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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Osseous metaplasia in an inflammatory polyp of the anal canal – a case report and a review of literature

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SUMMARY
Introduction Osseous metaplasia is a heterotopic formation of bone and its appearance in benign gastrointestinal polyps is exceedingly rare. The mechanism responsible for this type of metaplasia is not fully understood, however it seems to be an innocent rare phenomenon.
Case outline We present a case of a 31-year-old male with mesenchimal osseal metaplasia in a large inflamatory polyp measuring 57 × 23 × 20 mm in diameter, located in the anal canal region.
Conclusion According to our knowledge, this is the largest gastrointestinal polyp with osseous metaplasia described so far. Although a rare phenomenon, there are certain characteristics of this disease, so we conducted a literature review and summarized these characteristics.
Keywords: osseous metaplasia; gastrointestinal polyps; inflamatory polyps

INTRODUCTION

Heterotopic formation of bone (mesenchymal osseous metaplasia) is rarely found in the gastrointestinal tract. Most cases are associated with colon adenocarcinoma, but also can be found in the benign lesions of the bowel wall, such as necrosis, chronic inflammation foci, and mucin extravasation [1]. The appearance of heterotopic bone in benign colon polyps is exceedingly rare, and only a few cases have been reported in literature. The first case of heterotopic bone formation in gastrointestinal polyp was described by Todd [2] in 1963. The mechanism responsible for this type of metaplasia is not yet fully understood [3].

Herein, we shall describe a case of mesenchymal osseous metaplasia (OM) in a large inflammatory polyp located in the anal canal region in a 31-year-old male, after which we shall make an accompanying literature review.

CASE REPORT

We report a case of a 31-year-old male who visited the hospital with a chief complaint of pain and evacuation of fresh blood from the anal canal during defecation. Clinical exam revealed a polypoid tumefaction with contact bleeding in the anal canal region. Concomitant clinical findings were grade I internal hemorrhoidal nodules without signs of bleeding or inflammation. Total colonoscopy confirmed lobulated and vulnerable polyp about 5 cm in diameter, located at 1–2 cm from the anocutaneous line. Colonoscopy biopsy revealed an inflammatory pseudopolyp. The patient underwent a transanal electrosurgical resection of the polyp. The polyp was sent to pathohistological analysis. The postoperative course was uneventful, and the patient was discharged on the first postoperative day.

The tissue fragment submitted for pathohistological analysis, was macroscopically a soft greyish white polyp measuring 57 × 23 × 20 mm in diameter. Histological analysis showed fragments of an inflammatory polyp of the large bowel mucosa, partly overlaid with superficial cylindrical epithelium and partly with fibrin deposits and groups of neutrophils. The stroma of the described specimen was edematous with florid fibrovascular granulation tissue and numerous foci of dilated and congested blood vessels, as well as with moderately intense mixed inflammatory infiltrate, made mostly of granulocytes and lymphocytes. In the central parts of the polyp, numerous foci of mineralized osteoid lined by osteoblasts without extramedullary hematopoiesis signs were found (Figure 1). The lesion was diagnosed as an inflammatory polyp of the anal canal with foci of OM.

DISCUSSION

Stromal ossification can occur in gastrointestinal cancers from the stomach to the anal canal and it seems to be result of bone morphogenetic protein production of tumor cells.

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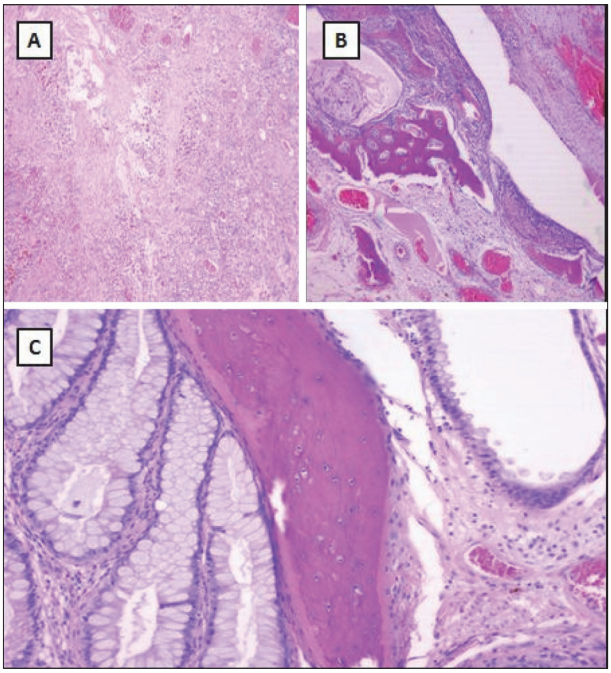

