Korean J Gastroenterol Vol. 83 No. 1, 33-36
https://doi.org/10.4166/kjg.2023.136
pISSN 1598-9992 eISSN 2233-6869

CASE REPORT

A Curious Case of Primary Gastric Mucosal Melanoma

Zahabia Sohail[1], Mirza Rameez Samar[2], Neelam Jawed Qureshi[3], Sidra Arshad[4] and Adeeba Zaki[2]

Departments of Gastroenterology[1], Medical Oncology[2], Medicine[3], and Pathology[4], The Aga Khan University Hospital, Karachi, Pakistan

Malignant melanoma is a neoplasm of melanin-producing cells predominantly of cutaneous origin, which uncommonly develops within gut mucosa. We present the case of a 58-year-old woman with complaints of abdominal pain, loss of appetite and weight. Esophagogastroduodenoscopy revealed a gastric mass and systemic imaging demonstrated widespread nodal and bilateral adrenal gland involvement. Histopathology of the gastric mass confirmed primary malignant mucosal melanoma of the stomach. The patient received three cycles of Nivolumab but did not respond, and thus, was then offered best supportive care. Although infrequent, mucosal melanoma can arise from the gastrointestinal tract, and in contrast to the cutaneous form, advanced disease usually has a dismal prognosis and responds poorly to immune checkpoint inhibitors. Primary gastric melanoma is an aggressive disease that is diagnosed by exclusion after the differential diagnosis of metastasis from a cutaneous or unknown primary site has been conducted. If available, patients with treatment-naïve mucosal melanoma should be considered for enrollment in clinical trials. **(Korean J Gastroenterol 2024;83:33-36)**

Key Words: Gastric neoplasm; Immunotherapy; Esophagogastroduodenoscopy; Malignant melanoma; Gastrointestinal tract

INTRODUCTION

Malignant melanoma is a neoplasm of melanin-producing cells. In the United States, mucosal melanoma (MM) accounts for only 1.3% of melanomas, and its incidence has remained stable over time despite a rapid increase in that of cutaneous melanoma.[1,2] In 2020, an estimated 325,000 people were diagnosed with melanoma.[3]

Although several risk factors, such as exposure to the ultraviolet component of sunlight and tanning beds and lamps, are known to increase the risk of cutaneous melanoma development, no clear environmental or other predisposing risk factor has been identified for MM. Most cases, when diagnosed at an early stage, are treated by surgical excision with curative intent, but those that present with metastasis require systemic therapy with palliative intent.

The treatment paradigm of melanoma has shifted since the introduction of immune checkpoint inhibitors (ICIs). Several ICIs have produced promising results in the setting of advanced melanoma. Inhibitors targeting PD-1 (programmed cell death 1), such as Nivolumab and Pembrolizumab, CTLA-4 (cytotoxic T lymphocyte-associated protein 4) inhibitors (e.g., Ipilimumab), and inhibitors of LAG-3 (lymphocyte-activated gene-3), like Relatlimab, are key therapeutic agents in this field. Here, we report a rare case of primary gastric MM, which, to the best of our knowledge, has not been previously reported in South Korea.

CASE REPORT

A 58-year-old Asian woman presented at our gastroenterology clinic with complaints of right upper quadrant pain of duration one month associated with loss of weight and appetite. The pain was mild in intensity, dull in character, and

Received November 13, 2023. **Revised** December 14, 2023. **Accepted** December 29, 2023.

Correspondence to: Mirza Rameez Samar, Department of Medical Oncology, The Aga Khan University Hospital, Karachi 74600, Pakistan. Tel: +92 324 2006239, E-mail: rameez_samar_1992@hotmail.com, **ORCID:** https://orcid.org/0000-0002-4553-4677

Financial support: None. Conflict of interest: None.

radiated to the right shoulder. Her medical history included diabetes, hypertension, and recent cholecystectomy (1.5 months previously), and the patient denied any significant family, allergic, or addiction history.

