

## Primary malignant melanoma of the stomach: report of a case

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**Abstract** We report a case of primary malignant melanoma (MM) of the stomach. The patient, a 73-year-old man, was referred to our hospital for investigation of an elevated lesion in the stomach, detected by gastroscopy. On admission, physical examinations and laboratory data were unremarkable. Gastroscopy revealed a pigmented, elevated tumor, approximately 2 cm in diameter, in the posterior wall of the stomach. A biopsy was taken, which resulted in a diagnosis of MM, based on the presence of melanin in tumor cells. F-18 fluorodeoxyglucose positron emission tomography showed no accumulation of tracer except for the tumor in the stomach, indicating that it was a primary MM of the stomach. The patient underwent distal gastrectomy, but died of recurrence 1 year later. Very few cases of primary MM of the stomach have been reported. Thus, we report this case, followed by a review of the literature.

**Keywords** Malignant melanoma · Primary lesion · Stomach

### Introduction

Occasionally, ectopic neoplasms arise in the gastrointestinal (GI) tract [1]. Malignant melanoma (MM) usually arises from typical sites where there are melanocytes:

namely, the skin, eyes, meninges, and anal region. While it is found occasionally in the GI tract, the vast majority of GI melanomas are metastases from a cutaneous primary tumor [2]. In fact, clinical GI tract involvement secondary to cutaneous melanoma has been reported in up to 4% of living patients and up to 60% at autopsy [3, 4]. Conversely, primary MM of the GI tract, particularly in the stomach, is extremely rare, although sporadic cases have been reported [5–14]. We present another case of primary MM of the stomach, which to our knowledge, is the first documented case of a primary MM of the stomach, from Japan.

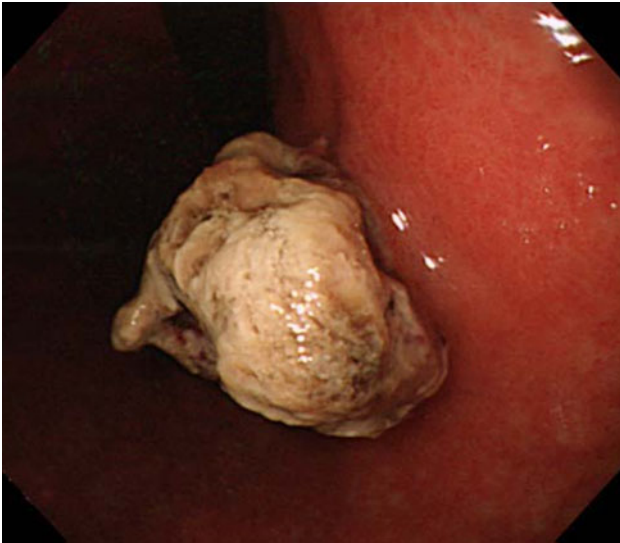
### Case report

A 73-year-old man was referred to our hospital after gastroscopy had shown an elevated lesion in the posterior wall of the stomach. On admission, he appeared in good health, without peripheral adenopathy, and laboratory data, including serum lactate dehydrogenase (LDH), were all within normal limits. Gastroscopy showed a pigmented, elevated lesion, approximately 2 cm in diameter, in the posterior wall of the stomach (Fig. 1). A biopsy was performed and histologic examination revealed sheet-like malignant cells with large nuclei and eosinophilic cytoplasm containing dark brown pigment (Fig. 2a). Immunohistochemically, the tumor cells were positive for S-100 proteins (Fig. 2b) and HMB-45 antibodies (Fig. 2c), and negative for pan-cytokeratin antibodies (AE1/AE3) and leukocyte common antigen. Based on these findings, we diagnosed MM. Ophthalmologic, dermatologic, and oral examinations were negative, as were computed tomography of the chest and anoscopy. Furthermore, F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) showed no accumulation of tracer, except in the tumor of the stomach (Fig. 3).

