AMERICAN JOURNAL OF MEDICAL CASE REPORTS

ISSN 2374-216X

Idiopathic cervical heterotopic ossification causing neck pain and immobility: A case report and review of the literature

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Abstract

Introduction: Heterotopic Ossification (HO) is an ectopic bone formation in the soft tissue outside the skeletal system. This rare disorder is mostly related to musculoskeletal trauma, burns, or central nervous system injury. HO may cause pain and immobility of the joints. In some cases, HO is difficult to diagnose in early stages due to non-specific symptoms. In later stages, differential diagnoses of HO include tumors such as osteomas, osteochondromas or osteoblastomas. An occurrence of idiopathic HO has not been described before, so far.

Case Presentation: This is the first case of an idiopathic symptomatic HO in the cervical muscles causing a painful progressive spinal immobility of the neck without preceding trauma. CT-Scan of the cervical spine revealed an enormous calcificated, well defined lesion in the nuchal muscles adjacent to the spinal processes. The patient was admitted to surgery due to progressive immobility of the cervical spine. Histopathologic examinations confirmed the diagnosis of HO.

Conclusions: HO is a primary benign, progressive disorder, leading to disability by restricted mobility and pain. At early stages medical treatment or radiotherapy may control HO. If a conservative approach fails, surgery is indicated to prevent a disabling loss of function and to restore normal mobility.

Keywords

idiopathic; heterotopic ossification; cervical spine; spinal immobility

Abbreviations

HO: Heterotopic ossification; BMP: Bone morphogenetic proteins; TGF: Transforming growth factor; CT: Computed Tomography

Introduction

Heterotopic Ossification (HO) is an ectopic bone formation in the soft tissue outside the skeletal system. HO develops and affects all layers of the skin adjacent to joints and may also occur in the wall of blood vessels and ligaments [1], or at intra-abdominal sites such as the mesentery [2].

HO is likely caused by direct trauma to the muscles or the skeletal system, joint dislocations or arthroplasties of the various joints (approximately 53% in total hip arthroplasty [3]). Also, it has been observed in neurogenic disorders as spinal cord injury (incidence ranging from 20%-30% [4]), traumatic brain injuries (incidence about 10%–20% [5]), and even non-trauma causes like strokes or

brain tumors. Furthermore, HO has been associated with abdominal visceral operations (incidence of around 25% for midline abdominal scars [6]). Rarely, HO is found in burns (incidence of 1%-3%, [7]).

To our best knowledge is this the first case of an idiopathic symptomatic HO in the cervical muscles causing a progressive painful spinal immobility of the neck with a few years' history. Surgical treatment is indicated in this case due to the progressive spinal immobility and the resulting pain, and to reveal a correct diagnosis. In addition, malignant transformation of HO into e.g. osteosarcoma has been reported arguing for removal of the lesion [8, 9].

Case Presentation

Case: A 67-year old female patient presented to our department with a history of progressive neck pain and spinal immobility. She claimed that she had noticed a solid knot, which had grown approximately over the past four years between the processus spinosus of the 2nd cervical vertebra and the 1st thoracic vertebra (Figure 1). The patient was not able to rotate the head to the left side due to a painful and physical restriction of motion because of the size of the HO. The examination of the neck revealed a firm and tender mass fixed to the muscle. Further clinical and neurological examination was without pathological findings.

Radiological findings: On plain X-ray of the cervical spine a large calcificated, well defined lesion in the nuchal muscles adjacent to the spinal processes was diagnosed. The CT-scan of the cervical spine showed a well demarcated lesion consisting of multiple smaller and larger ossicles between the processus spinosus of the 2nd cervical vertebra and the 1st thoracic vertebra (9.5cm x 6.1cm x 4.4 cm). No affection of the bony integrity of the cervical spine was shown (Figure 1). A whole body CT-scan or a scintigraphy was not performed as HO is not a systemic multilocular disease and literature did not show any advantage of a screening.

