Metastatic Intramucosal Colorectal Adenocarcinoma A Case to Support Review of Current Concepts (and Staging) of Early Colorectal Cancer

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Sir: A 70-year-old male presented with rectal bleeding and was found to have a rectosigmoid polyp, clinically 30 mm diameter. The polyp was received in two pieces (18 × 15 × 15 mm and 15 × 15 × 10 mm). The largest piece demonstrated focal high-grade dysplasia with a distinct area of lamina propria invasion by dyscohesive clusters of vacuolated 'malignant' cells (highlighted by cytokeratin MNF116; see Figure 1). The endoscopist noted that the centre of the polyp would not lift adequately and deeper invasion was suspected. Subsequent anterior resection revealed residual/recurrent villous adenoma with focal high-grade dysplasia and transmural venous invasion (see Figure 2) with lymph node metastases. No other malignancy was demonstrated clinically or radiologically. The patient subsequently developed liver deposits and died of metastatic disease.

KRAS testing revealed the same codon 13 mutation [c.38G>A (p.Gly13Asp)] in the original adenoma, adenoma in the resection specimen and the intravascular tumour. Complete examination of all the

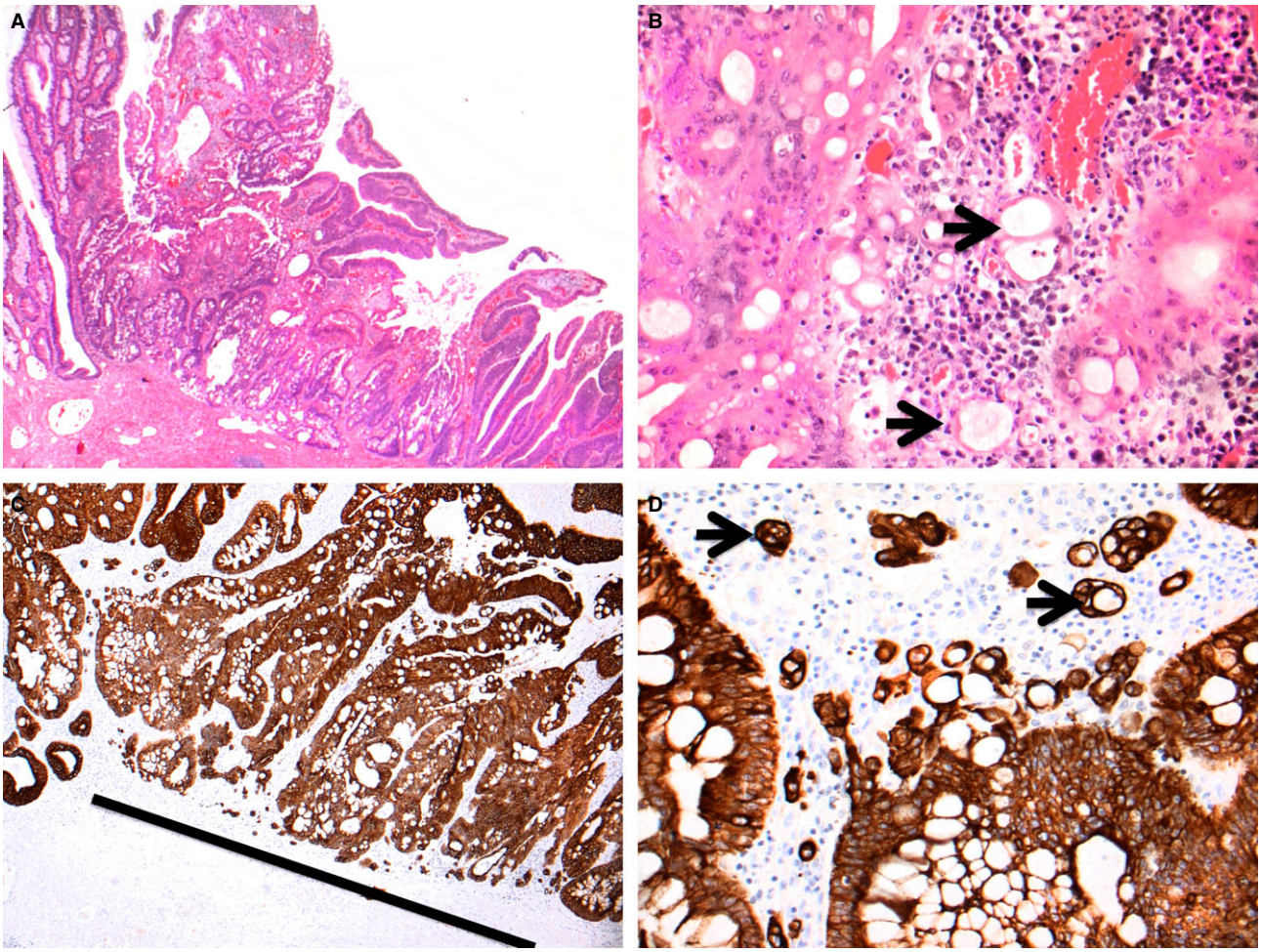

Figure 1. Low-power view (**A**) of adenoma with high-grade dysplasia, and (**B**) higher-power view demonstrating signet ring-like cells (arrowheads) in lamina propria, demonstrated more clearly by MNF116 immunohistochemistry (**C**,**D**). The black line in C demonstrates the approximate location of the muscularis mucosae.

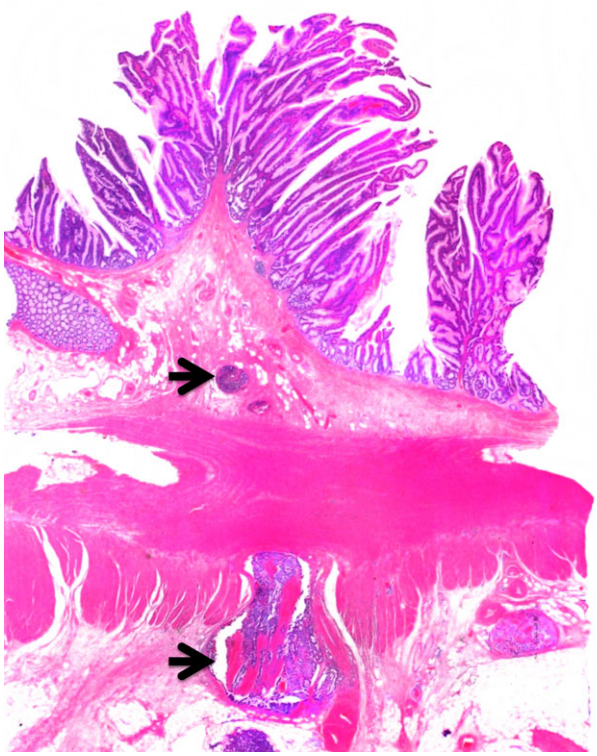

Figure 2. Residual villous adenoma in resection specimen showing transmural intravenous carcinoma (arrowheads) without submucosal stromal invasion.

submitted tissue (levelling through all relevant blocks) showed no evidence of submucosal stromal invasion.

