylosis has been reported[13–21].

The reported incidence of acquired HO after total knee and hip replacement is as high as 23–30% after primary surgery, and 56% after revision surgery. Risk factors for the development of HO have been reported to include the male sex, cemented implants, bilateral hip replacements, pre-implant ankylosis, ankylosing spondylitis, infection, heterotopic osteoarthritis, and patients not compliant with post-implantation physical therapy[22–24]. The prevalence of neurogenic HO is reported to be 10–53% after central neurological injury[25], 0.2–4% after burns[26], 20% after spinal cord injury[27], and 40% after elbow fracture[28].

HO of the TMJ may be seen in children with juvenile idiopathic arthritis (JIA) and is associated with particularly severe TMJ arthritis, joint destruction, and pannus formation. Pathology findings from these joints suggest that the HO may result from multiple pathological processes[29].

After infection (2.74%), acquired HO (1.24%) is the second most common post-implantation complication associated with alloplastic TMJ replacement (TMJR)[30]. Understanding the etiology of HO and the diagnosis of HO are essential to its management.

Although the risk factors and diagnosis of HO are discussed in the orthopedics literature, the etiology of HO, as well as its prevention and management, remain theoretical. Furthermore, there is a lack of information in the literature regarding HO in TMJR. This article provides a qualitative review of information relative to the etiology, diagnosis, and management of HO to inform and encourage further investigation in TMJR.

Materials and methods

The orthopedic HO literature considered for this qualitative review was drawn from a comprehensive examination of the subject published previously by one of the authors[1]. Using the key words ''heterotopic ossification'' or ''heterotopic bone''; citations in the PubMed database from both the dental and oral and maxillofacial surgery literature were reviewed.

Results

Based on a qualitative review of the literature selected for this article, as discussed in detail below, it appears that the etiology, diagnosis, imaging, laboratory testing, risk factors, prophylaxis, and non-surgical and surgical options available for the management of TMJR-related HO are similar to those for orthopedic HO, but further elucidation is required for TMJR.

Discussion

The etiological mechanisms at the molecular and cellular level leading to HO are not well understood. However, recent studies suggest that the innate immune system[31,32], central and peripheral nervous systems[27], and inflammation trigger the development of HO[33].

The inflammatory response to injury and surgical wounding plays a critical role in the development of HO and requires three components: (1) osteoinductive factors, (2) skeletal progenitor cells, and (3) a permissive tissue environment[34]. The induction of cells of mesenchymal origin, present in a permissive tissue environment created in the peri-articular tissues, leads to their transformation into osteogenic cells. This has been postulated to be the pathogenesis of HO. This leads to overactivation of the bone morphogenetic protein (BMP) cascade through activation of the activin type 1 receptor (ACVR1), resulting in abnormal bone formation (HO)[35].

Tissues prone to HO demonstrate an abnormally heightened or increased inflammatory response to wounding[36]. HO occurs because of the pathological recruitment of local and distant circulating cellular precursors. Mesenchymal stem cells demonstrate an increased osteogenic potential through increased BMP-4 expression, leading to increased vascular proliferation (Tie2-expressing cells) and osteogenesis. Fibroblasts also differentiate into osteoblasts and chondrocytes, contributing to HO formation[37–41].

In addition, local factors play a role in the development of HO. BMPs are central to tissue homeostasis and osteogenesis as part of the transforming growth factor beta (TGF-β) superfamily. The BMP-2/4 subfamily is relevant for its osteoinductive properties, and activation of the BMP-2 receptor is one of the major pathways leading to HO formation. Studies have demonstrated upregulation of this pathway after injury[33,42,43]. Oxygen tension, pH, micronutrients, and mechanical stimuli also impact HO formation[44].

The HO process recapitulates the cellular and molecular events of endochondral bone formation in embryonic skeletal development and fracture healing. However, these events are temporally and spatially unsynchronized, resulting in disorganized and non-homogeneous HO bone[4].

Classically, the clinical signs and symptoms of HO, namely pain with joint movement and restricted joint mobility and function, develop 3–12 weeks after trauma or joint replacement surgery. Since the early signs and symptoms of HO are relatively non-specific, diagnosis can be difficult. Consequently, reduced joint range of motion may lead to complete ankylosis[11].

The diagnosis of HO is primarily based on imaging. Conventional imaging techniques (plain films, computed tomography (CT), and magnetic resonance imaging (MRI)) and three-phase bone scanning will demonstrate bone formation and confirm the diagnosis. Since bony radiographic findings are typically 1 to 4 weeks behind what is occurring biologically, the most sensitive imaging for the early detection of HO is three-phase scintigraphy using a technetium-99m methylene radiotracer[45].

HO maturity can be assessed using serial three-phase bone scans, as there is a decrease and normalization of blood flow and blood-pool activity as HO reaches maturity[46,47]. This can be important clinically, as there is evidence that the surgical resection of mature HO bone results in fewer intraoperative complications and better long-term outcomes, including lower recurrence rates[46–49].

In the orthopedic literature, CT and MRI do not have a confirmed role in the diagnosis of HO. However, in the early stages of HO, the lesions can appear as enhanced bony masses with disorganized or absent mineralization. MRI findings in early HO include a heterogeneous T2 signal and a mass-like enlargement of the surrounding affected tissues. Additionally, there may be a rim of low signal intensity. Also, HO demonstrates enhancement with gadolinium contrast uptake[45]. To date, no specific studies exist on CT or MRI imaging in TMJR-related HO cases.

Most orthopedic patients with HO will have elevated alkaline phosphatase (ALP) levels, which makes this a highly sensitive test in that patient population. ALP levels begin to rise within 2 weeks of the etiological event and reach abnormal levels after 3 weeks. ALP levels will peak at 10 weeks after the etiological event and return to normal after 18 weeks[49,50].

Since the release of cytokines as a result of acute inflammation is involved in early

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