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Case Report / Приказ случаја

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

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

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SUMMARY

Introduction Osseous metaplasia is exceedingly rare in benign gastrointestinal polyps.

The aim of this paper was to present a rare case of osseous metaplasia in an inflammatotory polyp of the anal canal.

Case Outline We present a case of a 31-year-old male with mesenchimal osseal metaplasia in a large inflammatory polyp measuring 57x23x20mm in diameter, located in anal canal region.

Conclusion According to our knowledge this is the largest gastrointestinal polyp with osseous metaplasia described so far.

Keywords: osseous metaplasia; gastrointestinal polyps; inflammatory polyps

САЖЕТАК

Увод Коштана метаплазја је врло ретка појава у бенигним гастроинтестиналним полипима.

Циљ обог рада је био да прикаже ретку појаву коштане метаплазије у инфламаторном полипу аналног канала.

Приказ болесника Приказујемо мушкарца, старог 31 годину, са мезенхималном коштаном метаплазијом у великом инфламаторном полипу промера 57x23x20мм у аналном каналу.

Закључак Према нашим сазнањима, ово је највећи гастроинтестинални полип са коштаном метаплазијом описан до сада.

Кључне речи: коштана метаплазија; гастроинтестинални полипи; инфламаторни полипи

INTRODUCTION

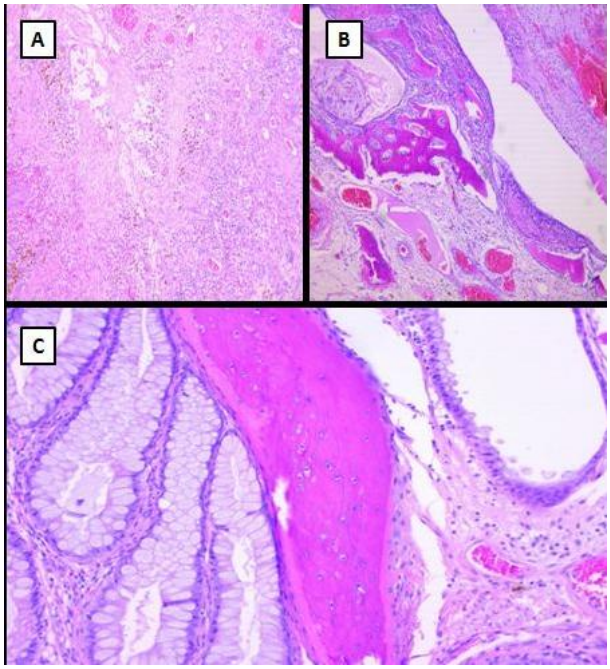
Heterotopic formation of bone (mesenchymal osseal metaplasia) is rarely found in the gastrointestinal tract. Most cases are associated with colon adenocarcinoma, but also can be found in the benign lesions of the bowel wall, such as necrosis, chronic inflammation foci and mucin extravasation [1]. The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

The aim of this work was to describe a case of mesenchymal osseal metaplasia (OM) in a large inflamatory polyp located in anal canal region in a 31-year-old male with an accompanying literature review.

CASE REPORT

We report a case of a 31-year-old male who visited our hospital with a chief complaint of of pain and evacuation of fresh blood from the anal canal during defecation. Clinical exam revealed a polypoid tumefact with contact bleeding in the anal canal region. Concomitant clinical finding were grade I internal haemorrhoidal nodules without signs of bleeding or inflammation. Total colonoscopy confirmed lobulated and vulnerabile 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 patient was discharged first postoperative day.

The tissue fragment submitted for pathohistological analysis, was macroscopicaly a soft greyish white polyp measuring 57x23x20mm in diameter. Histological analysis showed fragments of an inflammatory polyp of the large bowel mucosa, partly overlayed 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 dialated 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 hematopoesis signs, were found (Figure 1). The lesion was diagnosed as an inflammatory polyp of the anal canal with foci of OM.



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

DISCUSSION

Stromal ossification can occur in gastrointestinal cancers from the stomach to the anal canal and it seems to be result of bone morphogenic protein production of tumor cells. 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 5 were female patients, while in 3 cases gender as well as age were not described. Patient age ranged from 3 to 85 years, with mean age of 34 years. Our patient was 31-year-old male. Out of 24 described polyps, 3 were smaller than 10 mm, 11 were betwen 10 and 20 mm in diameter, and 6 were larger than 20 mm, while in 4 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 rectum where 60% of polyps (12/20) were found. In 30% (6/20) polyps were located in colon, and in 10% (2/20) polyps were found in the junction of the sigmoid colon and rectum. In 4 remaining cases exact location was not defined. Our patient had polyp in the anal canal which is another curiosity of our case. Histologically, 7 lesions were neoplastic (4 tubular adenomas, and 3 tubulovillous adenomas), while 15 lesions were non-neoplastic (7 juvenile polyps, 6 inflammatory polyps, and 2 serrated adenomas). In 2 lesions histology finding was not specified [1, 3–8]. Our patient had non-neoplastic inflammatory polyp.

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	AI-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: Indicates not informative.

The pathogenesis of heterotopic ossification is still not fully investigated. Many theories about pathogenesis are published. At the beginning of the 20th century Huggins conducted a set of experimental studies on dogs and demostrated OM in soft tissue of abdominal wall after transplantation of bladder tissue with 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, 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 [8]. Zemheri et al. noticed that OM, especially in benign lesions, is most often seen in lesions with active chronic inflammation and/or ulceration [3]. 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 fenotype of other types of cells of mesodermal tissue by the process of metaplasia, especially osteoblasts [3, 8, 9]. 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. conducted a immunohistochemistry study of BMP expresion 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. Also, BMP-2 and BMP-4 were found in tumor cells, but staining was week. Authors concluded that BMPs may have a significant role in heterotopic ossification in colon adenocarcinoma [10]. Study of Kypson et al. showed BMP-2 overexpression in rectal adenocarcinoma tumor cells with OM compared to rectal adenocarcinomas without bone production [8]. Later on, Liu et al. found BMP-1, BMP-4, and BMP-6 expression in stroma as well as epithelium in different cancers with OM [11]. Genetic studies of Takahasi et al. 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, 12, 13]. Other genetic studies found incrised expression of bone matrix synthesis markers e.g. collagen type I, osteocalcin and osteonectin in the foci of metaplastic bone formation [8, 14].

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 mesenchimal 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 agrees that clinically, the presence of the metaplastic bone seems to be innocent phenomenon [1].

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