

CASE REPORT

Heterotopic ossification in skeletal muscle metastasis from colonic adenocarcinoma – a case report

Venkatesh R. NAIK *M.D [Path]*, Hasnan JAAFAR *MPath*, Samarendra S. MUTUM *M.D [Path]*.

Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia,

Abstract

Colonic adenocarcinoma metastasising to the skeletal muscle is rare. A 56-yr-old Malay man was diagnosed to have adenocarcinoma of the right colon [Dukes B] for which a right hemicolectomy was performed, followed by radiotherapy and chemotherapy. Five years later the patient presented with a mass in the rectus abdominis muscle. The serum carcinoembryonic antigen was 71ng/ml. The mass was resected. Gross and microscopical examination showed multiple deposits of mucin-secreting adenocarcinoma with prominent heterotopic ossification in the stroma. The exact pathogenesis and significance of heterotopic ossification is not clear, but bone morphogenetic proteins may play an important role.

Key words: adenocarcinoma, colon, metastasis, skeletal muscle, heterotopic bone

INTRODUCTION

Colorectal cancer is the third most common cause of cancer death in Malaysia. Data from the Ministry of Health of Malaysia confirms an increase in colorectal cancer admission rates from 8.1% in 1987 to 11.9% in 1995. Metastasis of colonic carcinoma to skeletal muscle is very rare. Heterotopic bone formation is known to occur occasionally in colorectal polyps, Peutz–Jeghers syndrome, Barrett's oesophagus, colorectal carcinoma, mucocele of the appendix, etc¹ but it rarely occurs in metastatic tumour deposits.^{2,3} We report here a very rare combination of metastasis of colonic adenocarcinoma to the rectus abdominis muscle and extensive heterotopic ossification within the tumour deposit occurring 5 years after the surgical resection of the tumour and radiotherapy.

CASE REPORT

A 56-year-old Malay male presented to the surgical clinic with complaints of lower abdominal pain and loose stools for a few days. The pain was dull aching in nature and present diffusely in the lower abdomen. He denied any change in bowel or bladder habits or malaena. On questioning he gave the history of passing fresh blood in his stools for a few days many years

previously. He had not taken any treatment for this and it subsided on its own. He was a known hypertensive on medication.

Abdominal examination revealed a mass in the right lumbar region measuring approximately 4x5cm. This mass was firm, non-tender and was ballotable. Barium enema showed a persistent constriction in the recto-sigmoid junction and it was diagnosed as carcinoma of the colon. He underwent a right hemicolectomy and the resected specimen was submitted for histopathological examination.

Microscopical examination revealed a moderately-differentiated adenocarcinoma of colon with prominent mucin secretion. The stage of the tumour was B [Dukes stage].

With this diagnosis the patient was given 8 cycles of radiotherapy followed by chemotherapy and the condition of the patient improved with this treatment. He was on regular follow-up.

Five years later, on one of his regular follow-ups, he complained of pain in the lower abdomen and also a mass in the suprapubic region. During this visit his serum carcinoembryonic antigen level was found to be 71ng/ml.

On examination of the lower abdomen, there was a firm to hard mass, which was non tender and not mobile. C.T. scan showed a mass within the rectus abdominis muscle on the right side,

which was multinodular with solid and cystic areas. The anastomotic site was free of tumour and no other metastatic deposit was seen. With an impression of metastatic tumour deposit, the mass was resected.

The patient is currently doing well on follow-up assessment.

Pathology

Grossly, the resected specimen was enclosed in muscle tissue. The mass was gritty to cut and serial sections showed multiple greyish nodules of varying sizes with areas of haemorrhage and cystic change.

Microscopical examination showed multiple tumour deposits within the muscle tissue. The tumour was composed of moderate to poorly differentiated glands lined by tall columnar cells with vesicular pleomorphic nuclei, arranged back-to-back and forming papillary structures as seen in the main tumour earlier. Islands of mature bone were seen in the core of the papillae (Fig. 1). These bony lamellae were rimmed by osteoblasts and contained osteocytes. There was no bone marrow formation or cartilage tissue seen. Pools of mucin and areas of necrosis were seen in other areas.

DISCUSSION

Skeletal muscle is one of the most unusual sites for metastasis of any malignancy. The most common neoplasms metastasising to the

muscle are from the breast or the lungs and the most common muscles involved are psoas and paravertebral muscles.⁴ The low incidence of muscular metastasis may be related to the anatomical characteristics and or biochemical environment of the skeletal muscle. Inflammatory oncotaxis has been offered as the most likely explanation for this phenomenon.⁵

Formation of heterotopic bone within metastatic tumour deposits in skeletal muscle is still rare.⁶ Gastrointestinal cancers and their metastasis are liable to calcify and ossify and they, particularly the mucin-secreting variety, are more liable to do so than other epithelial tumours.^{1,2,7,8} It has also been reported in other conditions like colorectal polyps, Peutz-Jeghers syndrome, Barrett's oesophagus and in abdominal laparotomy scars.^{1,7,9} The rectum is the most common site.¹⁰