Physical examination revealed noticeable pallor accompanied by tenderness in the right upper quadrant. No associated jaundice, cyanosis, clubbing of hands, or any palpable lymph nodes was observed, and no cutaneous or mucosal lesion was detected by cutaneous, mucosal, digital rectal, and per-vaginal examinations. However, abdominal ultrasound (US) of the abdomen visualized a cystic mass in the left hepatic lobe, and subsequent computed tomography (CT) of the chest, abdomen, and pelvis revealed multifocal enhancing nodular gastric wall thickening at the gastric cardia, a 2.3 cm mass at the gastric body, a 1.4 cm mass at the greater omentum, and bilateral adrenal gland masses suggestive of widespread involvement. Esophagogastroduodenoscopy (EGD) then demonstrated three ulcerated masses in the stomach body, that is, two in the proximal and one in the distal stomach (Fig. 1).

1. Diagnosis and management

A biopsy was taken from the edges of all three masses. Histopathology revealed fragments of gastric mucosa with widened stroma and atypical cellular proliferation featuring large cells with little cytoplasm and large nuclei with conspicuous nucleoli, apoptotic bodies, and abnormal mitoses. Immunohistochemical staining exhibited reactivity for SOX-10, HMB-45, and S100 (patchy) with Ki67 being high whereas Cytokeratin AE1/AE3, LCA, CD30, CD79a, CD138, DOG1 and Synaptophysin were negative (Fig. 2). Malignant melanoma was diagnosed based on these findings. Staging positron emission tomography-computed tomography revealed a large mass arising from the lesser curvature of the stomach with

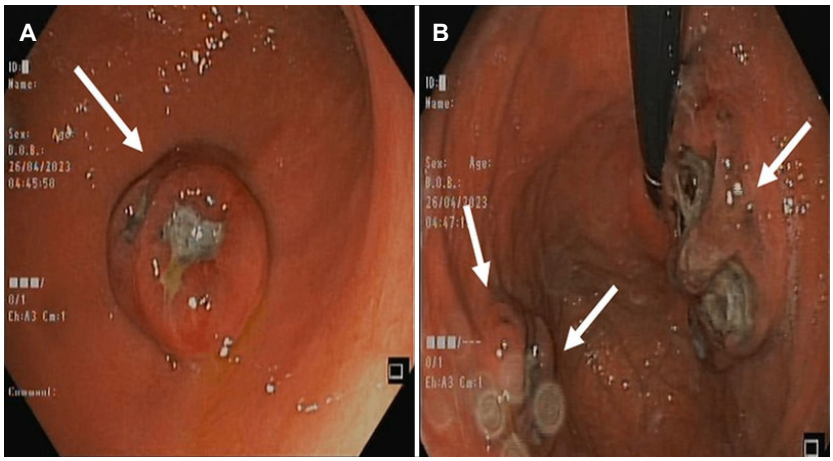

Fig. 1. Endoscopy showing: (A) An ulcerated gastric mass. (B) Three ulcerated masses in the body, one large, one small, at the proximal gastric body along lesser and greater curvature (arrows) respectively with a small mass at distal gastric body.

