

CASE REPORT

Malignant melanoma of the gastrointestinal tract presenting as a bleeding gastric ulcer

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Abstract

Malignant melanoma involving the gastrointestinal tract is diagnosed antemortem in only a small percentage of patients with the disease. Presenting symptoms are often non-specific, causing a diagnostic problem. The vast majority of such melanomas are metastatic from a cutaneous primary, however there is evidence that the tumour can arise *de novo* in the gastrointestinal system. We report a 74-year-old man with malignant melanoma with an unusual presentation simulating a symptomatic gastric ulcer. He presented with epigastric pain, haematemesis and melaena. Explorative laparotomy revealed a large ulcerated tumour with several pigmented satellite nodules in the proximal stomach, multiple ileal nodules and widespread nodal and liver metastases. Proximal gastrectomy and limited small bowel resection was performed. Histology revealed the tumour to be composed of nests of epithelioid cells with melanin pigment. The tumour cells showed immunohistochemical positivity for S100 protein and HMB45 antibodies. This report emphasizes that melanoma should be a diagnostic consideration in patients with gastric ulcer.

Key words: Gastrointestinal tract, melanoma, diagnosis

INTRODUCTION

Although the vast majority of gastrointestinal tract (GIT) melanoma is metastatic, primary melanoma can also arise from the mucosal epithelial lining of the GIT.¹ Preoperative diagnosis is often difficult due to non-specific symptoms. Signs and symptoms may occur late and these include nausea, vomiting, abdominal pain, weight loss and anaemia.² Aggressive surgical therapy has been shown to prolong survival and provide important symptomatic palliation.³ Accurate diagnosis is therefore important to decide on the most appropriate therapy.

Primary malignant melanoma of the GIT is recognised to occur in the anorectum⁴ and the oesophagus.⁵ Rare cases have been reported in the small bowel⁶ and stomach.⁷ Pathologically the tumour grows as a submucosal lesion which may enlarge into a polypoidal mass and undergo ulceration. The well recognized morphological diversity of malignant melanomas may cause diagnostic difficulties in differentiating it from adenocarcinoma, gastrointestinal stromal tumours (GIST), hemangiopericytoma and lymphoma, particularly in biopsy specimens where a primary

tumour has not been identified.^{8,9} We describe here a case of malignant melanoma to the gastrointestinal tract presenting as a bleeding ulcer in the stomach, in the absence of a clinically obvious primary lesion elsewhere.

CASE REPORT

A 74-year-old man presented with a one week history of epigastric pain, haematemesis and melaena. He had no previous history of peptic ulcer disease or chronic analgesic ingestion. Clinically he was very pale. The abdomen was soft with mild tenderness in the epigastrium. The Hb was 5.1 gm/dL.

An upper gastrointestinal endoscopy revealed a large ulcer on the lesser curve of the stomach with raised edges and blood clot on the ulcer floor. There were three to four other nodules adjacent to the ulcer. A biopsy was taken and histologically an epithelioid stromal sarcoma was the primary diagnostic consideration. A differential diagnosis of metastatic melanoma was also considered.

Due to persistent melaena, a laparotomy was carried out. A large lobulated mass with central ulceration was found in the proximal stomach

with several pigmented umbilicated satellite nodules. Multiple metastatic nodules were also seen in the ileum, root of the mesentery, paraaortic nodes, paraaortic nodes and the liver. Proximal gastrectomy, splenectomy and limited small bowel resection with end to end anastomosis was performed. A thorough search for a primary lesion was unsuccessful.

Postoperatively recovery was uneventful. The patient was well on discharge but defaulted follow-up.

Pathology

Gastric biopsy

The specimen, comprising of two mucosal fragments, showed proliferation of epithelioid cells arranged in nesting pattern, expanding the submucosa but sparing the overlying mucosa (Fig. 1). The cells were not pigmented and displayed large pleomorphic nuclei with prominent eosinophilic nucleoli (Fig. 2). The cytoplasm was abundant and exhibited cytoplasmic vacuolation. Mason Fontana stain did not reveal any melanin pigment and mucin stains were negative. Immunohistochemistry showed weak cytoplasmic staining for vimentin. Staining for S100 protein which was performed much later was also positive. Cytokeratin, leucocyte common antigen, chromogranin and desmin were negative. A diagnosis of epithelioid stromal sarcoma with a differential diagnosis of metastatic melanoma was made.

