CASE REPORT

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Heterotopic mesenteric ossification of ileostomy – "intraabdominal *myositis ossificans*"

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Abstract

Heterotopic mesenteric ossification is a rare clinical entity with less than 40 reported cases. Moreover, heterotopic mesenteric ossification around a stoma is described in fewer cases. *Case presentation*: An 81-year-old male patient, who underwent a sigmoidectomy two years ago for a sigmoid colon cancer, was admitted in our Department in order to be investigated for a local recurrence of his disease. Because of unresectable pelvic lesions, the patient was taken in the operating room for a palliative double barrel ileostomy. The patient presented two weeks after the ileostomy clinical signs suggesting its obstruction. A revision of the ileostomy is performed. Macroscopically, the end part of the ileostomy was inflamed and resected. Histological findings revealed heterotopic ossification of the mesentery. *Conclusions*: The surgeon should be alert to the possibility of heterotopic ossification, especially within a previously operated wound and be prepared for the difficulties it may cause during reopening of an incision, during the operation itself, at closure of the wound and, if not removed, also in the postoperative setting.

Keywords: heterotypic mesenteric ossification, fibroblastic stroma, obstruction.

Introduction

Heterotopic ossification is a metaplastic phenomenon in which new bone is formed in tissues that do not normally ossify [1]. Ossification of soft tissues following orthopedic surgery, trauma, and/or prolonged immobilization has been well-described [2]. However, intra-abdominal occurrence remains relatively rare [3]. The pathophysiology of this condition remains unknown. Heterotopic mesenteric ossification (HMO) is a rare clinical entity with less than 40 reported cases in the literature. Of these reported cases, most are associated with prior abdominal trauma or surgery. A wide range of presentations have been reported. Herein, an extremely rare case of HMO developed around a stoma is presented. The diagnosis requires a high index of suspicion and is often confounded by radiological contrast agents [4, 5]. Due to the extremely low incidence, the surgical community is yet to define the optimal treatment strategy for HMO.

Aim

We aim to present a rare case of heterotopic ossification of the mesentery in an 81-year-old patient who underwent sigmoidectomy.

Case presentation

An 81-year-old male patient, who underwent a sigmoidectomy two years ago for a sigmoid colon adenocarcinoma, was admitted in our Department in order to be investigated for a local recurrence of the disease. Because of unresectable pelvic lesions, the patient was taken in the operating room for a palliative double barrel ileostomy. Concomitantly, a conservative treatment of first line radiotherapy combined with chemotherapy was decided. On day 14, the patient presented abdominal distension, bloatness, inability to pass stool and gas through the stoma. From the clinical examination, there was a suspicion of obstruction of the ileostomy. The patient was taken again in the operating room for a revision of the ileostomy. The end part of the double barrel ileostomy, macroscopically inflamed, was resected and a new end ileostomy was performed.

Harvested material was fixed in 10% formalin solution and sent to the pathology laboratory where paraffin was included following the standard histopathology protocol. We performed microtome sections with a thickness of 4 μm, which were stained with Hematoxylin–Eosin (HE) and Goldner–Szekely (GS) trichromic. In addition, we took histological sections, which were collected onto slides with poly-L-lysine for immunohistochemical studies. In our study, believing it might be a local inflammatory process, we used the following antibodies: CD68 (M0814 clone KP1, 1:200, Dako) for highlighting macrophages, CD20 (M0755 clone L26, 1:100, Dako) for highlighting B-lymphocytes and CD3 (A0452, F7.2.38 clone, 1:100, Dako) for highlighting the T-lymphocytes.

