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GASTRIC MELANOMA IN A 19-YEAR-OLD PATIENT: A RARE CASE AND A REVIEW OF DIAGNOSTIC PITFALLS

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ABSTRACT

Background: Gastric melanoma is exceptionally rare, typically metastatic and found in older adults. Primary cases are even rarer. We present a novel case in a 19-year-old male, underscoring unique diagnostic challenges due to his youth and lack of a known primary lesion.

Case description: A previously healthy 19-year-old male presented with postprandial vomiting, weight loss, constipation, and fatigue. Endoscopy revealed multiple pigmented gastric nodules. Biopsies confirmed malignant melanoma via immunohistochemistry (S100, HMB45, Melan A positive; cytokeratin, CD117, DOG1 negative). Imaging showed widespread metastases (hepatic, pulmonary, osseous). The patient deteriorated rapidly and died before a primary lesion could be identified. An autopsy was not performed.

Discussion: This case presents a profound diagnostic dilemma. The patient's age and absence of a primary lesion are highly atypical for metastatic melanoma. While the metastasis burden suggests a secondary origin, a primary gastric source could not be ruled out. This underscores that melanoma must be considered in the differential diagnosis of pigmented gastric lesions in all age groups. Immunohistochemistry is indispensable for confirming the diagnosis and excluding more common malignancies when faced with an atypical clinical presentation.

Conclusion: This report describes the youngest documented patient with gastric melanoma. It highlights the critical need to include melanoma in the differential diagnosis of young patients with gastrointestinal symptoms and endoscopic findings of pigmented lesions. The case emphasizes the aggressive potential of this disease and the essential role of immunohistochemical staining for timely and accurate diagnosis.

KEYWORDS

Gastric melanoma, melanocytic lesions, differential diagnosis, pigmented gastric tumors, endoscopic findings

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LEARNING POINTS

- Gastric melanoma, while rare, must be considered in the differential diagnosis of young patients presenting with non-specific gastrointestinal symptoms and pigmented endoscopic lesions, as it can occur in the absence of classic risk factors.
- A definitive diagnosis relies on a specific immunohistochemical panel (S100, HMB45, Melan-A) to confirm melanocytic origin and rule out more common gastric malignancies like carcinoma or gastrointestinal stromal tumour.
- This malignancy can be exceptionally aggressive and progress very rapidly in young adults, underscoring the critical importance of a prompt diagnosis and urgent intervention to improve outcomes.

INTRODUCTION/BACKGROUND

Melanoma is a malignant tumour arising from the transformation of melanocytes—pigment-producing cells normally found in the skin, mucous membranes, and certain deep tissues. In the vast majority of cases (approximately 95%), melanomas are cutaneous, with a steadily increasing global incidence, particularly among young adults and women[1]. Extracutaneous, or so-called mucosal or internal melanomas, are much rarer and often associated with a poor prognosis due to late diagnosis[2]. Among mucosal forms, the most common sites are the vulvovaginal region (18–40%), anorectal area (17–24%), and head and neck region (31–55%)[3]. In contrast, melanomas of the deep gastrointestinal tract, especially the stomach, are extremely rare, accounting for less than 1% of mucosal melanomas[4]. A recent systematic review identified only a few cases of primary gastric melanoma in the adult population[4]. In most cases, gastric involvement represents metastases from an advanced primary cutaneous melanoma[5]. These cases are typically diagnosed late, often in the context of multi-organ dissemination and occasionally postmortem[6].

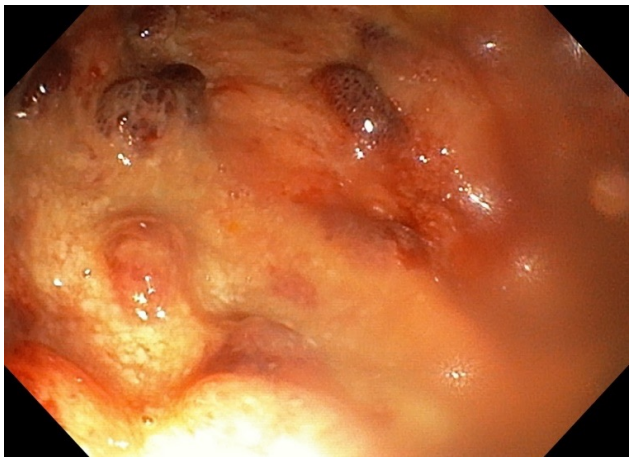


Figure 1. Endoscopic image showing multiple nodular blackish lesions.