Surgical treatment: The patient was admitted to surgery due to the progressive neck pain and the restricted range of motion of the cervical spine. Informed consent was obtained. The operation was carried out with the patient in prone position. The enormous lesion could be easily removed via a median incision by blunt dissection of the autochthone muscles of the neck (Figure 2).

Histopathology: Histopathologic examination revealed trabeculae of mature lamellar bone with foci of haematopoiesis as well as foci of metaplastic chondrocytes within connective and adipose tissue. There was no connection to the skeletal system. Signs of malignancy were not found. Thus, the diagnosis of heterotopic ossification was made (Figure 3).

Postoperative course and Follow up: The postoperative stay at the hospital was uneventful. The patient recovered well and the deficit in rotation of the cervical spine could not be observed any longer. The postoperative X-Ray two weeks after surgery showed a regular result (Figure 4). At latest follow up two years after surgery, the patient remained well-being without any neck pain and with normal cervical mobility and without any clinical sign of a recurrence of the HO. The Oswestry Disability Index two years after surgery showed a score of 6% [10]. The modified Japanese Orthopaedic Association scale also showed normal values of 17/18 [11]. It has to be kept in mind that a two-years follow up in our patient does not exclude a later recurrence of HO as the initial lesion progressed slowly over several years.

Discussion

Heterotopic Ossification is an ectopic bone formation in the soft tissue outside the skeletal system. It is hypothesized that injured cells release cytokines that induce differentiation of mesenchymal cells into chondro- and osteoblasts [12]. Such signaling proteins like the bone morphogenetic proteins (BMP, especially BMP types 1-12), or growth differentiation factors (GDFs, types 5–7), have been identified as crucial actors in the pathogenesis of HO [13].

Chondrogenic and osteogenic properties are exhibited in vivo by BMPs 2—7 and GDFs 5–7. The majority of those molecules belong to the transforming growth factor (TGF) ß family [14]. Micha et al. showed that the pharmacological inhibition of TGF β signaling resulted in the attenuation of osteogenic transdifferentiation and suggested that an inhibition of the TGF ß might decrease the ongoing ossification in patients with fibrodysplasia ossificans progressiva [15]. Those morphogenic proteins are also playing a role in normal embryonic development. The axis of the embryo, the differentiation of individual skeletal structures and the supporting tissue are specified by BMPs [16].

Another pathway in the development of HO might be the expression of prostaglandins that regulate the bone formation by affecting pluripotent mesenchymal stem cells such as osteoblasts and osteoclasts. Vanden Bossche and Vanderstraeten proved that the specific prostaglandin E 2 is a dose-dependent inducer of periostal lamellar bone formation [17].

The management of HO is generally agreed to be a conservative treatment, including physiotherapy, pharmacotherapy and radiotherapy. Surgery should be performed in case of neurologic deficits, progressive immobility or pain, only. Active physiotherapy within the pain-free range has a positive impact on the patients with HO [18].

The use of systemic medications has been documented. Yet, there is no consensus about the best treatment regimens and when to start the treatment of HO. Some authors recommend to start with the systematic therapy directly after detecting HO. Elevated alkaline phosphatase levels might be noted or imaging studies may be used to establish the presence of HO [19].

Diphosphonates and nonsteroidal anti-inflammatory drugs (such as indomethacin and ibuprofen) have been successfully used for the treatment and the prophylaxis of HO after adequate trauma, for example after total hip arthroplasty or spinal cord injury. Diphosphonates may impede the osteoid calcification, but the effect on osteoid formation and the overall efficacy is limited. Even more, the treatment with nonsteroidal anti-inflammatory drugs probably leads to a systemic inhibition of prostaglandine synthesis promoting osteoprogenitor development. A widely used and effective therapy regimen can be orally administered indomethacin (e.g. 25–50 mg t.i.d. for 6 weeks) [20].