Microscopic analysis of histological preparations highlighted the presence of various lesions in the small intestine wall thickness. Thus, we noted a significant thickening of the intestinal wall, especially of the subserosal area as a whole and the mesentery (Figure 1). The

intestinal mucosa showed atrophic or ulcerated areas, with an abundant inflammatory infiltrate, and areas of normal appearance (Figure 2). The muscular bowel tunica was slightly hypertrophic, without other morphological changes. At the subserous and mesentery levels, we identified proliferating fibroblasts, without being able to identify cells or nuclear alterations. Fibroblasts were enlarged, arranged in bundles with abundant slightly acidophilic cytoplasm, large nuclei and nucleoli (Figure 3). We observed rare typical mitosis within these fibroblasts. In some areas, subserous stroma and mesenteric fibroblasts suffered a bone-like metaplasia. In these areas, fibroblasts had withdrew their extensions, becoming oval or round, with intense basophilic cytoplasm possibly by increasing intracellular organelles involved in biochemical synthesis of extracellular matrix components and the round nucleus and nucleolus. Extracellular matrix in these areas has become intensely acidophilic, leading to the emergence of young bone islands, with similar images of embryonic osteogenesis of desmal type (intramembranous ossification) (Figures 4 and 5). In some areas, the process of ossification was intense, generating multiple anastomosed trabeculae and areola-like bone cavities with an architecture similar to a young spongy bone (Figure 6). Some bone trabeculae were made of calcium salts, which led to intense basophilic areas (Figure 7). Deposition of calcium salts in the bone matrix was heterogeneous, from a trabecula to another and even from one cell to another. The thickness of these cells appeared round, oval, similar to young osteoblasts. At the periphery of the bone trabeculae, we have relatively frequently identified large cells with intensely basophilic cytoplasm, arranged in a single row, similar to cells of the periosteum or endostum (Figures 8 and 9).

In few areas, these fibroblasts were arranged randomly in a myxoid stroma (Figure 10). In other areas of the mesentery, we identified microbleeds and vascular congestion (Figures 11 and 12).

Immunohistochemistry examinations revealed the presence of a relatively high number of macrophages, particularly in the areas of necrosis or stroma in myxoid stroma areas. Amongst these, we identified rare multinucleated cells (Figure 13). We found few T- and B-lymphocytes.

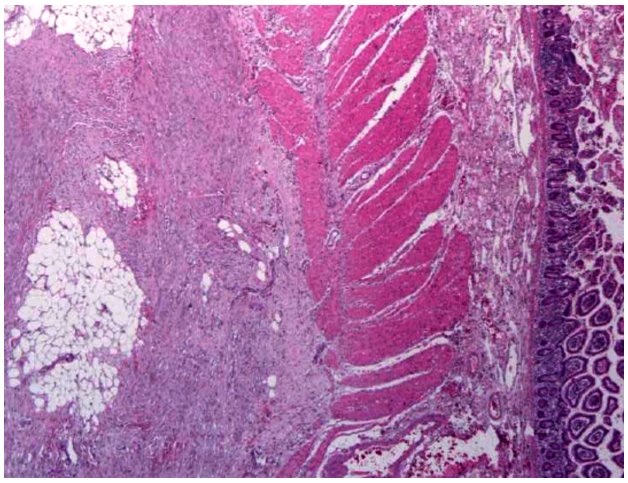

Figure 1 – ***Transverse section through the ileon in which we can see the significant thickening of the intestinal wall, especially of the subserosa and mesenterum, with dense connective tissue and myxedematous areas. HE staining, ×40.***