Stomach, ileum and spleen

The gastrectomy specimen revealed two large ulcerated polypoid tumour measuring 7 cm and 4 cm respectively with six smaller pigmented satellite nodules. A segment of the ileum measuring 7 cm long was received separately and revealed two ulcerated pigmented nodules measuring 1.5cm and 1cm respectively.

Microscopically, sections from the stomach and ileum showed sheets of pleomorphic epithelioid cells expanding the submucosa, infiltrating the overlying surface mucosa and invading the underlying muscular and serosal layers. In the smaller nodules, the tumour was confined mainly to the submucosa leaving the surface mucosa intact. The malignant cells were pigmented, exhibited large vesicular nuclei with prominent nucleoli and abundant granular eosinophilic cytoplasm. Numerous mitotic figures and a few multinucleated giant cells were present. In the ileum, spindled malignant cells were seen adjacent to epithelioid areas. *In-*

situ change was not observed in the overlying or adjacent gastrointestinal epithelium. Mason Fontana stain indicated intracytoplasmic melanin pigment. Immunohistochemical staining for S100 protein and HMB45 were positive.

The splenectomy specimen did not show any diagnostic abnormality.

DISCUSSION

In this report we describe a case of malignant melanoma of the stomach in a patient where a thorough search for a primary lesion elsewhere proved futile. The case is of interest in several respects. It demonstrates that gastric melanoma may simulate a symptomatic gastric ulcer clinically and endoscopically. Preoperative diagnosis is often difficult and delayed. In the present case, the clinical and pathological evidence support a diagnosis of a primary melanoma of the stomach. Lack of concurrent or previous history of melanoma or atypical melanocytic lesion from the skin and the presence of extensive involvement of the stomach, are important features which support the diagnosis. Microscopical examination however failed to show *in situ* change in the overlying or adjacent epithelium, an important criteria in the diagnosis of primary melanoma. This feature is reported in 40-100% of primary GIT melanomas.¹⁰ Despite the presenting features described above, the possibility of the tumour being metastatic cannot be totally excluded as metastatic melanoma may occur in the absence of a clinically obvious primary lesion. The patient's disease could have resulted from an undiscovered, spontaneously regressing, primary cutaneous lesion.

The initial gastric biopsy posed a diagnostic problem and a definite histological diagnosis could not be made. Clinically the lesion was thought to be a primary tumour and epithelioid stromal sarcoma being more common than primary melanoma, was the preferred diagnosis at that time. It was supported by vimentin positivity and cytokeratin negativity in the immunohistochemical studies. Even though there was positive staining for S-100 in the biopsy, the definitive diagnosis of melanoma was made from the resected specimen only 5 weeks later. The delay in diagnosis can be attributed to several reasons. Firstly, the possibility of malignant melanoma was not thought of, as it is a rare primary tumour of the stomach. Secondly and more importantly, the tumour cells from the gastric biopsy were not pigmented and were

composed of epithelioid cells, without a spindle cell component. This closely resembled a carcinoma or an epithelioid GIST. The nesting pattern of the tumour cells and their polygonal shape also suggest the possibility of a neuroendocrine tumour. The morphological similarity between melanoma and other tumours

and the recruitment of immunohistochemical markers are points of interest discussed here.

Like GIST, malignant melanoma may be composed of proliferation of spindle-shaped cells and epithelioid cells. The typical nuclear features of melanoma which include round nuclei with prominent nucleoli, glassy eosinophilic