Maender et al. showed that the perioperative radiation therapy has a positive impact as a prophylaxis of HO [21]. For patients, who already have developed HO after a previous operation or who have contraindications receiving indomethacin, a single irradiation of 7 Gray should be applied as prophylaxis [22]. The preoperative and postoperative radiation therapy appears equally effective to prevent HO. Most studies recommend administering 6 to 7 Gray within the first 2 postoperative days [20]. In our patient postoperative radiotherapy was not administered after interdisciplinary discussion as there are no evidence based data that radiation serves as a postoperative adjunctive therapy after

surgical removal of HO in contrast to the above mentioned prophylactic treatment.

Surgical treatment should be considered, if there are any limitations in the motion of the joints which interfere the activities of the daily life [23], or if there are acute signs of nerve entrapment with resulting neurological deficits to avoid any irreversible nerve damage [24]. In addition, malignant transformation of HO into e.g. osteosarcoma has been reported in several cases arguing for removal of the lesion [8, 9]. Nevertheless, one has to keep in mind that a further trauma is caused by the operation and this might also increase the risk of recurrent HO.

If no neurological deficits or immobility are present, surgical treatment is indicated after HO has fully matured to decrease the risk of a postoperative recurrence [25].Time of maturation might be estimated using the alkaline phosphataselevels as a measurement of the osteoblastic activity. Unfortunately, in our patient the preoperative alkaline phosphatase level was not measured and, thus, we did not employ this as a follow up parameter. Nevertheless, it might be a quick and non-invasive method to monitor patients in the follow up. A normalization may indicate the completion of ossification [19].

Conclusion

HO is a benign disorder and should be operated if neurological deficits or immobility of the spine or the joints occur to prevent disability. Furthermore, the diagnosis has to be revealed knowing that HO might mutate into malignancy and to further differential diagnosis like osteosarcoma.

Figures

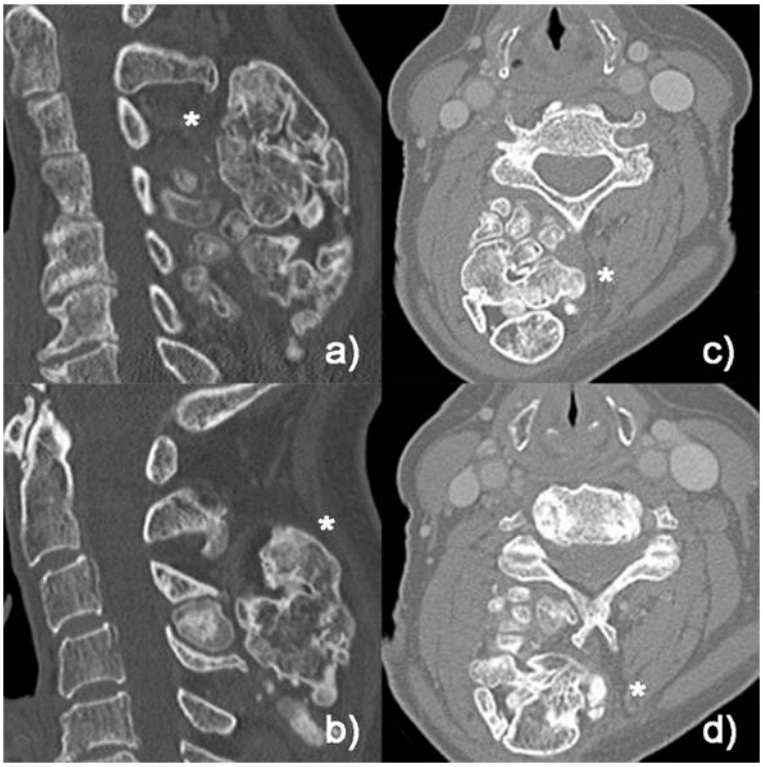

Figure 1: a) and b) preoperative CT-Scan of the cervical spine showing HO ranging from the 2nd cervical vertebra to the 1st thoracic vertebra; c) and d) axial view.