The exact pathogenesis of heterotopic ossification is not well known but it has been commonly seen in tumours that produce abundant mucin.^{1,8,10} This has led to the speculation that mucinous malignant tumours may secrete a substance that stimulates bone formation and that tumour necrosis provides a nidus for metaplastic ossification.⁷ Thus, there is proliferation of local mesenchymal tissue and differentiation of mesenchymal cells into osteoblasts induced by the tumour cells.^{2,6,10} Significant concentration of alkaline phosphatase was found in osteoblasts, proliferating mesenchymal cells surrounding

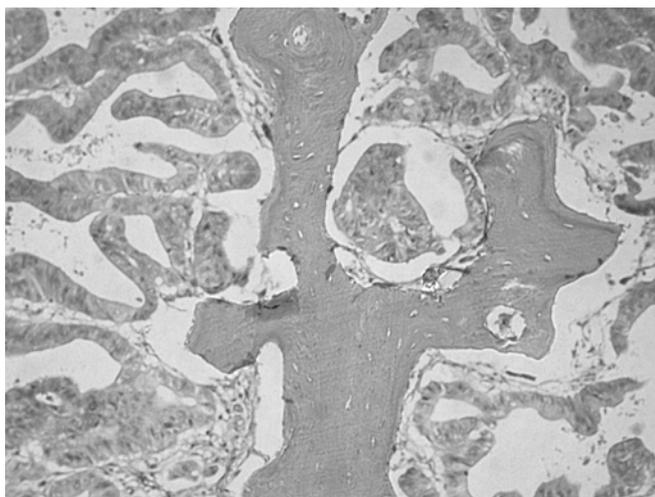


FIG. 1: Island of mature bone is seen in the stromal core of the tumour [H&E x100].

osseous foci and to a lesser degree on the apical membrane of glandular cells by immunohistochemical stains suggesting that it can promote heterotopic ossification.³ This does not, however, account for the ossification occurring in benign lesions like colorectal polyps where there are no mucin pools or necrosis.

Bone morphogenetic proteins [BMP] are known to be primary inducers of new bone formation. Immunohistochemistry in colonic adenocarcinoma has shown BMP-5 and BMP-6 to be prominent in the cytoplasm of tumour cells and weakly staining in osteoblast-like cells adjacent to newly formed bone. Cytoplasmic staining for BMP-2 and BMP-4 was weak in tumour cells, osteoblast-like cells and stromal fibroblasts. Thus, BMP may play an important role in heterotopic ossification.¹¹

Heterotopic ossification is a rare occurrence whether in the primary lesion or its metastatic deposits. Its significance and pathogenesis needs further investigation.

REFERENCES

1. Haque S, Eisen RN, West AB. Heterotopic bone formation in the gastrointestinal tract. *Arch Pathol Lab Med* 1996; 120: 666-70.
2. Caluori D, Gallo P. Case report of heterotopic bone formation in metastatic carcinoma of the colon. *Tumori* 1979; 65: 345-51
3. Randall JC, Morris DC, Tomita T, Anderson HC. Heterotopic ossification: a case report and immunohistochemical observations. *Hum Pathol* 1989; 20: 86-8.
4. Pons SM, Moreno SI, Vila PJ, Arevalo ND, Grau AJ. [Muscular metastasis in a patient with adenocarcinoma of the colon. An infrequent complication][article in Spanish]. *An Med Interna* 1997; 14: 412-4.
5. Palazzo FF, New NE, Cullen PT. An unusual cause of thigh pain in colonic cancer. Inflammatory oncotaxis? *Acta Chir Belg* 2000; 100: 28-30.
6. Bettendorf U, Remmele W, Laaff H. Bone formation by cancer metastases: case report and review of literature. *Virchows Arch A Pathol Anat Histol* 1976; 369: 359-65.
7. McPherson F, Maldonado M, Truitt CA, Mamel JJ, Morgan MB. Metaplastic ossification of a benign colonic polyp: case report. *Gastrointest Endosc* 1999; 49: 654-6.
8. Alper M, Akyurek N, Patiroglu TE, Yuksel O, Belenli O. Heterotopic bone formation in two cases of colon carcinoma. *Scand J Gastroenterol* 2000; 35: 556-8.
9. Myers MA, Minton JP. Heterotopic ossification within the small-bowel mesentery. *Arch Surg* 1989; 124: 982-3.
10. Ansari MQ, Sachs IL, Max E, Alpert LC. Heterotopic bone formation in rectal carcinoma. Case report and literature review. *Dig Dis Sci* 1992; 37: 1624-9.
11. Imai N, Iwai A, Hatakeyama S, Matsuzaki K, Kitagawa Y, Kato S, Hokari R, Kawaguchi A, Nagao S, Miyahara T, Itoh K, Miura S. Expression of bone morphogenetic proteins in colon carcinoma with heterotopic ossification. *Pathol Int* 2001; 51: 643-8.