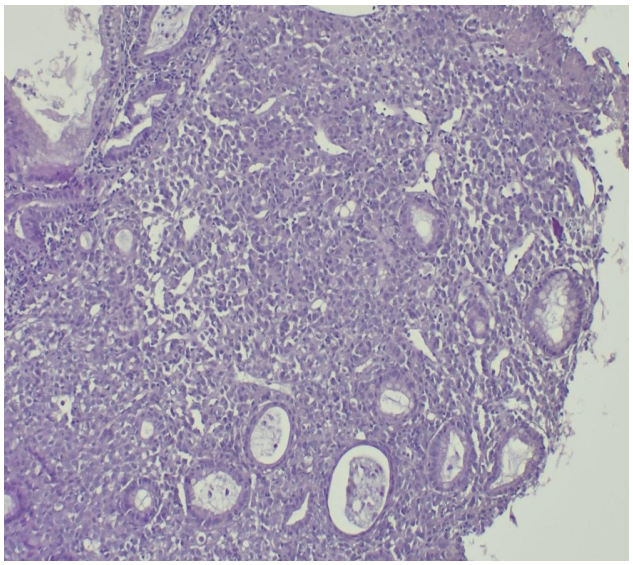


Figure 2. Melanin bleach technique: disappearance of melanin pigment and atypical tumor cell proliferation (×100).

Primary gastric melanoma represents an even more exceptional entity. Its diagnosis relies on strict criteria: the presence of a single histologically compatible lesion, the absence of current or prior cutaneous or ocular melanoma, and the exclusion of other primary sites through comprehensive clinical evaluation[4,7]. These criteria—defined in the World Health Organization (WHO) classification—can only be confirmed following a rigorous diagnostic workup that includes clinical, endoscopic, histopathological, immunohistochemical, and ideally, molecular analyses[8].

Diagnosis is particularly challenging when clinical symptoms are non-specific—such as vomiting, abdominal pain, and weight loss—and endoscopic findings mimic other pigmented (e.g., melanosis, pseudomelanosis) or non-pigmented tumours (e.g., poorly differentiated carcinomas, gastrointestinal stromal tumours (GIST), or clear cell sarcomas). In such cases, histochemical stains (e.g., melanin bleach) and immunohistochemistry (HMB45, S100, Melan A, SOX10) are essential for definitive diagnosis. At the molecular level, mucosal melanomas display a mutation landscape that differs significantly from that of cutaneous types. They show a higher prevalence of mutations in KIT, NF1, or SF3B1, along with a generally lower tumour mutational burden—features that influence both diagnosis and therapeutic strategies[8].

Age is also a critical factor in diagnostic assessment. Mucosal melanomas predominantly affect elderly patients, with a median age between 60 and 70 years[9]. Therefore, the occurrence of gastric melanoma in an adolescent or young adult is extremely unusual. To our knowledge, no case of gastric melanoma in a 19-year-old patient has been reported in the scientific literature to date. In this context, we report an exceptional clinical case of gastric melanoma in a 19-year-old young adult, investigated through endoscopic, histochemical, and immunohistochemical examinations. This

case presents significant diagnostic challenges due to the rarity of the location, the absence of an identifiable primary site, and the patient's unusually young age. We aim to raise awareness among pathologists and clinicians to consider this diagnosis, even in atypical clinical scenarios.

CASE DESCRIPTION

A 19-year-old male with no notable medical history presented 3 months prior to diagnosis with delayed postprandial vomiting—initially food-based, then bilious—associated with chronic constipation, dizziness, intermittent fever, and unquantified weight loss.

An upper gastrointestinal endoscopy revealed multiple blackish nodules in the fundus and body of the stomach *(Fig. 1)*. Gastric biopsies were obtained for histopathological evaluation. Microscopic examination revealed moderate chronic gastritis with lymphoid follicles, along with numerous clusters of tumour cells containing brown intracellular deposits that obscured nuclear details. Perls' stain was negative, excluding hemosiderin pigmentation. However, melanin bleach staining effectively removed the pigment, confirming its melanin nature and allowing for better cytological assessment *(Fig. 2)*. The tumour was composed of cells of varying morphology—ovoid, polygonal, and epithelioid—with moderately abundant eosinophilic cytoplasm, anisokaryotic nuclei, and irregular chromatin. The mitotic rate was estimated at 9.43 mitoses/mm^2.