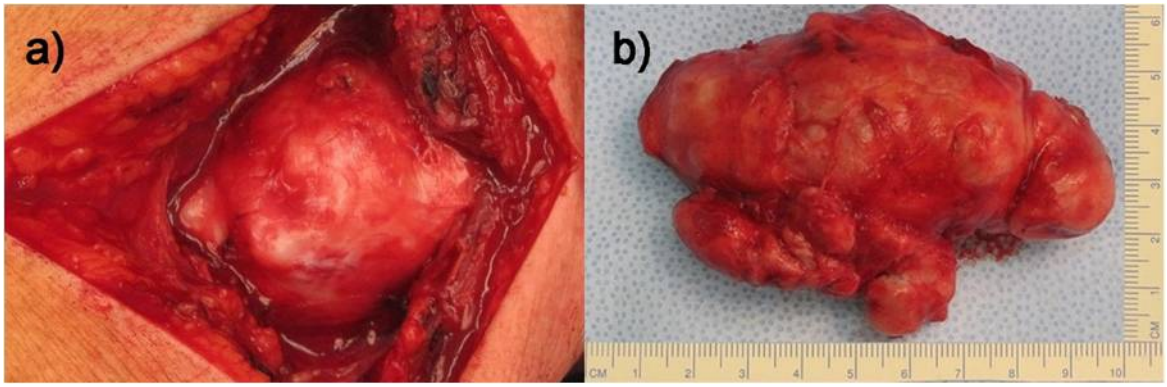

Figure 2: a) intraoperative view showing the HO in situ; b) HO after resection (9.5 cm x 6.1 cm x 4.4 cm).

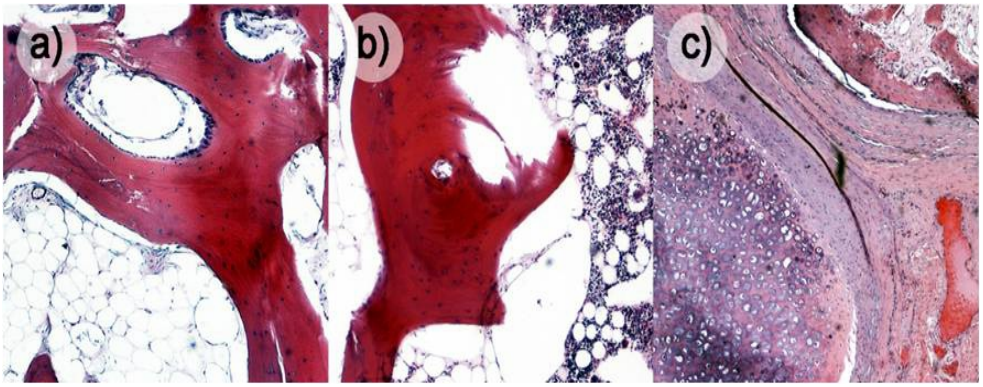

Figure 3: Trabeculae of mature lamellar bone within adipose tissue (a) with blood-building bone marrow (b) and foci of metaplastic chondrocytes (c). Haematoxylin-eosin staining, Magnification: 40fold.

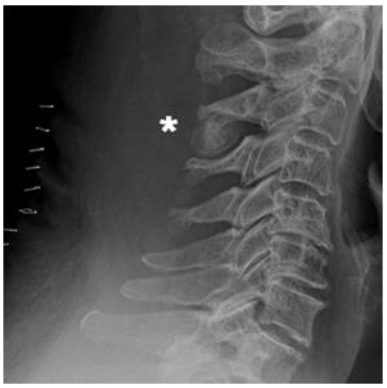

Figure 4: postoperative X-Ray-control two weeks after surgery.

Author's Contributions

Oliver Gembruch was a major contributor in writing the manuscript and was part of the neurosurgical team. Yahya Ahmadipour was part of the neurosurgical team and was a contributor in writing the manuscript. Sarah Teuber-Hanselmann performed the pathological examination and was also a contributor in writing the manuscript. Ulrich Sure was also a contributor in writing the manuscript. Oliver Müller performed the neurosurgical procedure and was a contributor in writing the manuscript. All authors read and approved the final manuscript.

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