

Collision adenoma-carcinoid tumour of the colon complicated by carcinoid syndrome

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ABSTRACT Tumours consisting of a glandular component, either an adenoma or adenocarcinoma, and a carcinoid component are uncommon. These tumours can be differentiated into collision, composite or amphicrine tumours. Most cases reported in the literature were mixed adenocarcinoma-carcinoid tumours. To date, only four cases of mixed adenoma-carcinoid tumours have been reported in the literature. This case report describes a unique case of collision adenoma-carcinoid tumour in the colon complicated by carcinoid syndrome in a 45-year-old woman who presented with a one-month history of diarrhoea and weight loss. She developed recurrence of the carcinoid component of the tumour four months after endoscopic resection. We conclude that carcinoid syndrome can occur in an adenoma-carcinoid tumour; however, the prognosis of this condition is uncertain.

Keywords: adenoma-carcinoid tumour, carcinoid syndrome, collision tumour, colon
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INTRODUCTION

Tumours consisting of a glandular component (either an adenoma or adenocarcinoma) and a carcinoid component are uncommon. These tumours can be differentiated into collision, composite or amphicrine tumours. Tumours that are in intimate contact without intermixture between the cell types are classified as collision tumours. Tumours where the two cell types merge and intermingle, with an identifiable transition between the two tumours, are classified as composite tumours.^(1,2) On the other hand, amphicrine tumours are differentiated by the presence of both endocrine and non-endocrine epithelial cells within the same cell.^(1,2) Although our understanding and knowledge of mixed glandular carcinoid tumours have increased over the years, this case report describes a unique case of collision adenoma-carcinoid tumour in the colon complicated by carcinoid syndrome.

CASE REPORT

A previously healthy 45-year-old Chinese woman presented with a one-month history of diarrhoea and weight loss of 6 kg. A colonoscopy showed a 1.5 cm sessile polyp at the rectum, 15 cm from the anal verge (Fig. 1a). The polyp was removed *en bloc*. Histology of the polyp showed tubulovillous proliferation of the large intestinal glands with cribriform glands arising from the overlying dysplastic epithelium, in keeping with high-grade dysplasia (Fig. 1b). At the deeper section, the colorectal mucosa contained tiny clusters, nests and tubules of relatively bland-looking and mitotically inactive, small, round cells in the lamina propria. These cells possessed round hyperchromatic nuclei, inconspicuous nucleoli and scanty cytoplasm consistent with rectal carcinoid (Fig. 1c). These components were adjacent to

each other and were histologically distinct. There was no evidence of invasion into the submucosal region. A clear resection margin of more than 2.0 mm was achieved.

Immunostaining for synaptophysin and chromogranin A was performed on the dysplastic glands of the adenomatous and carcinoid components. The carcinoid component of the tumour was positive for both synaptophysin and chromogranin A, while the adenomatous component showed no staining for these two markers. Upon the finding of an adenoma-carcinoid tumour, the patient was investigated for evidence of carcinoid syndrome three days after endoscopic resection. Her serum serotonin and serum chromogranin A levels were both elevated at 540 (normal range [NR] 90–195) ng/mL and 28 (NR 1.9–15.0) ng/mL, respectively. Her 24-hour urine 5-hydroxyindoleacetic acid level was 48.7 (NR < 42.6) μ mol/day. Echocardiogram showed moderate tricuspid regurgitation. The right ventricular systolic pressure was normal, and there was no significant gradient across the pulmonary valve. Helical computed tomography (CT) of the whole abdomen was normal. Whole body positron emission tomography-computed tomography (PET-CT) showed no 18F-fludeoxyglucose-avid lesion.

The patient declined a hemicolectomy and preferred to have routine surveillance colonoscopy. Her diarrhoea slowly improved and subsided one month post polypectomy. Her serum serotonin level one month after polypectomy was 108 ng/mL, serum chromogranin A level was 18 ng/mL, and 24-hour urine for 5-hydroxyindoleacetic acid level was 23.7 μ mol/day. A colonoscopy was repeated one month after the polypectomy. Biopsies from the previous tumour site showed mild, nonspecific chronic inflammatory infiltrate in the lamina propria and submucosa with regenerative changes. The biopsy tissues showed

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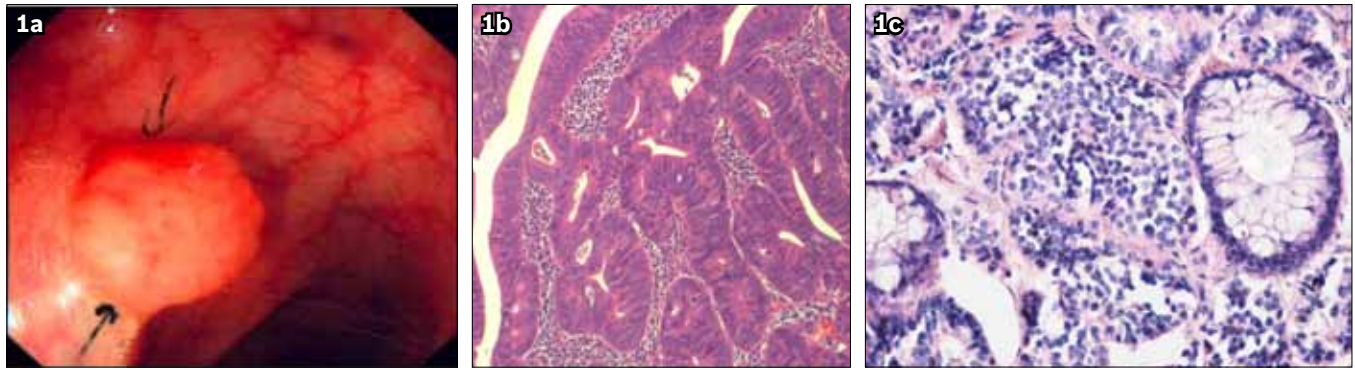