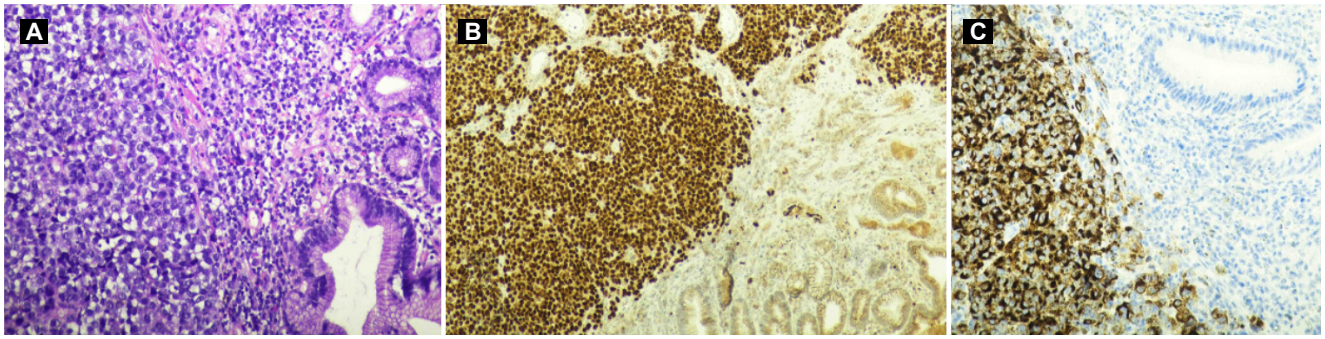

Fig. 2. (A) H&E stain under 20× magnification, showing large tumor cells with pleomorphic nuclei and abundant cytoplasm. (B) Tumor cells under 20x magnification, show diffuse nuclear positivity for immuno-histochemical marker SOX-10. (C) Tumor cells under 20x magnification, show diffuse cytoplasmic positivity for immuno-histochemical marker HMB-45.

bilateral adrenal gland deposits, a metastatic deposit in the left pleura infiltrating the 6th rib, multiple abdominal lymph nodes in the suprapancreatic, preaortic, paraaortic, and aortocaval regions and a large confluent mass in the left axilla, confirming metastatic disease.

Laboratory investigations, including complete blood count, biochemistry profile, and liver function tests, were all within normal limits. She was started on intravenous Nivolumab immunotherapy at 240 mg once every two weeks. However, after three cycles, her clinical condition deteriorated, and oral candidiasis and a purulent discharge from the left axillary mass developed. She was treated with intravenous antibiotics and antifungals. However, on admission day 3, her Glasgow Coma Scale (GCS) score fell . Brain magnetic resonance imaging suggested diffuse sulcal enhancement, suggesting leptomeningeal involvement, but lumbar puncture and cerebrospinal fluid analysis failed to reveal any abnormality. The patient was then administered intravenous steroids, but unfortunately, her GCS score dropped. Her family was then counseled, and due to a persistently low GCS, best supportive management was provided.

DISCUSSION

Melanomas are usually cutaneous in origin and can develop anywhere in the body, though most are encountered in skin areas more exposed to the sun, i.e., trunk, extremities, head, neck, and face. Less commonly, melanoma involves other sites, such as nail beds, palms, or soles. Melanoma can also arise in areas where neural crest cells migrate during the prenatal period, including the eyes, brain, nasal cavity, throat, and gastrointestinal tract.[4] In clinical practice, cutaneous melanoma is more commonly encountered than MM, which arises from melanocytes within the mucosal epithelium in different regions, such as the respiratory tract, alimentary canal, or genitourinary tract. Unlike the cutaneous form, there is no proper morphological classification of MM.[5] The American Joint Association of Cancer has proposed a staging classification for head and neck, vulvovaginal, and anorectal MM, but no consensus has been reached for those of gastric or intestinal origin.

A systematic review found that the principal symptoms associated with malignant melanoma of the stomach were abdominal pain (64%), weight loss (48%), and hematemesis or melena (32%),[6] which indicated our patient had a typical presentation. In general, patients diagnosed with MM are 60 and 70 years old[7] and tend to be female.[8] On the other hand, cutaneous melanomas are usually observed in individuals with a fair complexion, whereas MMs occur more in Black, Asian, and Hispanic individuals. Nonetheless, despite this epidemiologic variation, the absolute incidence of MM is higher among Caucasians.[9] Furthermore, approximately 40 percent of MMs are amelanotic,[10] possibly because of an enteric neuroendocrine tissue origin and subsequent malignant conversion or because they originated from neuroblastic Schwann cells of the intestinal autonomous nervous system.[11]

Patients with MM tend to present with de novo metastatic disease more often than patients with cutaneous melanoma (23% vs. 5%).[12] Also, malignant melanomas usually metastasize to the gastrointestinal tract, whereas primarily melanomas of gastric origin are uncommon[13]; this may be explained by a lack of visibility at primary sites and the absence of clinical symptoms. Furthermore, MM is an aggressive entity that proliferates rapidly and, when left unchecked, can lead to widespread involvement and poor prognoses.