Figure 1. Microscopic pictures of H&E stained sections of the inflammatory polyp of the anal canal with focus of OM; (A) 10× magnification, (B) 10× magnification, (C) 20× magnification

Ossification in benign colon tumors has been documented only rarely, and only a few cases have been documented [1]. We reviewed and summarized the related literature on OM in gastrointestinal polyps (Table 1). We found 24 cases described in literature, of which 16 were male and five were female patients, while in three cases gender as well as age were not specified. Patient age ranged 3–85 years, with mean age of 34 years. Our patient was a 31-year-old male. Out of 24 described polyps, three were smaller than 10 mm, 11 were 10–20 mm in diameter, and six were larger than 20 mm, while in four cases size was not specified. The mean size was 17.05 mm (range: 3–50 mm). In our case, the polyp was very large with 57 mm in diameter, which is to our knowledge the largest gastrointestinal polyp with OM described so far. The most frequently involved site was the rectum where 60% of polyps (12/20) were found. In 30% (6/20) polyps were located in the colon, and in 10% (2/20) polyps were found in the junction of the sigmoid colon and the rectum. In four remaining cases, exact location was not defined. Our patient had a polyp in the anal canal, which is another curiosity of our case. Histologically, seven lesions were neoplastic (four tubular adenomas, and three tubulovillous adenomas), while 15 lesions were non-neoplastic (seven juvenile polyps, six inflammatory polyps, and two serrated adenomas). In two lesions histology finding was not specified [1, 3–8]. Our patient had non-neoplastic inflammatory polyp.

The pathogenesis of heterotopic ossification is still not fully investigated. Many theories about pathogenesis are published. At the beginning of the 20th century, Charles Brenton Huggins [9] conducted a set of experimental studies on dogs and demonstrated OM in soft tissue of abdominal wall after transplantation of bladder tissue with

Table 1. Summary of our and previously reported cases of OM in gastrointestinal polyps

Case	Author	Year	Sex	Size (mm)	Location	Age	Histology
1	Todd	1963	NI	NI	NI	NI	NI
2	Marks	1964	M	NI	NI	10	Juvenile polyp
3	Sperling	1981	M	10	Rectum	25	Inflammatory polyp
4	Castelli	1992	F	10	Rectum	22	Inflammatory polyp
5	Drut	1992	M	10	Rectosigmoid	5	Juvenile polyp
6	Drut	1992	M	5	Rectum	4	Juvenile polyp
7	Groisman	1994	M	18	Rectum	67	Tubulovillous adenoma
8	Groisman	1994	F	20	Rectum	3	Juvenile polyp
9	Cavazza	1996	NI	NI	NI	NI	Tubulovillous adenoma
10	Monzon	1997	M	12	NI	59	Tubular adenoma
11	McPherson	1999	M	20	Cecum	73	Tubulovillous adenoma
12	Rothstein	2000	NI	25	Sigmoid colon	NI	Tubular adenoma
13	Al-Daraji	2005	F	15	Sigmoid colon	85	Tubular adenoma
14	White	2008	F	NI	Transverse colon	63	Tubular adenoma
15	Oono	2009	M	12	Rectum	39	Inflammatory polyp
16	Ahmed	2009	M	10	Rectum	15	Juvenile polyp
17	Wilsher	2010	M	25	Rectosigmoid	50	Serrated adenoma
18	Bowman	2012	M	45	Descending colon	28	NI
19	Odum	2012	M	7	Ascending colon	74	Inflammatory polyp
20	Montalvo	2012	M	50	Rectum	62	Serrated adenoma
21	Bhat	2012	F	14	Rectum	5	Juvenile polyp
22	Bhattachary	2013	M	10	Rectum	14	Juvenile polyp
23	Garg	2013	M	15	Rectum	6	Inflammatory juvenile polyp
24	Zemheri	2015	M	8	Rectum	9	Inflammatory polyp
25	Our case	2016	M	57	Anal canal	31	Inflammatory polyp

