

CASE REPORT

Colonic adenosquamous carcinoma and mucinous adenocarcinoma with microsatellite instability

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Abstract

A 43-year-old man presented with two-month history of fatigue, weakness, paleness, rectal bleeding, sweating, and weight loss of 10 kg in the past one month. A complete blood count revealed anaemia. The patient underwent a right hemicolectomy. The microscopic examination revealed an adenosquamous carcinoma associated with a mucinous adenocarcinoma in a patient with microsatellite instability due to loss of MLH1 and PMS2 expression and retention of MSH2 and MSH6 expression in both the squamous and glandular components. We also observed an atypical immunohistochemical phenotype in the adenocarcinoma component showing CK7 expression and reduced CK20 and CDX2 expression.

Keywords: Adenosquamous carcinoma, mucinous adenocarcinomas, microsatellite instability

INTRODUCTION

Histological variants of colorectal adenocarcinoma have been described but most are classical adenocarcinomas (AC)¹. Other subtypes include adenosquamous carcinomas (ASC), a rare entity comprised malignant squamous and glandular elements, accounting for 0.05% to 0.20% of colorectal malignancies^{2,3}, and mucinous adenocarcinomas (MAC), accounting for 1.6-25.4%,⁴ and defined by >50% of the tumour volume composed of extracellular mucin.¹ These two variants carry a worse prognosis than classical adenocarcinomas^{3,4} and curiously may occur in patients with microsatellite instability (MSI).^{5,6} We described an interesting case, to our knowledge, the first case of colon ASC and MAC with MSI.

CASE PRESENTATION

A 43-year-old man presented with a two-month history of fatigue, weakness, paleness, rectal bleeding, sweating, and body weight loss of 10 kg in the past one month. A complete blood count revealed anaemia (haemoglobin 4.3 mg/dl and haematocrit 15.10 mg/dl). A colonoscopy showed a multi-lobular polypoid lesion with ulceration involving 60% of the circumference and occluding 60% of the lumen in the ascending colon. Histologic examination of the biopsy sample revealed a moderately differentiated adenocarcinoma.

The patient underwent a right hemicolectomy. On gross examination the colon specimen

measured 25 x 6 x 4 cm and evidenced an ulcerated mass measuring 10 x 8 x 9 cm, occluding 90% of the lumen. Microscopic examination revealed an adenosquamous carcinoma characterised by sheets of moderately differentiated malignant squamous cells and scattered keratinisation. A mucinous adenocarcinoma was observed in the glandular component (Fig. 1). The final diagnosis was an adenosquamous carcinoma with a predominant component of mucinous adenocarcinoma (95%) and moderately differentiated squamous keratinising cell carcinoma (5%). The tumour penetrated the visceral peritoneum (pT4a). Three of the 42 mesenteric lymph nodes retrieved were positive. There was no distant metastasis.

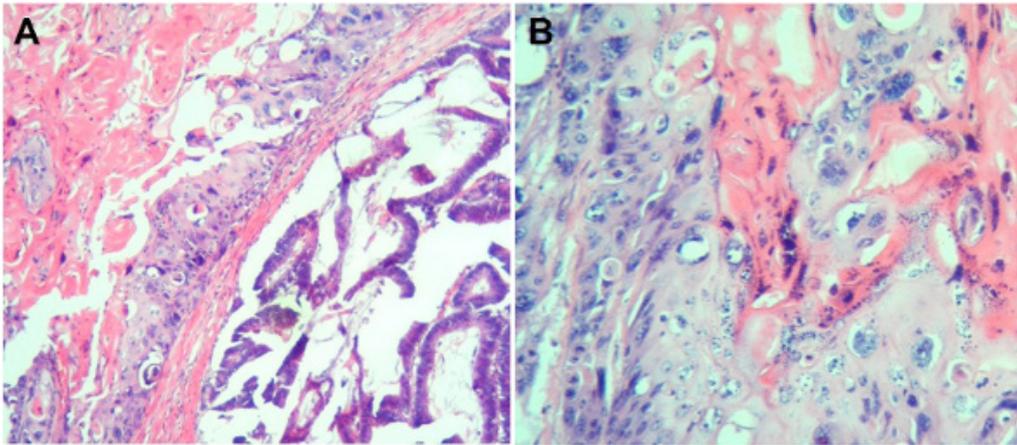


FIG. 1: (A) Adenosquamous carcinoma with mucinous adenocarcinoma component composed of glands and pool of mucin (H&E, x20). (B) Higher magnification showing areas of keratinisation (H&E, x40).