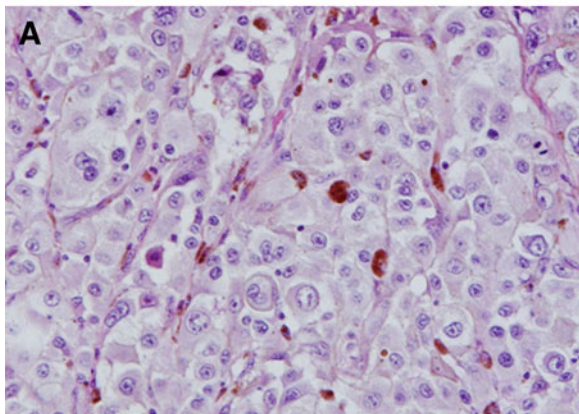
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Therefore, we performed distal gastrectomy for assumed primary MM of the stomach without metastases. The resected specimen contained a brown-pigmented fungiform tumor, 2 cm in diameter, in the posterior wall of the stomach (Fig. 4). Postoperative histological and immunohistochemical examinations confirmed the diagnosis.



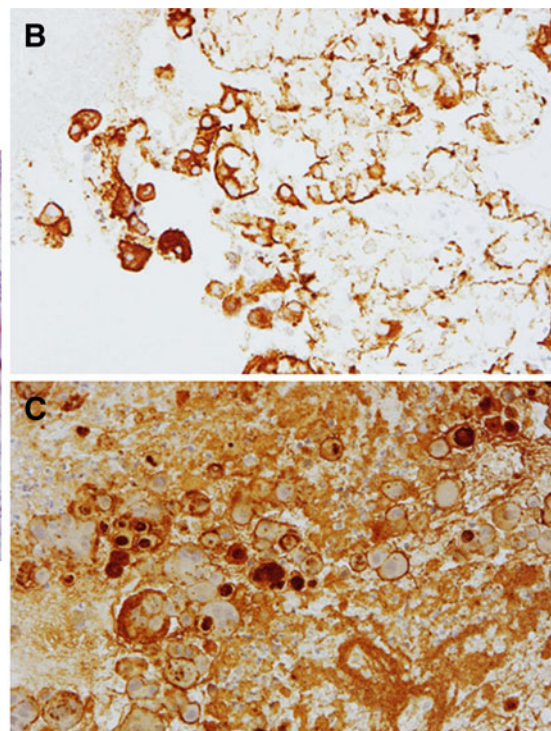
**Fig. 1** Endoscopic examination showed a pigmented elevated lesion in the posterior wall of the stomach



Tumor cells were spreading through the submucosal layer of the stomach, but the resection margins were clear of tumor. Six of 27 resected lymph nodes were positive for metastases. The patient was discharged from our hospital after an uneventful recovery, and was followed up at another hospital. He was readmitted to our hospital 9 months later with abdominal pain, general fatigue, and anorexia. A subcutaneous tumor in his back was resected and pathological examination revealed a metastasis of MM (Fig. 5). Computed tomography showed ascites and pleural effusions, but cytological examinations of the fluid were negative. He became extremely cachectic and died approximately 2 months later; 1 year after the gastrectomy.

## Discussion

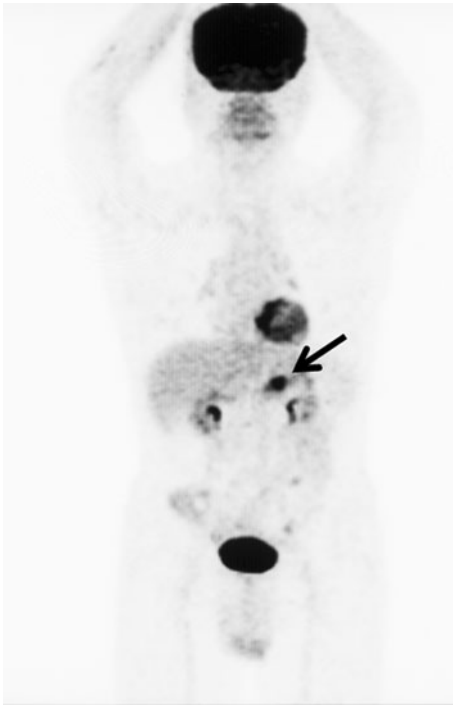
Primary MM of the stomach is extremely rare. Since normal stomach epithelium lacks melanocytes, the cell of origin remains obscure, although possible etiologies of primary MM have been suggested. For example, ectopic migration of melanocyte precursors or differentiation of the APUD cells (amine precursor uptake and decarboxylation cells) to melanocytes has been suggested as a possible mechanism of the development of MM [8, 15, 16]. Criteria for the diagnosis of primary MM include the absence of other primary site melanomas and no history of the