Fig. 1 (a) Photograph shows sessile polyp at the rectum. Photomicrographs show (b) tubulovillous adenoma with high-grade dysplasia (Haematoxylin & eosin, $\times 400$); and (c) carcinoid component (Haematoxylin & eosin, $\times 400$).

no evidence of adenocarcinomatous or carcinoid element. A third colonoscopy was repeated three months later (four months after the endoscopic resection). Multiple biopsies at the previous tumour site showed recurrence of the rectal carcinoid. However, there was no evidence of the adenomatous component. The patient was asymptomatic despite a recurrence of rectal carcinoid. Her serum serotonin level was 373 ng/mL and serum chromogranin A level was 24 ng/mL. Despite the raised serum serotonin and chromogranin A levels, her 24-hour urine sample for 5-hydroxyindoleacetic acid was normal at 31 $\mu\text{mol/day}$. She declined further investigation and intervention, and subsequently defaulted follow-up.

DISCUSSION

Cases of mixed glandular carcinoid tumours in the large intestine are uncommon.⁽¹⁻⁵⁾ Most of the cases reported were mixed adenocarcinoma-carcinoid tumours.^(6,7) Only four were mixed adenoma-carcinoid tumours.^(3,4) These tumours are usually detected as polyps, and their sizes have been reported to range from 1.5 cm to 3.0 cm. The adenomatous component consists of either tubular or villous type with low- or high-grade dysplasia and carcinoid component.⁽¹⁾ It usually occupies the periphery of the polyp, extending to involve the stalk. The carcinoid component, on the other hand, is usually located in the centre of the polyp.⁽¹⁻³⁾

The carcinoid component can be argyrophil, chromogranin A or synaptophysin positive. Although hormonal immunoreactivity for serotonin or glucagon has been reported,^(1,3) this is the first reported case of an adenoma-carcinoid tumour complicated by carcinoid syndrome. The presence of tricuspid regurgitation, and raised serum serotonin and chromogranin A levels suggested the development of carcinoid syndrome. Surprisingly, we were unable to find any evidence of liver metastases on PET-CT, as 90% of those who develop carcinoid syndrome would usually have metastatic disease of the liver.⁽⁸⁾

The pathogenesis of carcinoid syndrome in this patient was uncertain. The venous drainage of the rectum is to the portal or systemic system. The lower rectum is drained by the middle rectal vein. The middle rectal vein drains into the internal iliac veins and the systemic system.⁽⁹⁾ As the tumour in this patient was located between the middle and lower rectum, serotonin

secreted by the tumour may have been released into the middle rectal veins by retrograde flow and entered the systemic system. Thus, biologically active products may have reached the systemic circulation before being passed through the liver to be metabolised.⁽⁹⁾ Another reason may be the presence of metastases in the liver that were not picked up by PET or CT, as the sensitivity of PET and CT in detecting small, slow-growing tumours, like a carcinoid tumour, is limited. In retrospect, magnetic resonance (MR) imaging of the liver should have been performed in view of its higher sensitivity for detection of metastases compared to CT, as shown in one study.⁽¹⁰⁾

The prognosis of adenoma-carcinoid tumour seems to be good. In those who underwent surgical hemicolectomy, no residual tumour or invasion into the muscularis propria was detected. Furthermore, there was no evidence of tumour recurrence on follow-up for 1–6 years.⁽¹⁾ However, the optimal treatment in this case is uncertain. It may depend on the behaviour of the independent elements of the collision tumour. This is because the prognosis of patients with carcinoid tumour complicated by carcinoid syndrome is worse than those with metastatic disease without carcinoid syndrome.⁽⁸⁾

Based on current recommendations, as a clear resection margin of more than 1.5 mm was achieved in this patient, the adenomatous element should be completely cured.^(11,12) Her serotonin and chromogranin A levels, and 24-hour urine 5-hydroxyindoleacetic acid level normalised one month after endoscopic resection of the tumour. Diarrhoea and weight loss also stopped, indicating that her symptoms were due to carcinoid syndrome. Any complication or metastases would thus depend on the carcinoid component of the tumour. As the patient declined a hemicolectomy, colonoscopy was repeated at one and four months after endoscopic resection. Multiple biopsies at the previous tumour site showed recurrence of the rectal carcinoid four months after endoscopic resection.

There was no evidence of the adenomatous component on biopsy. Hence, the patient only developed a recurrence of the carcinoid component of the tumour. Although she was asymptomatic at the time the rectal carcinoid was detected, she did have raised serum serotonin and chromogranin A levels. However, we are unable to ascertain whether she subsequently developed a

recurrence of the symptoms of carcinoid syndrome, as she was lost to follow-up.

In conclusion, carcinoid syndrome can occur in an adenoma-carcinoid tumour, but the prognosis of adenoma-carcinoid tumour with carcinoid syndrome is still uncertain.

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