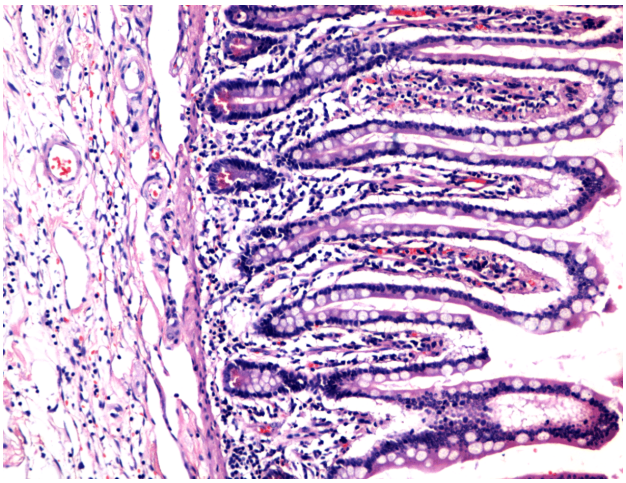

Figure 2 – ***Normal ileal mucosa. HE staining, ×100.***

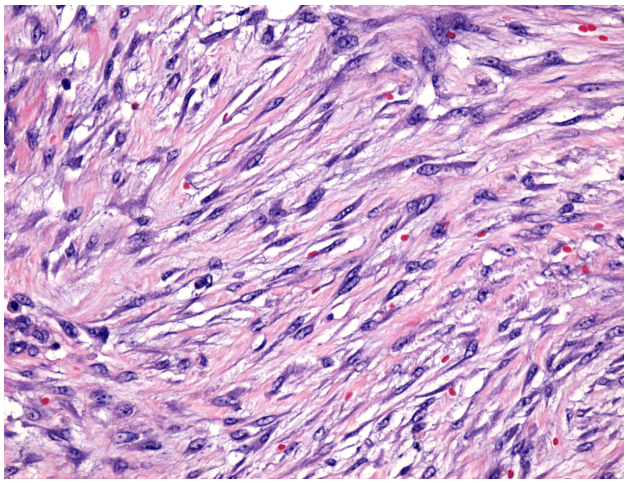

Figure 3 – ***Multiple fibroblasts within the subserosa, arranged as fascias. HE staining, ×200.***

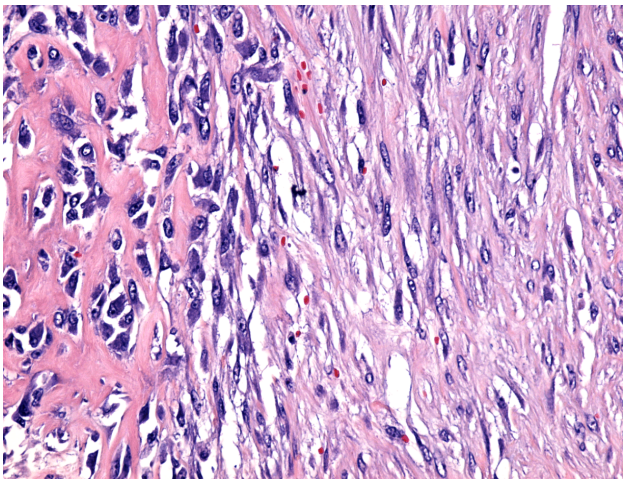

Figure 4 – ***Area of bone metaplasia of stromal fibroblasts. HE staining, ×200.***

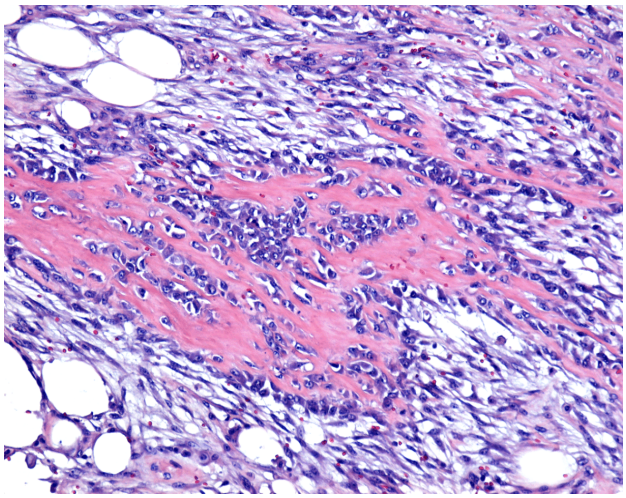

Figure 5 – ***Bone bays of young tissue surrounded by fibroblasts and areas with myxoid stroma. HE staining, ×100.***

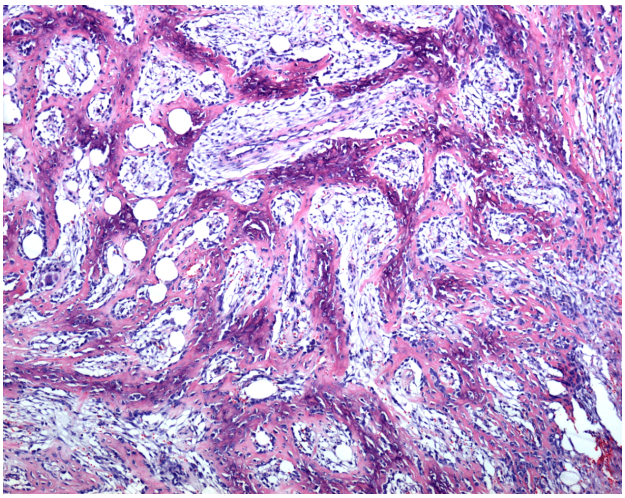

Figure 6 – ***Overview image of a mesenteric area with intense ossification, with anastomosed bone bays, similarly to young bone tissue. HE staining, ×40.***

