Resesrch Article

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Unusual Osseous Metaplasia in Colonic Polyp: Two Case Reports and Review of the Literature

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Abstract

Background: *Osseous metaplasia occurring within the gastrointestinal tract is a rare phenomenon. Only a few of cases have been documented that osseous metaplasia can occur in colorectal polyps, although its underlying pathogenesis has not yet been elucidated.*

Methods: *Two cases of osseous metaplasia within inflammatory and adenomatous polyps of colon, respectively. The clinical and histological features of this lesion, as well as suggested mechanisms for its pathogenesis are discussed.*

Results: *Under the histological examination, both cases demonstrate the typical normal-looking osseous trabeculae rimmed by a layer of scattered osteoblasts in the stroma of inflammatory polyp or tubular adenoma of colon. To the best of our knowledge, they are possible the first cases of osseous metaplasia in colorectal polyps in Chinese.*

Conclusion: *Although it has not been found to have any significance in clinical treatment and prognostic evaluation, our data suggest that persistent inflammatory process and/or pluripotent stromal cells in polyps might contribute to the formation of osseous metaplasia in colonrectal neoplastic and non-neoplastic polyps.*

Keywords: Osseous metaplasia, Colonic polyps, Colon, Pathogenesis.

Introduction

Osseous metaplasia, also known as heterotopic bone, occurring within the gastrointestinal tract is a rare phenomenon. The most of previous reports are associated with mucin-producing colonic adenocarcinomas [1]. Only a few of reported cases have been documented that osseous metaplasia can occur in a variety of benign conditions, such as colorectal polyps and lesions associated with inflammation and ulceration [2-18]. Despite of distinctive morphology, the underlying pathogenesis of osseous metaplasia in gastrointestinal tract has not yet been elucidated. Herein, we present two cases of rare osseous metaplasia within colonic polyps occurring in 58-year old female and 34-year old male patients, respectively. To the best of our knowledge, they are possible the first cases of osseous metaplasia in colonic polyps presented in Chinese. The clinical and histological features of this lesion, as well as suggested mechanisms for its pathogenesis are discussed.

Materials and Methods

Case 1: A 58-year old female patient presented with a 3 weeks history of change in her bowel habits in the form of alternating diarrhoea and constipation. There was some rectal bleeding noted. But she had no family history of colorectal cancer or polyps. Physical examination showed the patient was fit. There was no fever, weight loss and no palpable lymphadenopathy or organomegaly. The laboratory results, including blood count, differential, liver and renal function, were within the normal range. Flexible sigmoidoscopy revealed a 2.5 cm polyp 30 cm from the anus. It had a slightly irregular surface with ulceration and it was reddish in colour. The polyp was removed during the sigmoidoscopy by electrocautery and sent for histological examination.

Case 2: A 34-year old male patient with 3 months history of intermittent diarrhoea and abdominal distention. On physical examination he was fit and had no organomegaly or palpable lymph nodes. All haematological and biochemical investigations were within normal limits. A colonoscopic examination revealed

a solitary polypoidal growth in the sigmoid colon, which measured approximately 0.5 cm in diameter. A polypectomy with sclerotherapy was performed under general anaesthesia and the polypoidal mass was sent for histological examination.

The surgical specimens were routinely fixed in 10% neutral buffered formalin and embedded in paraffin. Four micrometer-thick sections were stained with H&E in our laboratory.

Results

Histopathological findings

Case 1: Under the microscopy, the polypoid tissue was lined by surface epithelium and well-formed, mucin secreting mucosal glands. An area of surface ulceration and granulation tissue was noted. Surface epithelium and mucosal glands were infiltrated by a mixed acute and chronic inflammatory cell infiltrates. The granulation tissue was comprised of fibrous tissue and prominent small blood vessels. The polyp stroma contained multiple areas of osseous metaplasia consisting of normal-looking osseous trabeculae rimmed by a layer of scattered osteoblasts. There was no adenomatous proliferation of mucosal glands found in the polyp. The polyp base demonstrated normal mucosa with complete excision margins (Figure 1). Based on the pathological findings, a final diagnosis of colonic inflammatory polyp with osseous metaplasia was made.

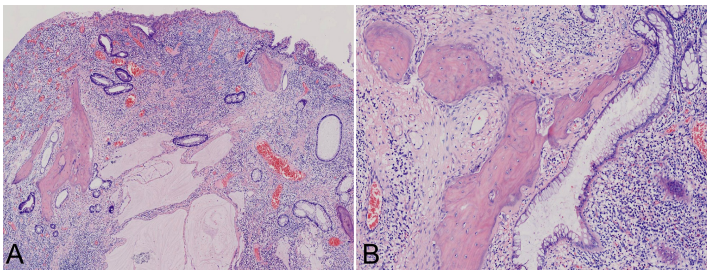

Figure 1: Photomicrographs of the inflammatory polyp of colon in Case 1.