Metastatic disease is typically treated with palliative systemic therapy. However, cutaneous melanomas that do not metastasize are largely curable, and even those that do may respond quite successfully to ICIs. However, the same cannot be said for MMs. In a systematic review of 25 patients with primary gastric melanoma, six had metastatic disease, and their 5-year survival rate was <5 percent.[14] Furthermore, ICI treatment only increased the 5-year overall survival rate to 25 percent,[15] which we ascribe to a lack of understanding of the biology and treatment of MM in different anatomical locations.

This case highlights the clinical presentation, diagnosis, and challenges associated with the diagnosis of non-cutaneous malignant melanoma, which demands thorough cutaneous, ophthalmic, and mucosal examinations to ensure timely detection and treatment. Malignant melanoma with a gastrointestinal tract, especially stomach, origin has rarely been reported. Immune checkpoint inhibitors offer potential cures, but not all patients respond favorably due to the aggressive nature of the disease. More studies are needed to understand the pathogenesis of this uncommon neoplasm and to enhance the effectivenesses of diagnostic and therapeutic approaches.

REFERENCES

1. Bishop KD, Olszewski AJ. Epidemiology and survival outcomes of ocular and mucosal melanomas: a population-based analysis. Int J Cancer 2014;134:2961-2971.
2. Saginala K, Barsouk A, Aluru JS, Rawla P, Barsouk A. Epidemiology of melanoma. Med Sci (Basel) 2021;9:63.
3. Samar MR, Merchant S, Zehra NE, Idrees R, Khan SR. Thin on the ground: Primary mucosal melanoma of the nasal cavity. Int J Surg Case Rep 2023;111:108929.
4. Heistein JB, Acharya U, Mukkamalla SKR. Malignant melanoma. In: StatPearls. Treasure Island, FL: StatPearls Publishing, 2023.
5. Zechariah P, Surendran S, Abraham V, Samarasam I. Primary malignant melanoma of the stomach: a rare entity. BMJ Case Rep 2020;13:e234830.
6. Ionescu S, Nicolescu AC, Madge OL, Simion L, Marincas M, Ceausu M. Intra-abdominal malignant melanoma: Challenging aspects of epidemiology, clinical and paraclinical diagnosis and optimal treatment-a literature review. Diagnostics (Basel) 2022; 12:2054.
7. Konuthula N, Khan MN, Parasher A, et al. The presentation and outcomes of mucosal melanoma in 695 patients. Int Forum Allergy Rhinol 2017;7:99-105.
8. Al-Haseni A, Vrable A, Qureshi MM, et al. Survival outcomes of mucosal melanoma in the USA. Future Oncol 2019;15:3977-3986.
9. Bai X, Mao L, Guo J. Comments on Chinese guidelines for diagnosis and treatment of melanoma 2018 (English version). Chin J Cancer Res 2019;31:740-741.
10. Takehara K, Nakamura H, Mizunoe T, Nogawa T. Primary malignant melanoma of the vagina with a survival of longer than 5 years after recurrence: case report and review of the literature. Gynecol Obstet 2013. doi:10.4172/2161-0932.1000183.
11. Kohoutova D, Worku D, Aziz H, Teare J, Weir J, Larkin J. Malignant melanoma of the gastrointestinal tract: Symptoms, diagnosis, and current treatment options. Cells 2021;10:327.
12. Tomicic J, Wanebo HJ. Mucosal melanomas. Surg Clin North Am 2003;83:237-252.
13. Goral V, Ucmak F, Yildirim S, et al. Malignant melanoma of the stomach presenting in a woman: a case report. J Med Case Rep 2011;5:94.
14. Schizas D, Tomara N, Katsaros I, et al. Primary gastric melanoma in adult population: a systematic review of the literature. ANZ J Surg 2021;91:269-275.
15. Haimowitz S, Cohen DA, Dhanda A, Barron K, Povolotskiy R, Roden D. Mucosal melanoma of the oral cavity: What is the role of elective neck dissection? Laryngoscope 2023;133:317-326.