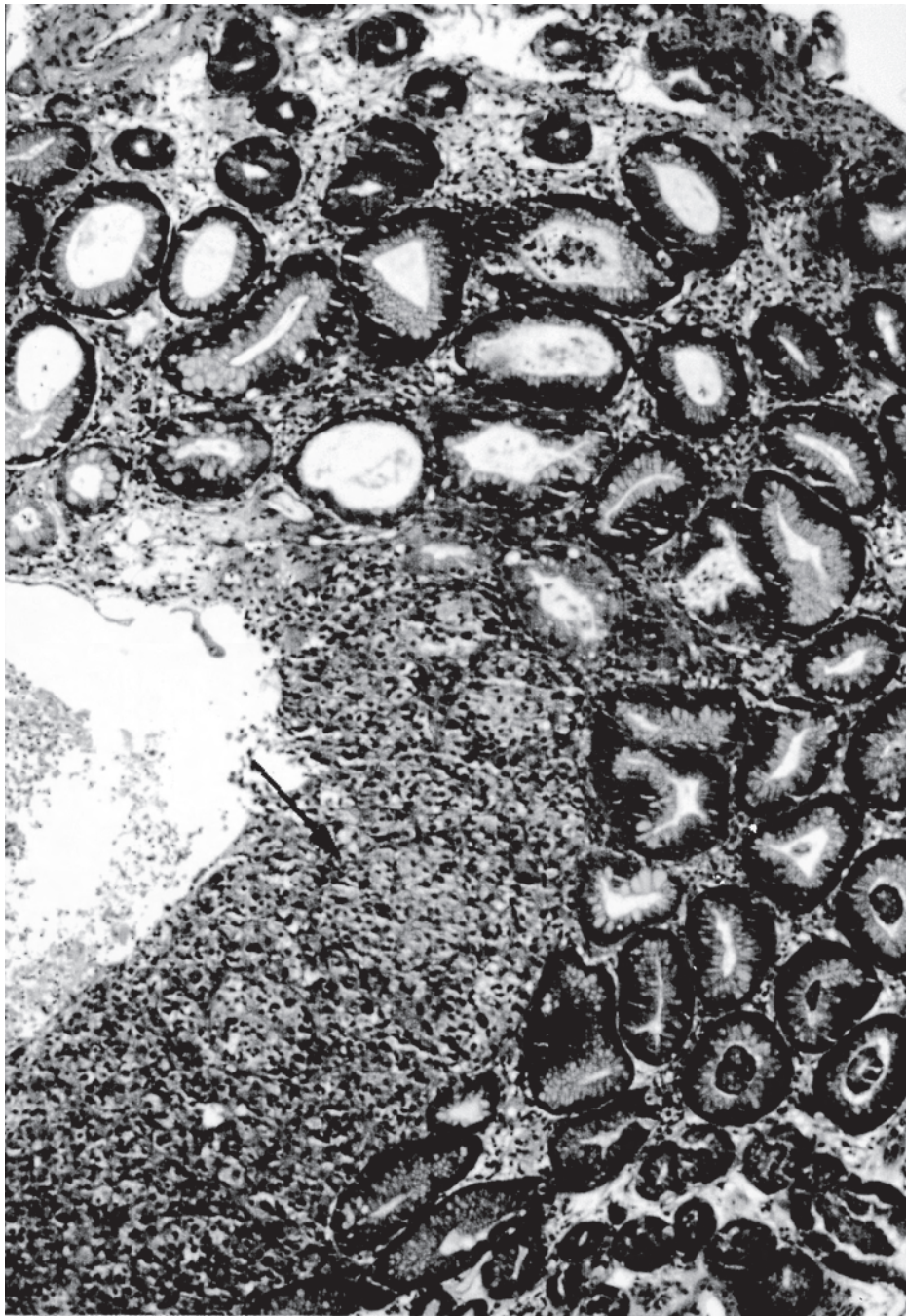


FIG. 1: Arrow shows melanoma cells filling the gastric submucosa. The overlying mucosa is intact. H&E X40.