**Fig. 2** **a** Histology showed sheet-like malignant cells with large nuclei and eosinophilic cytoplasm containing dark brown pigment. **b** Tumor cells were positive for HMB-45 antibody. **c** Tumor cells

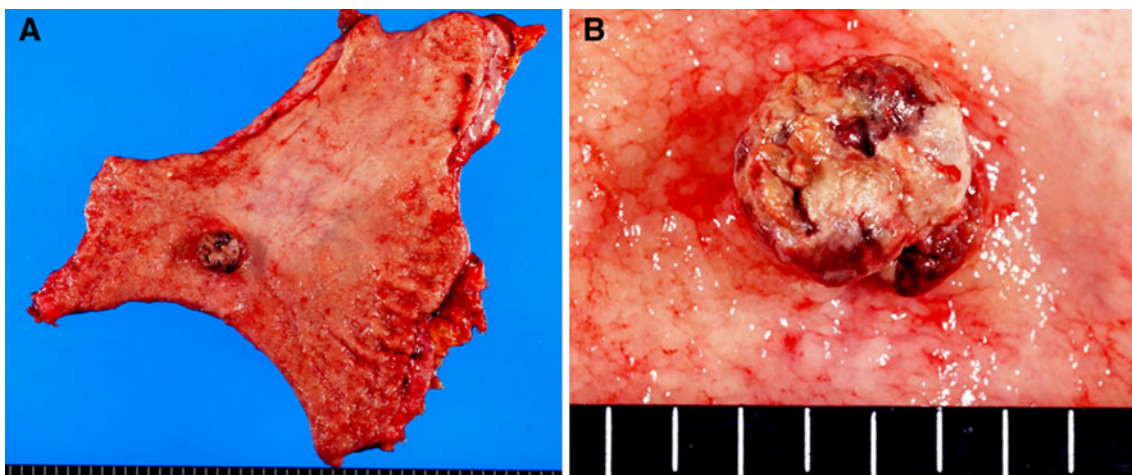
were also positive for S-100 protein. **a** H&E, ×400; **b** and **c** immunohistochemistry, ×200

removal of a melanoma or atypical melanocytic lesion from the skin or other organs [5, 17]. It is recognized that spontaneous regression of primary melanoma occasionally occurs [5, 7, 18, 19]. Moreover, metastatic melanoma of the GI tract is found in up to 60% of autopsies of patients who have died with primary cutaneous melanoma [3, 4]. Therefore, it is important to be aware of the danger of misinterpreting metastasis to the gastric wall. Our patient



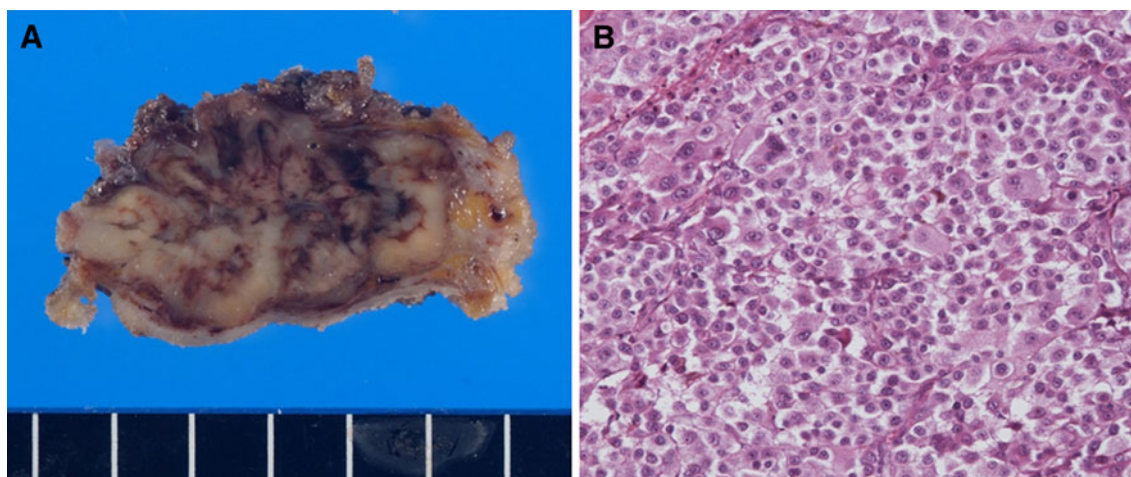
**Fig. 3** FDG-PET showed accumulation of tracer in the gastric tumor (arrow). No accumulation was observed in any other site