Immunohistochemical studies showed that tumour cells were negative for cytokeratin, CD117, and DOG1, thereby excluding diagnoses such as poorly differentiated carcinoma and GIST. In contrast, the tumour exhibited nuclear and cytoplasmic positivity for S100, and diffuse cytoplasmic positivity for HMB45 and Melan A, supporting the diagnosis of malignant melanoma.

A computed tomography scan of the chest, abdomen and pelvis revealed a nodular liver, mild ascites, and multiple metastatic lesions in the peritoneum, lungs, and bones, indicating an advanced stage of metastatic disease. A comprehensive staging workup was scheduled to identify a potential primary melanoma site. This included total skin dermhscopy, ophthalmologic examination (to assess for uveal melanoma), ear, nose and throat evaluation, anorectal examination, and colonoscopy. Unfortunately, the patient died due to rapid disease progression before these evaluations could be completed. No autopsy was performed, per the family's wishes, limiting the ability to definitively classify the gastric melanoma as primary or secondary.

DISCUSSION

Gastric melanoma is a rare and atypical entity, most frequently encountered as a metastatic manifestation of advanced cutaneous melanoma. The small intestine, colon, and stomach represent the most common gastrointestinal sites affected by melanoma metastases[5]. In contrast, primary gastric melanoma is extremely rare, with only a few cases reported in the literature[4]. When such a lesion

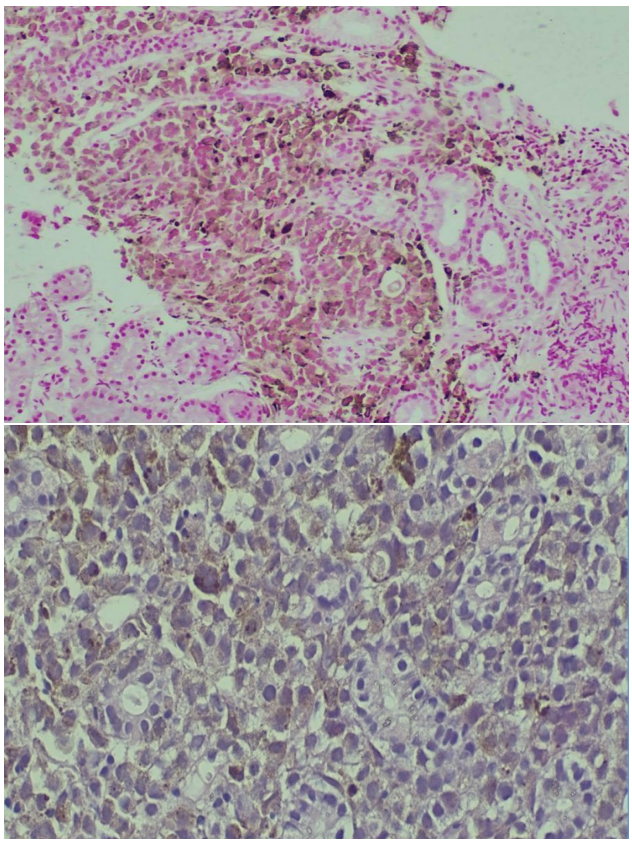


Figure 3. Tumor cells with cytonuclear atypia (H&E, ×400).

is identified, it is crucial to distinguish between a primary and metastatic origin. Several diagnostic criteria have been proposed to support a diagnosis of primary gastric melanoma. These include histologically confirmed melanoma localized to a single gastric site, absence of current or prior cutaneous melanoma or atypical pigmented skin lesions, and no evidence of ocular, anal, or other mucosal melanomas[3]. In our case, none of these potential extra-gastric primary sites were detected, though the confirmation remained incomplete due to the patient's early death.

The patient's age—19 years—is exceptionally uncommon for both cutaneous and mucosal melanoma. To our knowledge, this is the first documented case of gastric melanoma in a young adult. Mucosal melanoma typically affects older patients, with a median age around 70 years[2]. Orbital melanoma cases reported by Li et al.[9] and Chao et al.[10] involved patients with a median age of 50 and a young patient, 39 years old, respectively. While cutaneous melanomas do occur in young individuals—especially females[1]—our patient was male, further contributing to the clinical rarity.