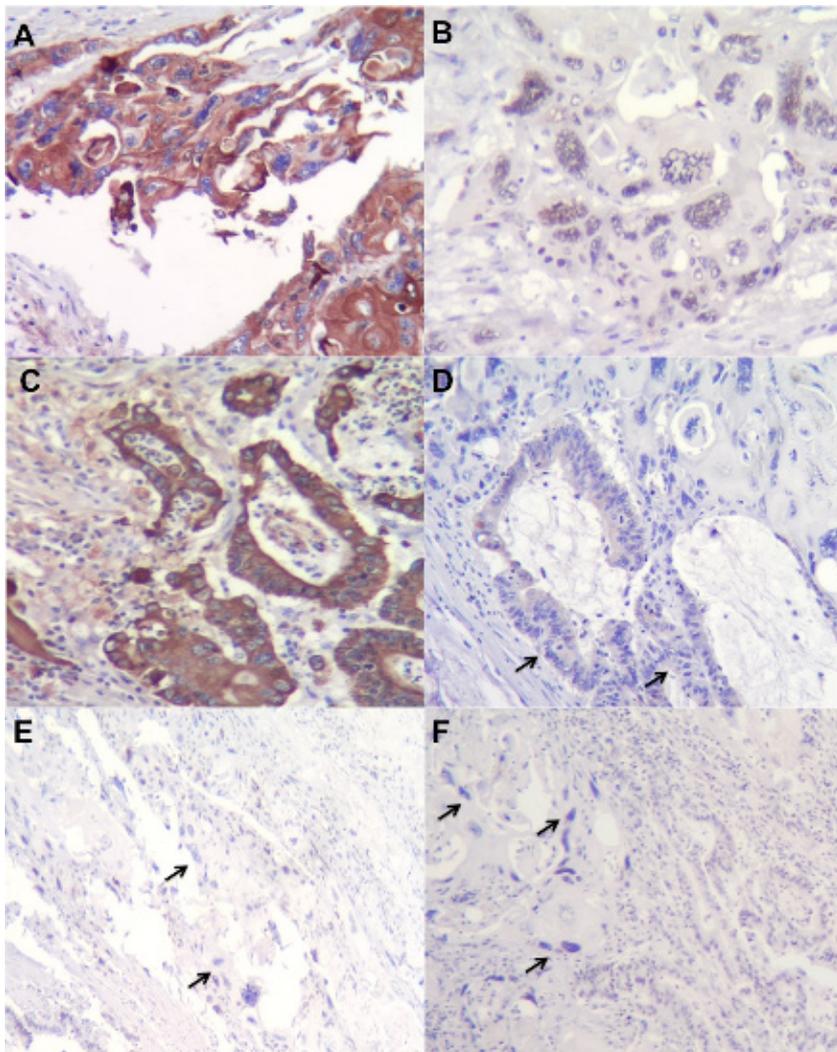


FIG. 2: Immunohistochemistry studies. CK5/6 (A) and p63 (B) immunoreactivity of the adenosquamous carcinoma. Adenocarcinoma component showed CK7 expression (C) and reduced expression of CK20 (arrow) (D). Loss of MLH1 (arrow) (E) and PMS2 (arrow) (F) expressions.

Immunohistochemical stains showed CK5/6 and p63 expression in the squamous component (Fig. 2 A-B). The adenocarcinoma component showed CK7 expression and reduced expression of CK20 (Figure 2 C-D) and CDX2, as well as, loss of MLH1 and PMS2 expression in the adenosquamous carcinoma and the adenocarcinoma component (Fig. 2 E-F) and retention of MSH2 and MSH6 expression in both squamous and glandular components, suggesting loss of MLH1 function.

DISCUSSION

Colorectal cancer shows variable underlying molecular changes with two major mechanisms of genetic instability: chromosomal instability and MSI⁷. MSI tumours occur in approximately 15% of colorectal adenocarcinomas (and of these 15% to 20% are due to Lynch syndrome), caused by loss-of-function defects in DNA mismatch repair (MMR) genes (MLH1, MSH2, MSH6, PMS2), inherited in an autosomal dominant mode.^{1,7,8} Pathologic examination in patients with MSI showed a trend to develop tumour-infiltrating lymphocytes, a Crohn-like lymphoid response, mucinous or signet-ring differentiation or a medullary growth pattern.¹

It has been proposed that ASC associated with MSI is another histologic subtype. Its molecular mechanisms remain uncertain.⁵ Similar to colonic ASC, stomach ASC may also be associated with MSI.⁹ Our case is the first reported ASC with MAC in a patient with MSI, and immunohistochemistry studies revealed loss of MLH1/PMS2 expression and retained MSH2/MSH6 expression in the squamous and glandular components, indicative of MSI.

ASC is composed of malignant squamous and glandular elements. The origin of squamous component is unknown. Several hypotheses have been proposed, including the presence of embryologic nests of ectodermal and pluripotent stem cells capable of squamous differentiation, squamous metaplasia, and abnormal mucosal stimulation derived from inflammatory conditions leading to carcinogenesis (ulcerative colitis, schistosomiasis, radiation, or human papilloma virus).¹⁰ Clinical manifestations are very similar to those of AC. The most common location is the right and transverse colon. ASC carry a worse prognosis than AC (HR 1.67, 95% CI 1.33 to 2.10).³ The squamous components behave more aggressively and have a higher metastatic potential.¹⁰

On the other hand, MAC is defined by

showing >50% of the tumour volume composed of extracellular mucin. Tumours with >10% but <50% of mucinous component are defined as adenocarcinomas with mucinous features or mucinous differentiation.¹ MAC is usually present in a more advanced stage than classical adenocarcinomas (AC), MAC is more frequent in females and proximal disease stage at diagnosis is similar in MAC and AC. Moreover, MAC has a slightly worse prognosis than AC (HR 1.05, 95% CI 1.02 to 1.08).⁴

We also observed an atypical immunohistochemical phenotype. The most common immunophenotype of colorectal adenocarcinomas is positivity for CDX2 (>90%) and CK20 with negativity for CK7.¹¹ Curiously, we observed expression of CK7, and reduced expression of CK20 and CDX2. These findings involving loss of CDX2 expression and CK7 positivity with reduced CK20 expression may be seen in patients with MSI.^{12,13} In our case, they were useful to determine the presence of MSI.

In summary, we present an interesting case report. To the best of our knowledge, this is the first reported case of colonic ASC with mucinous adenocarcinoma and with MSI. This atypical immunohistochemical phenotype may be useful to determine the presence of MSI, in spite of not exhibiting the other histologic features of MSI (tumour-infiltrating lymphocytes or Crohn-like lymphoid response). Further studies on the presence of MSI in patients with ASC are required. The ASC may represent an additional variant in patients with MSI.

Conflict of interest: The authors declare that there are no conflicts of interest

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