(A) Microscopic examination demonstrated that polypoid tissue was lined by surface epithelium and well-formed, mucin secreting mucosal glands. An area of surface ulceration and granulation tissue was noted. Multiple areas of osseous metaplasia and numerous inflitrated inflammatory cell were observed in the polyp.

(B) Under the high-power fields, the osseous metaplasia was normal-looking osseous trabeculae rimmed by a layer of scattered osteoblasts. (A, H&E staining with original magnification × 100; B, H&E staining with original magnification × 400).

Case 2: Microscopically, the polypoid tissue demonstrated an adenomatous polyp with a mostly tubular growth pattern and mild epithelial dysplasia. There was no surface ulceration with granulation tissue found in the tissues. A single small focus of stromal osseous metaplasia consisting of irregular islands of mineralized osteoid bone and scattered osteoblasts was detected (Figure 2). Based on the pathological findings, a final diagnosis of tubular adenoma of colon with osseous metaplasia was made.

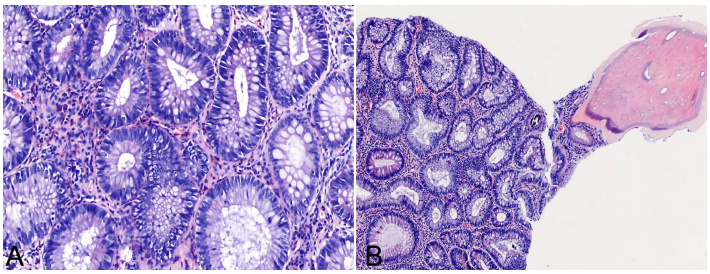

Figure 2: Photomicrographs of the tubular adenoma of colon in Case 2.

(A) The polypoid tissue demonstrated an adenomatous polyp with a mostly tubular growth pattern and mild epithelial dysplasia. There was no surface ulceration and remarkable inflammation infiltrating found in the polyp.

(B) A single small focus of stromal osseous metaplasia consisting of irregular islands of mineralized osteoid bone and scattered osteoblasts was detected. (A, H&E staining with original magnification × 400; B, H&E staining with original magnification × 200).

Discussion

Mesenchymal metaplasia, especially osseous metaplasia, is a rare and incidental finding in the gastrointestinal tract, although epithelial metaplasia is a common occurrence in the upper gastrointestinal tract. In 1913, Gruber was the first to describe a case of osseous metaplasia in a gastric adenocarcinoma [19]. In 1939, Dukes described four cases of osseous metaplasia in colonic adenocarcinomas [20]. Since then, osseous metaplasia has been described in both benign and malignant lesions in gastrointestinal tract, including Barrett's esophagus, carcinoid tumor and adenocarcinoma of stomach, Peutz-Jeghers syndrome, hyperplastic polyp, tubular adenoma and adenocarcinoma of colon and rectum. However, osseous metaplasia which occurs in colonic polyps is extremely rare. The first description of the phenomenon of bone formation within a rectal polyp was given by Marks in 1964, in which the authors termed this phenomenon as "heterotopic bone" [2].

In 1981, Sperling and his colleagues firstly designed this lesion as "osseous metaplasia" in colon polyp [3]. Although it is definitely a striking morphological feature, it has not been found to have any significance in clinical treatment and prognostic evaluation [5,19]. To the best of our knowledge, so far around 18 osseous metaplasia in various benign colorectal polyps have been described, including neoplastic and non-neoplastic polyps (Table 1). Amongst the cases, juvenile polyps and adenomatous polyps are the major lesions with osseous metaplasia. There are four cases of inflammatory polyp and three cases of serrated adenoma. A majority of these lesions are located in the rectum, and the polyp sizes vary from 0.5 cm to 5.0 cm, with a mean size of 1.5 cm. There no risk association has been determined for sex, age or polyp size, but adenocarcinoma can develop in a serrated adenoma with osseous metaplasia [14]. In the present cases, osseous metaplasia is detected in an inflammatory polyp and tubular adenoma of colon, respectively. To the best of our knowledge, they are possibly the first reported