The initial clinical presentation was non-specific but aggressive, with symptoms including dizziness, vomiting, unquantified weight loss, and constipation appearing 3 months before diagnosis. Gastrointestinal symptoms such as fatigue, abdominal pain, anorexia, hematemesis, and melena are typical, although obstruction or perforation may also occur in rare instances. Endoscopic evaluation revealed multiple darkly pigmented nodules in the gastric fundus and body. At the time of diagnosis, the patient already had metastases to the liver, peritoneum, lungs, and bones.

Pigmented vs. non-pigmented lesions	Differential diagnosis	Definition	Microscopic examination	Histochemical examination	Immunohistochemical or molecular study
Pigmented lesion	Melanosis	Non-inflammatory bowel disease Associated with anthraquinone-based laxative use	Brownish lipofuscin pigment in lamina propria macrophages	PAS+	Not required for diagnosis
	Gastric and duodenal pseudomelanosis	Linked to increased oral iron intake, hypertension, diabetes, or end-stage renal failure	Brownish iron pigment in macrophages of gastric/duodenal lamina propria	Perls+	Not required for diagnosis
Non-pigmented lesion	Gastrointestinal stromal tumour	Mesenchymal tumour with variable behaviour, differentiated toward interstitial cells of Cajal	Broad morphological spectrum: spindle, epithelioid, or pleomorphic sarcomatoid cells		CD117+ DOG1+
	Clear cell sarcoma	Typically affects aponeurotic/tendinous areas of extremities; rarely visceral	Monomorphic proliferation of round/oval cells with clear cytoplasm and prominent nucleoli		S100+ HMB45+ Melan-A+ t(12;22)(q13;q12) translocation
	Malignant peripheral nerve sheath tumour	Malignant tumour often arising from peripheral nerves, pre-existing benign nerve sheath tumours, or neurofibromatosis type 1	Monomorphic spindle cells, necrotic areas, large vascular spaces, perivascular infiltration		Focal S100+ Focal Sox10+
	Poorly differentiated carcinoma	Primary gastric epithelial tumour	Anaplastic cells lacking specific cytological/ architectural differentiation		Cytokeratin AE1/AE3+

Abbreviation: PAS, Periodic acid Schiff.

Table 1. Main differential diagnoses of gastric melanoma.

Gastrointestinal metastases from melanoma are rarely isolated and usually appear in the context of widespread disease, which was consistent with our findings.

Endoscopically, primary gastric melanoma may present as a pigmented ulcerated lesion—a feature often considered pathognomonic[4]. Metastatic lesions, however, show greater variability, often presenting as multiple pigmented, ulcerated nodules, submucosal masses, diffuse ulcerations, or lesions mimicking gastric melanosis. Amelanotic metastases, though rare, may also occur[6].

Histologically, melanoma is usually composed of sheets or nodules of pleomorphic epithelioid or spindle-shaped malignant melanocytes. Pigmentation can range from abundant to absent. In our patient, melanin pigment was prominent, masking cytological detail and impeding identification of in situ components, which are essential to confirming a primary origin[3,4]. The use of the melanin bleach technique, a robust method for both histological and molecular analysis, allowed removal of pigment and facilitated better visualization of cytologic and nuclear features, including cytonuclear atypia. However, no in situ component was observed *(Fig. 3)*.

Given the unusual age and location, immunohistochemical analysis was crucial. The tumour demonstrated nuclear and cytoplasmic S100 positivity, nuclear SOX10 staining, and cytoplasmic expression of Melan-A (MART1) and HMB-45. PRAME positivity, if present, could aid in identifying a primary melanoma. It is noteworthy that dedifferentiated metastatic melanomas may lose melanocytic markers and aberrantly express cytokeratin or muscle markers[4]. In our case, the immunoprofile was consistent with melanoma and confirmed the diagnosis *(Fig. 4)*.

The differential diagnosis for pigmented gastric lesions of young patients includes pseudomelanosis and melanosis, although the latter is undocumented in gastric locations. In our case, pseudomelanosis was considered due to the patient's age and chronic constipation. Perls' stain for hemosiderin was negative, and melanin bleach confirmed the pigment's melanocytic origin *(Fig. 2)*. Other differential diagnoses, especially in the setting of amelanotic lesions, include GIST, clear cell sarcoma, malignant peripheral nerve sheath tumours, and poorly differentiated carcinomas. These entities were excluded based on morphology and immunohistochemistry: CD117 and DOG1 negativity excluded GIST, cytokeratin negativity ruled out carcinoma, and the morphology was inconsistent with peripheral nerve sheath tumours and clear cell sarcomas *(Table 1)*.