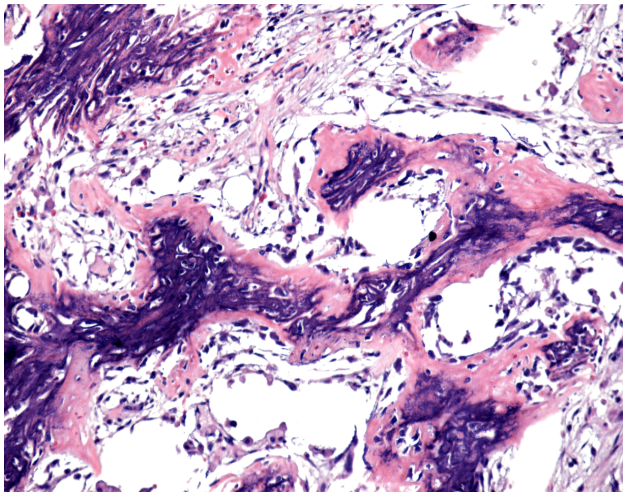

Figure 7 – ***Bone bays with inhomogeneous mineralization. HE staining, ×100.***

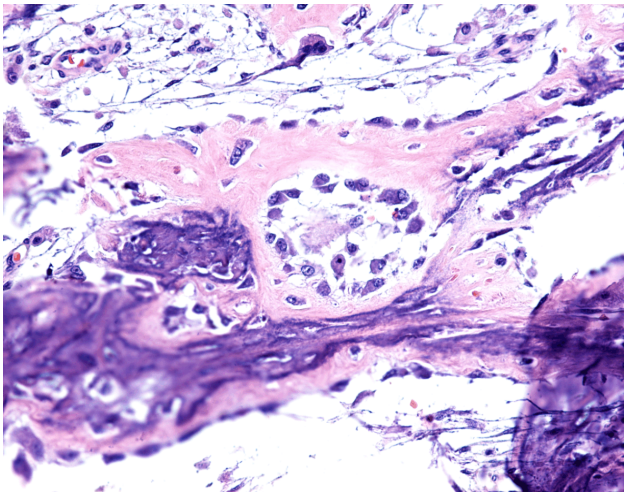

Figure 8 – ***Bone bays delimited by peri- and endosteum. HE staining, ×100.***

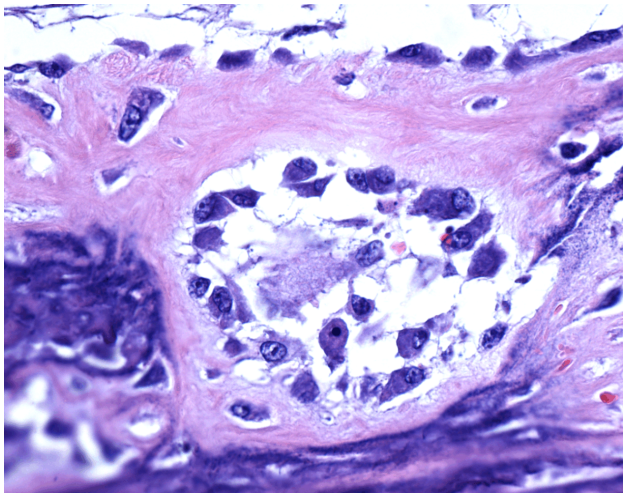

Figure 9 – ***Detail from the previous figure. HE staining, ×400.***

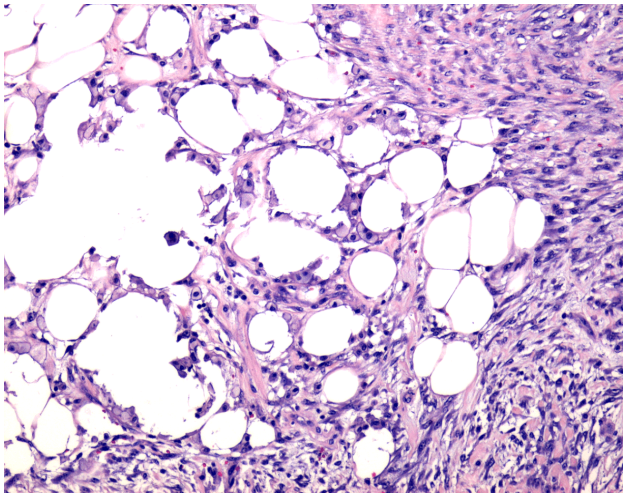

Figure 10 – ***Area of myxoid stroma, within the mesenteric thickness. HE staining, ×100.***