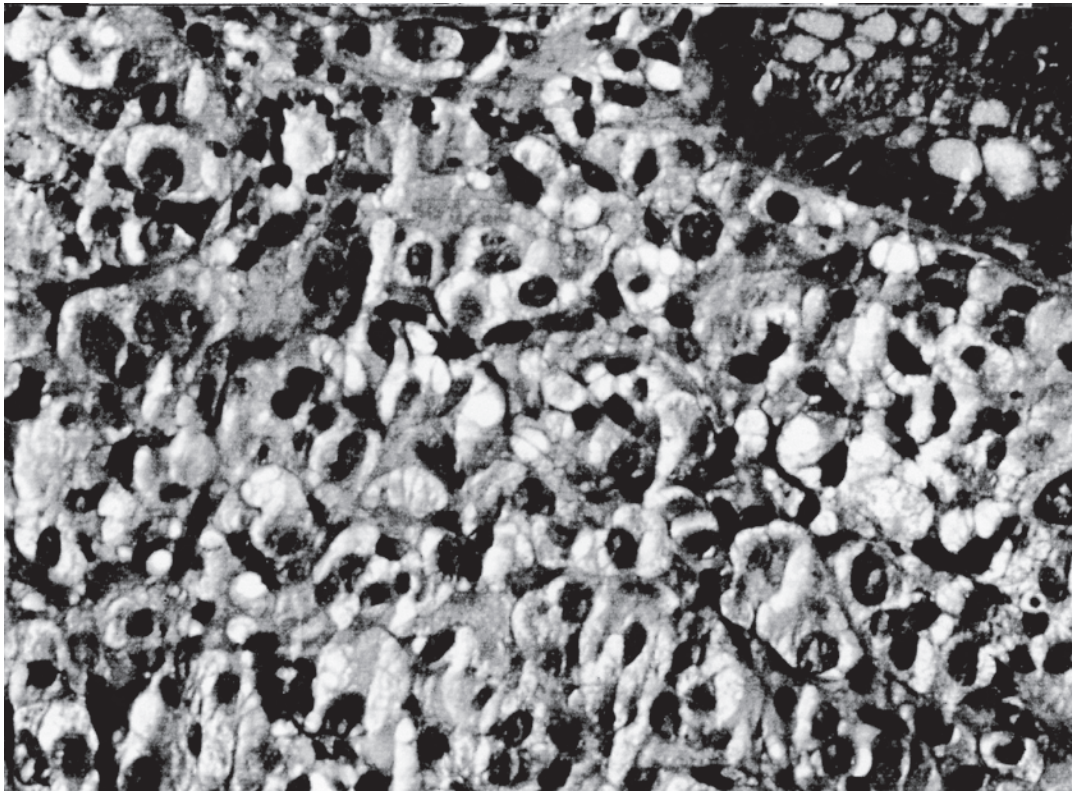


FIG. 2: The malignant cells are polygonal and display pleomorphic and hyperchromatic nuclei with vacuolated cytoplasm. H&E X200

cytoplasm and the presence of intranuclear pseudoinclusions, are diagnostically helpful but may be absent. The diagnosis of melanoma is made easy when intracellular melanin can be identified. Fifty to 70% of mucosal lesions are pigmented leaving others amelanotic.¹¹ In the present case, the biopsy was not pigmented and Mason Fontana conventionally used to demonstrate melanin was negative. Based on morphology, besides epithelioid stromal sarcoma, other lesions considered in the differential diagnosis include poorly differentiated carcinoma, small cell carcinoma and lymphoma. In a review of 335 malignant melanomas by Nakleh⁸ to identify the variant morphologic patterns, unusual histological features were found in 27 amelanotic neoplasms. These included adenoid and pseudopapillary pattern, small cell neoplasms, hemangiopericytoma-like tumours, tumours with prominent myxoid stroma and tumours with signet-ring cell configuration.

Differentiation from other diagnoses depends on positive immunohistochemical staining for S-100, HMB-45 and Melan A/Mart1. In general, melanomas react strongly with S-100 and is

widely used in the immunoprofile screen to support a diagnosis of melanoma. However it has been reported to be negative in signet-ring cell melanoma¹² and small cell melanoma.¹³ An additional marker is recommended in conjunction with S-100 protein when confirming the morphological diagnosis. In a study of 56 cases of melanoma, Duray⁹ found that monoclonal HMB-45 reacted with over 90% of all tumours. It appears specific for melanoma cells, with no cross reactivity with nonmelanocytic malignant tumours, unlike polyclonal anti S-100 protein. Melan-A/Mart 1 is a recently identified new melanocytic differentiation marker. It has been found to be more sensitive than HMB-45 especially in metastatic tumours.¹⁴ The antibody was not used in this case as it was not available in our laboratory. Some melanomas may exhibit an aberrant immunophenotype and may express cytokeratin¹⁵ and also some melanomas are negative for HMB-45 by immunoperoxidase.¹² In these cases, it has been recommended that a panel of antibodies with more than one marker in each category should be used for identifying melanosomes.

It can be concluded that malignant melanoma

should be included in the differential diagnosis of a gastric ulcer even though a history of a primary tumour is not elucidated. Ancillary studies designed to detect melanocytic differentiation are important in such a tumour with diverse histological guise.

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