Short reports

Early diagnosis of signet ring cell carcinoma of the stomach: role of the Genta stain

Hala M T El-Zimaity, Kemal Itani, David Y Graham

Abstract

Signet ring cell carcinoma is a poorly differentiated adenocarcinoma in which the tumour cells invade singly or in small groups. Early stages of the disease can be missed easily when using regular haematoxylin and eosin staining. This is a report of a case in which routine screening of gastric biopsies with the Genta stain was responsible for rapid identification of signet ring carcinoma. The patient, a 29 year old woman, had a large portion of the antrum excised surgically for signet ring cell gastric carcinoma. Follow up endoscopy six years later showed no evidence of tumour. Twenty six large cup biopsies were obtained and a single focus of signet ring tumour cells infiltrating the surface mucosa in single files was seen. The diagnosis was missed on haematoxylin and eosin stain by three senior pathologists but owing to the Alcian blue component of the Genta stain the tumour cells were recognised easily. Thus, the Genta stain not only facilitates detection of *Helicobacter pylori* but also allows for simultaneous visualisation of gastric morphology as well as signet ring carcinoma that can be missed with conventional stains.

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The Department of
Medicine, Veterans
Affairs Medical
Center, Baylor College
of Medicine, Houston,
Texas, USA

H M T El-Zimaity
D Y Graham

Department of
Surgery
K Itani

Correspondence to:
Dr El-Zimaity, VA Medical
Center (111-D), 2002
Holcombe Blvd (Room
3A352), Houston, TX
77030, USA.

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Diffuse gastric carcinoma can occur at any age, and the incidence may be increasing,¹⁻³ particularly among young women.^{1 2 4-6} Owing to the innocuous appearance of these tumour cells and the lack of specific symptoms, usually patients are seen late in the course of their illness and curative treatment is uncommon.¹ The recent interest in *Helicobacter pylori* led to the development of the Genta stain that allows the simultaneous visualisation of *H pylori* organisms and gastric mucosal histology with or without intestinal metaplasia.⁷ Our unit uses the Genta stain routinely on all gastric mucosal biopsies. We report a case of signet ring cell carcinoma in which routine use of the Genta stain in screening gastric biopsies not only facilitated the identification of *H pylori* infec-

tion, but also allowed the detection of malignant cells in an unsuspected case that might otherwise have gone unnoticed.

Case report

In 1990, a 29 year old woman with a history of peptic ulcer disease presented with nausea, vomiting, and decreased appetite of a few weeks duration. Upper gastrointestinal endoscopy with biopsy showed a pyloric stricture, 4-5 mm in greatest diameter. Repeat biopsy revealed signet ring cell carcinoma. An antrectomy with Billroth II anastomosis was performed. The tumour was multifocal, formed an ulcer at the gastroduodenal junction, and extended to the muscle layer. Frozen sections of the surgical margins were all negative for tumour as were regional lymph nodes, the peritoneum, and the liver. Gross staging, according to Borrmann's classification and TNM staging, showed type IIb,⁸ and T2 N0 M0 (stage I), respectively.

The patient returned six years later and endoscopy showed a normal postoperative stomach. Twenty six large cup mucosal biopsies were obtained and a single focus of signet ring tumour cells infiltrating the surface mucosa in single files was identified, with an identical histological pattern to the original tumour. The diagnosis was missed on haematoxylin and eosin stain by two senior pathologists. As part of our routine, additional slides are always stained with the Genta stain; owing to the Alcian blue component in the Genta stain, both *H pylori* infection and the tumour cells were recognised easily (fig 1).

The patient underwent gastrectomy with regional lymph node dissection. The resected stomach was opened along the lesser curvature based on the information of the known topographical site from which the positive biopsy specimen had been taken. The resected stomach showed no gross identifiable tumour. The areas around the positive biopsy site were sectioned serially at ~3 mm intervals for histological examinations, 32 sections being prepared. Microscopic examination showed marked foveolar hyperplasia (fig 2) as is seen frequently in postgastrectomy specimens, but the tumour could not be identified in the initial microscopic sections, and 30 additional

Figure 1 Signet ring cells showing a positive reaction (light blue colour) for mucin (Genta stain; original magnification $\times 10$).

Figure 2 Signet ring cell carcinoma infiltrating the lamina propria. The background is hyperplastic foveolar epithelium typical of chemical gastropathy (haematoxylin and eosin; original magnification $\times 10$).

sections were cut. Histological examination in one single section showed mucosal infiltration by a population of uniform, plump, mucous containing cells with eccentrically compressed hyperchromatic nuclei (signet ring cells). The tumour was 0.5 cm in the greatest dimension. The main lesion was confined to the lamina propria above the muscle layer, did not involve the overlying surface epithelium, and showed no fibrous reaction. The diagnosis was missed by three senior pathologists on haematoxylin and eosin stain (fig 2). Staging according to Borrmann's macroscopic types was IIb.⁸

Discussion

Gastric carcinomas hidden beneath intact mucosal surface epithelium are rarely discovered. Not only is the diagnosis incidental in the early stages but, usually, it is also unexpected.⁹ Needless to say, a significant diagnostic delay exists in younger patients owing to the higher numbers of diffuse carcinoma³ and the low level of suspicion by both the endoscopist and the pathologist.^{4 10 11} Early gastric cancer has a higher proportion of signet ring cells.^{6 9} The imperceptible IIb carcinomas are most often poorly differentiated.⁹ It seems reasonable to postulate that most carcinomas start as microcarcinomas of the endoscopic type IIb. Likewise, it seems reasonable to assume that if diffuse carcinoma is diagnosed in its early stages, the prognosis would be much better.⁹ Unfortunately, these malignant cells are missed very easily as they usually occur in non-metaplastic mucosa.^{5 9} This is exaggerated further in post-gastrectomy specimens and in gastric carci-

noma complicating Menetrier's disease,¹² in which the hyperplastic changes of the overlying epithelium and glands allow an innocuous nest of tumour cells to be overlooked easily. Signet ring cell carcinoma is one of the few malignant tumours that is likely to be missed on microscopic examination⁹ because often it is misinterpreted initially as some type of benign process⁶ such as an aggregate of histiocytes, xanthelasma,¹³ or a cohesive cluster of pyloric cells with glassy cytoplasm.

Fortunately, the periodic acid Schiff (PAS) stain and mucin stains, such as mucicarmine or Alcian blue, are helpful in highlighting signet ring cells. Mucin stains are crucial for the identification of gastric carcinoma cells in normal mucosa and in hyperplastic epithelium, where their presence may be imperceptible. In poorly differentiated carcinomas, the number of tumour cells demonstrated by mucin stains is usually much higher than that seen in haematoxylin and eosin stained sections and the routine use of special stains such as the Genta stain has an additional benefit of alerting the unwary pathologist to the presence of carcinoma. For example, a high index of suspicion would exist when an expansion of the lamina propria with blue cells is noted on low power microscopic examination (fig 1). The differentiation from histiocytes, which may be mucicarmophilic,¹⁴ can be made by cytomorphological examination of tumour cells with the PAS stain and/or the immunohistochemical cytokeratin stain.

Usually, gastric carcinoma in young patients is lethal.^{3 11} Whether the remaining focus of signet ring cell carcinoma in this patient was residual tumour or new tumour is impossible to know but the long survival of our patient is unusual. In conclusion, routine staining of gastric biopsies with the Genta stain can facilitate detection of *H. pylori* infection and signet ring cells in unsuspected cases that otherwise might be missed with conventional stains.

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