NI – not informative

intact epithelium to abdominal wall fascia. These studies provided evidence that some component of the epithelial tissue may induce mesenchymal tissue ossification. Van Patter and Whittick [10] presented a series of OM cases in gastrointestinal tumors and suggested theory that the ossification resulted from the interaction between local physicochemical factors, such as mucin and calcium salts, and proliferating connective tissue. Zemheri et al. [3] noticed that OM, especially in benign lesions, is most often seen in lesions with active chronic inflammation and/or ulceration. Therefore, the pathogenesis might be a reactive change due to repeated local trauma, or be a peculiar characteristic of the intestinal mucosa itself [1]. One of the possible mechanisms of bone formation could be the ability of fibroblasts to achieve the phenotype of other types of cells of mesodermal tissue by the process of metaplasia, especially osteoblasts [3, 8, 11]. Recent studies showed important role of the bone morphogenetic proteins (BMPs) in the tissue where the formation of heterotopic bone takes place [3]. BMPs are members of the TNF-β group, and they have an important role in the new bone formation. Imai et al. [12] conducted an immunohistochemistry study of BMP expression in colon carcinoma with heterotopic ossification. They found that BMP-5 and BMP-6 were strongly stained in tumor cells but weakly stained in osteoblast-like cells on the surface of the bone matrix. In addition, BMP-2 and BMP-4 were found in tumor cells, but staining was week. Authors concluded that BMPs might have a significant role in heterotopic ossification in colon adenocarcinoma. The study of Kypson et al. [13] showed BMP-2 overexpression in rectal adenocarcinoma tumor cells with OM compared to rectal adenocarcinomas without bone production. Later on, Liu et al. [14] found BMP-1, BMP-4, and BMP-6 expression in stroma as well as epithelium in different cancers with OM. Genetic studies of Takahashi et al. [15] demonstrated that mouse somatic cells and human dermal fibroblast cultures, by transduction of four transcription factors ($Oct^{3/4}$, Sox2, Klf4, and c-myc), can be generated in induced pluripotent stem cells, which are similar to human embryonic stem cells. Additionally, these cells could differentiate into cell types of the three germ layers in vitro and in teratomas [3, 16, 17]. Other genetic studies found increased expression of bone matrix synthesis markers e.g. collagen type I, osteocalcin and osteonectin in the foci of metaplastic bone formation [8, 18].

All of the above point to the fact that the interaction between either neoplastic or non-neoplastic epithelium of the large bowel with the surrounding mesenchymal tissue is the key factor for the formation of bone tissue in the stroma, but their relationship and the precise mechanism of OM are still confusing the clinicians as well as pathologists. Most importantly, the majority of authors agree that clinically, the presence of the metaplastic bone seems to be an innocent phenomenon [1].

Confilct of interests: None declared.

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Коштана метаплазија у инфламаторном полипу аналног канала – приказ болесника и преглед литературе

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САЖЕТАК

Увод Коштана метаплазија представља хетеротопично формирање коштаног ткива и њена појава у бенигним гастроинтестиналним полипима је ретка.

Механизам настанка ове врсте метаплазије није потпуно разјашњен, али изгледа да представља само редак доброћудни феномен.

Приказ болесника Приказујемо мушкарца, старог 31 годину, са мезенхималном коштаном метаплазијом у великом инфламаторном полипу промера 57 × 23 × 20 *mm* у аналном каналу.

Закључак Према нашим сазнањима, ово је највећи до сада описан гастроинтестинални полип са коштаном метаплазијом. Иако редак феномен, постоје извесне карактеристике ове болести, због чега смо урадили преглед литературе и сумирали карактеристике.

Кључне речи: коштана метаплазија; гастроинтестинални полипи; инфламаторни полипи