Molecular profiling of melanoma has therapeutic relevance. Mucosal melanomas should be tested for BRAF and KIT mutations to guide potential targeted therapy. The

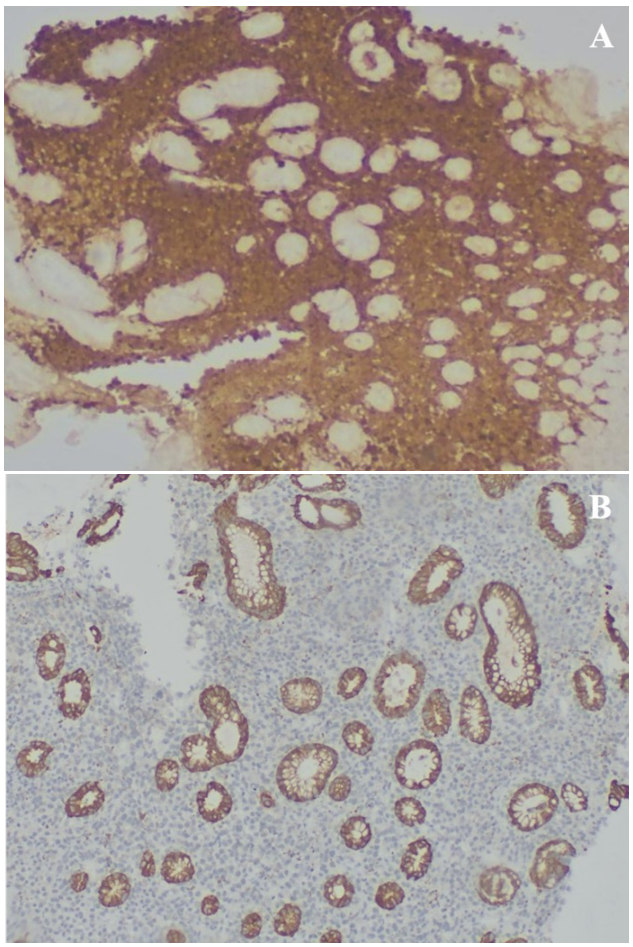


Figure 4. A) Tumor cells positive for S100 (nuclear/cytoplasmic, ×40), and B) negative cytokeratin staining (internal control: glandular structures, ×40).

identification of driver mutations may also help infer tumour origin. For example, KIT mutations are frequently found in mucosal or acral melanomas, while GNAQ/GNA11 mutations are typical of blue nevus–associated or uveal melanomas. Tumours with a high mutational burden generally respond better to immune checkpoint inhibitors. In our case, molecular testing could not be performed due to logistical limitations and the patient's rapid deterioration. Gastrointestinal melanomas, particularly primary gastric melanomas, have a poor prognosis. Reported median overall survival for mucosal gastrointestinal melanomas is approximately 17 months[6], while primary gastric melanomas specifically carry the worst prognosis with a median survival of only 5 months. For metastatic gastric melanoma, survival is typically under one year. Our patient succumbed to the disease just 4 months after symptom onset, which was consistent with its aggressive nature. This case is limited by the absence of a complete diagnostic workup to rule out other potential primary sites, owing to the patient's early death. No autopsy was performed. Nevertheless, it highlights the critical importance of considering melanoma in the differential diagnosis of atypical gastric lesions, even in young individuals. It also emphasizes the indispensable role of advanced histological, histochemical, immunohistochemical, and—when feasible—molecular techniques in establishing an accurate diagnosis when conventional criteria are insufficient.

CONCLUSION

This rare case highlights the diagnostic challenges associated with gastric melanoma, whether primary or metastatic, particularly when occurring in atypical clinical settings such as in young adults. It underscores the importance of considering melanoma in the differential diagnosis of poorly differentiated gastric tumors, even in the absence of classic pigmentation. Given the potential for deceptive histological and clinical presentations, a comprehensive diagnostic approach is essential—incorporating histological, histochemical, immunohistochemical, and, when feasible, molecular analyses. Vigilance is warranted when evaluating any unusual gastric lesion, as timely recognition of melanoma can significantly influence management strategies, despite the generally poor prognosis associated with this cancer.

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