Case	Author (yr.)	Age (yrs)/Gender	Location	Size (cm)	Histological diagnosis
1	Marks MM (1964) [2]	10/M	Rectum	not available	Juvenile polyp
2	Sperling MH (1981) [3]	25/M	Rectum	1.0	Inflammatory polyp
3	Castelli MF (1992) [4]	22/F	Rectum	1.0	Inflammatory polyp
4	Groisman GM (1994) [5]	3/F	Rectum	2.0	Juvenile polyp
5	Groisman GM (1994) [5]	67/M	Rectum	1.8	Tubulovillous adenoma
6	Cavazza A (1996) [6]	not available	Colon	not available	Tubulovillous adenoma
7	McPherson F (1999) [7]	73/M	Cecum	2.0	Dysplastic adenoma
8	Rothstein RD (2000) [8]	not available	Sigmoid colon	2.5	Dysplastic adenoma
9	Al-Daraji WI (2005) [9]	85/F	Sigmoid colon	1.5	Tubular adenoma
10	White V (2008) [10]	63/F	Transverse colon	not available	Adenomatous polyp
11	Ahmed R (2009) [11]	15/M	Rectum	1.0	Juvenile polyp
12	Oono Y (2010) [12]	39/M	Rectum	1.2	Inflammatory polyp
13	Wilsher MJ (2010) [13]	not available	Sigmoid colon	not available	Serrated adenoma
14	Wilsher MJ (2011) [14]	not available	Rectum	not available	Serrated adenoma
15	Bowman EA (2012) [15]	28/M	Descending colon	4.5	Adenomatous polyp
16	Montalvo NF (2012) [16]	62/M	Sigmoid colon	5.0	Serrated adenoma
17	Bhattacharya N (2013) [17]	14/M	Rectum	1.0	Juvenile polyp
18	Garg M (2013) [18]	6/M	Rectum	1.5	Juvenile polyp
19	Present case 1	58/F	Colon	2.5	Inflammatory polyp
20	Present case 2	34/M	Sigmoid colon	0.5	Tubular adenoma

Table 1: The clinicopathological characteristics of osseous metaplasia in colorectal polyps described in present and previous reports.

cases of osseous metaplasia within colonic polyps in Chinese.

The exact mechanism of osseous metaplasia in the lesions of the gastrointestinal tract is still unclear. Theoretically, the ossification process is initiated by a local osteogenic factor, which stimulates osteoblasts to differentiate and synthesise ground substance and collagen. Hydroxyapatite crystal formation, which is the final step in bone formation, depends on the presence of an adequate concentration of calcium and phosphate. Rhone postulated the metaplasia of a pluripotent cell into an osteoblast under the influence of factors generated by epithelial cells [21]. One possible mechanism includes the production of bone morphogenetic proteins (BMP)-5 and BMP-6 by epithelial cells and BMP-2 and BMP-4 by adjacent fibroblasts [22]. However, Randallet suggested that metastatic colonic carcinoma can promote heterotopic ossification, and that alkaline phosphatase is intimately associated with bone formation under these pathological conditions because immunostaining for alkaline phosphatase is not only seen in osteoblast-like cells, but also in apical membranes of the cancer cells next to areas of bone formation [23]. As for osseous metaplasia within benign colorectal polyps, Dukes suggested that a dystrophic calcification of the necrotic tissue in polyps might contribute to the bone formation [20]. Osseous metaplasia may also result from the ability of the fibroblasts to transform into other types of mesodermal tissues, especially osteoblasts in juvenile polyps [2,12], or a persistent inflammation may result in an osteogenic stimulation in inflammatory polyps of colon and rectum [3-4]. However, so far there has no reliable hypothesis of osseous metaplasia in adenomatous and hyperplastic polyps received in the literature yet.

In the present cases, chronic inflamamtion and granulation tissue could be found in the inflammatory polyp. It suggests that inflammatory process might be an important factor for osteogenic stimulation. Inflammation has previously been suggested as a trigger in a case of osseous metaplasia in an ulcer in Barrett's esophagus and in a rectal polyp found to have inflammatory infiltrate alongside the foci of osseous metaplasia [19]. The areas of ulceration and granulation tissue found in the polyp from our patient may be as a result of local damage. Osseous metaplasia may have then occurred secondary to this damage. However, there was no remarkable inflammatory cell infiltrating and granulation tissue formation in tubular adenoma in our presenting case. Osseous metaplasia in this lesion resulted from differentiation of immature connective tissue to osteoblasts is perhaps more applicable. It has also been reported that some factors released by abnormal epithelial cells can go on to induce differentiation and ossification [5]. Recent study has also demonstrated that the heterotopic ossification is more likely the result of pluripotent stromal cells that undergo differentiation to form osteoblasts rather than the tumor cells undergoing osseous metaplasia, but the certain mechanism involved in has not identified yet [24].

Conclusion

In conclusion, only a few cases of osseous metaplasia within colorectal polyps have been reported in the literature. Our additive cases are also presented for its rarity and possibly firstly described in Chinese. Although this lesion has distinctive morphological feature, it has not been found to have any significance in clinical treatment and prognostic evaluation. The persistent inflammatory process and/or pluripotent stromal cells in polyps might contribute

to the formation of osseous metaplasia.

Consent

Written informed consents were obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Authors' contributions

BCP made contributions to acquisition of clinical data, and analysis of the histological features. GFH carried out the H&E staining. CHW and XYT drafted the manuscript. ZL revised manuscript critically for important intellectual content and had given final approval of the version to be published. All authors read and approved the final manuscript.

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