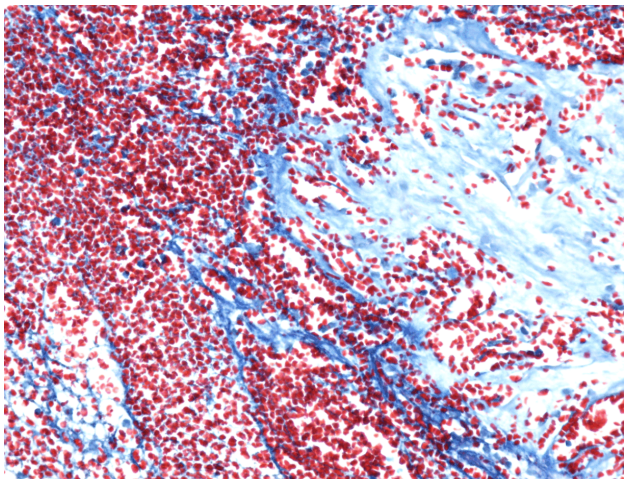

Figure 11 – ***Mesenteric stroma with microhemorrhages. Trichromic GS staining, ×200.***

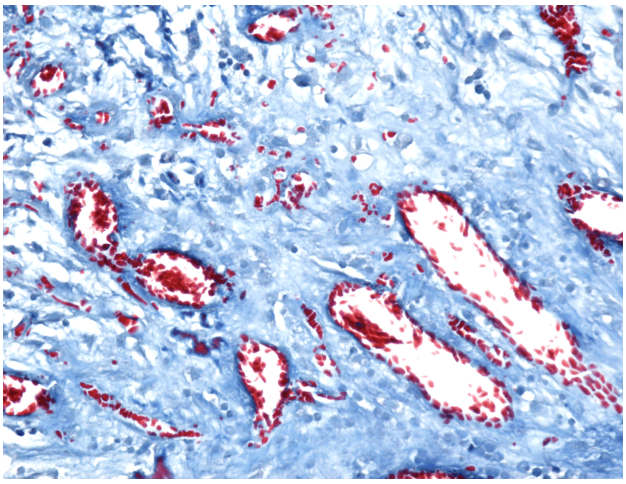

Figure 12 – ***Area of vascular congestion. Trichromic GS staining, ×200.***

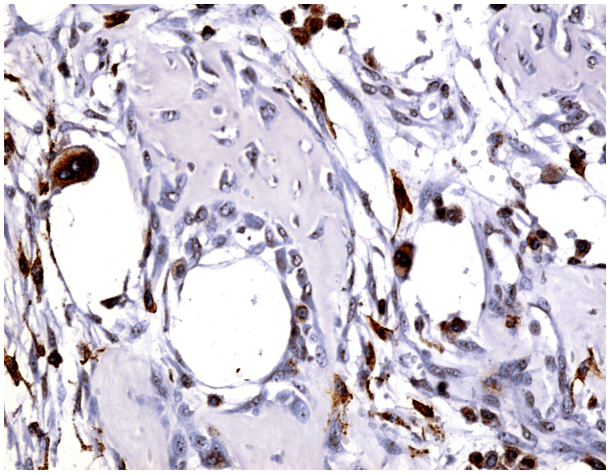

Figure 13 – ***Mesenteric area with a relatively high number of macrophages. Anti-CD68 immunostaining, ×200.***