had no remarkable history and FDG-PET showed no accumulation of tracer, other than the tumor in the stomach. Therefore, occult primary MM in another site seems highly unlikely. A definitive diagnosis of MM was made by immunohistological examination of harvested tissues. Since melanocytes are very sensitive to S-100 proteins and HMB-45 antibodies, immunohistochemical staining with those pigments is important to confirm the presence of melanocytes in a tumor [5, 7, 20]. Immunohistochemical examination of the tumor from our patient revealed a positive reaction with S-100 proteins and HMB-45 antibodies, which led us to assume a primary MM of the stomach. MMs that arise in mucosal surfaces appear to be more aggressive and associated with a worse prognosis than cutaneous MMs. This poorer prognosis may be related to late diagnosis, an inherently more aggressive behavior of mucosal MM, or earlier dissemination because of the rich lymphatic and vascular supply of GI tract mucosa [5, 7, 8, 10]. It has been reported that the median overall survival associated with primary MM of the GI tract is 17 months, whereas that associated with primary MM of the stomach is only 5 months [21]. Although there are no widely accepted treatment protocols for primary MM of the GI tract, surgical resection is the only identifiable treatment modality for which independent predictive prognostic values have been demonstrated [21]. It was also reported that age >70 years, stage (localized or distant), tumor location, and lymph node involvement are independently predictive of the prognosis of patients with primary MM of the GI tract [21]. The factors of age, tumor location, and lymph node involvement were applicable to our patient. On the other hand, some serum substances are known tumor markers of cutaneous MM. Although there are few markers that are useful for early detection of MM [22], some markers



**Fig. 4** Surgical specimen from the distal gastrectomy. **a** There was a tumor in the posterior wall of the stomach. **b** The tumor was 2.0 × 1.9 × 0.9 cm in size





**Fig. 5** **a** Resected subcutaneous tumor. **b** Histological examination revealed sheet-like malignant cells similar to those in the tumor of the stomach. H&E,  $\times 200$

such as LDH, S-100B protein, neuron-specific enolase, and 5-S-cysteinyldopa are recognized as significant prognostic factors [23, 24]. We examined only serum LDH levels, which were within normal limits in our patient. To our knowledge, there are no reports on tumor markers of primary MM of the GI tract. Therefore, clinical studies are required to identify markers that could be used for the early detection or prognosis of MM of the GI tract. A number of randomized controlled trials (RCTs) have been conducted to evaluate the efficacy of chemotherapy, non-specific immune stimulants such as bacillus Calmette–Guerin, *Corynebacterium parvum*, levamisole, or combinations of these agents with dacarbazine chemotherapy [25], but none of these therapies is recognized as efficient. However, the use of interferon alpha (INF- $\alpha$ ) in the adjuvant setting has been approved recently for prolonging disease-free survival in patients with high-risk cutaneous MM [26]. Although RCTs have not shown their significant effect on overall survival, a meta-analysis of the results of 14 RCTs indicated that INF- $\alpha$  adjuvant treatment achieved significant improvement in both the disease-free survival and the overall survival of patients with high-risk cutaneous MM [27]. It is possible that the prognosis of our patient could have been improved if we had given him adjuvant therapy after gastrectomy. Future studies are required to assess whether adjuvant therapies using agents such as INF- $\alpha$  can prolong the survival of patients with MM of the GI tract.

**Conflict of interest** None of the authors have a conflict of interest to disclose.

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