In our opinion, this is a rare case of metastatic adenocarcinoma that disseminated via mucosal venules. Although this single case by no means proves the hypothesis, we think it is biologically and clinically plausible that a small percentage of early colorectal cancers acquire the ability to disseminate without the necessity of prior submucosal stromal invasion (as is known to occur infrequently in cancers of the upper gastrointestinal tract).

We see no logical reason why carcinoma should be defined by invasion through the epithelial basement membrane in the stomach, and by invasion of the submucosa of the colorectum. Should infrequent metastasis or fear of overtreatment confuse a satisfactory definition of what constitutes a carcinoma? Compared with stomach, the paucity of lymphatic channels in colorectal lamina propria, the predominantly exophytic nature of colorectal precancers and lower frequency of poor differentiation in lower gastrointestinal tract cancers are all possible factors influencing the apparent rarity of colorectal mucosal metastatic spread. A recent study Lan *et al.*[2] unexpectedly identified metastatic spread in more than 1% of so-called '*in-situ*' colorectal adenocarcinoma.

These recent data have prompted a re-evaluation of these apparent metastatic mucosal carcinoma cases, as many will have undoubtedly been understaged or suboptimally sampled at original diagnosis. It does, however, raise the possibility that, like the stomach, metastasis may occur from the mucosa and predictably, once the concept gains acceptance among practising histopathologists, more cases will be reported in the literature. This will hopefully allow the eventual acceptance of a logical and coherent pan-gastrointestinal staging system, with clarification of factors predicting aggressive biological behaviour in early invasive colorectal neoplasms.

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