Discussion

Ossification of soft tissues following orthopedic surgery, trauma, and/or prolonged immobilization has been well described; however, intra-abdominal occurrence remains relatively rare [2, 3]. The neoplastic formation of bone in the abdomen, specifically the mesentery, was first reported by Lemeshev *et al.* in 1966 [6] and then in 1999 was termed heterotopic mesenteric ossification by Wilson *et al.* [7]. In 1975, Marteinsson described ossification of laparotomy scars and proposed that cells disrupted from the xyphoid were responsible for seeding the abdomen and leading to bone formation [8]. This explanation has been challenged by reports of ossification occurring without contact with the bony skeleton. In an effort to further define its pathogenesis, another hypothesis is that it is a result of immature multipotent mesenchymal cells differentiating into osteoblasts or chondroblasts as a reaction to local injury, ultimately resulting in bone formation [2]. This process might require additional contributing factors including venous stasis, edema, local trauma, inflammation, and secretion of local osteoinductive factors [9]. This hypothesis provides a better explanation for the pathogenesis of ossification in this reported case. However, despite ongoing investigation, a concise molecular explanation for heterotopic mesenteric ossification has been yet to be fully described.

Focusing solely on abdominal heterotopic ossification, there is a male preponderance with an average age of 55 [10–12]. There is a wide clinical presentation while patients usually present with intestinal obstruction (reports of nausea, vomiting, abdominal pain, distention, and obstipation) due to nodules of fibrous and bone tissue, or fistulas or leakage. The lesions usually developed after one or more intra-abdominal surgical procedures, although few patients have no previous surgery [4]. These lesions tend to grow rapidly, developing days or weeks after the injury or the procedure [4].

Diagnosing HMO preoperatively is difficult due to the rarity of the condition and the presence of radiological confounders. Radiologically, distinguishing among mesenteric ossification, osseous neoplasia, or oral contrast leakage is difficult, and early stages of the disease show only a slight increase in soft tissue density [3]. An extremely high index of suspicion is required for accurate preoperative diagnosis.

HMO is uncommon and may be missed or misdiagnosed, which can lead to complications. Once the right diagnosis is made, it has an excellent prognosis, although it represents a therapeutic challenge because of its tendency to recur. Some cases lead to intestinal obstruction requiring surgical excision; however, because the condition is clearly related to surgery, especially repetitive surgery, it would seem intuitive to try to avoid further surgical procedures. HMO is a benign, non-invasive condition, and aggressive resections may be associated with significant postoperative complications including high mortality. Surgical excision may be needed because of complications such as intestinal obstruction or recurrent fistulas. HMO can be a diffuse process encasing much of the abdominal viscera.

Radical excision is not without significant risks as demonstrated by the reported perioperative mortality. The literature reports the successful management of an extensive case of HMO with partial excision. If surgery is required, local radiotherapy or treatment with bisphosphonates or anti-inflammatory agents may be used to help prevent recurrence. Anti-inflammatory drugs have been shown to reduce the incidence of heterotopic bone formation [7].

We report this case to encourage accurate reporting of HMO and its morbidity and complications for the benefit of appropriate surgical planning and epidemiological tracking of outcomes. Given the scarcity of reports, description of the incidence and of the management and morbidity is helpful for improving understanding, operative planning and tracking of outcomes. It could be helpful to include in the preoperative setting (evaluation and imaging) of patients with multiple operations, also the possibility of heterotopic ossification in a previously operated wound and peri-operatively, to ensure the absence of heterotopic ossification in order to prevent a similar occurrence.

Conclusions

This case is presented in order to acquaint surgeons and pathologists with the possible development of heterotopic ossification also around a stoma. Pathologists should keep in mind this entity to avoid a misdiagnosis of benign or malignant soft tissue tumor. The surgeon should be alert to the possibility of heterotopic ossification, especially within a previously operated wound and be prepared for the difficulties it may cause during reopening of an incision, during the operation itself, at closure of the wound and, if not removed, also in the postoperative setting.

Conflict of interests

The authors declare that they have no conflict of interests.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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