

From Eye to Gut: A Melanotic Journey

Iskander, Peter MD ¹; Hayat, Umar MD ²; Daniel, Mina MD ¹; Ali, Khizar Amin MD ³; Shahzad, Muhammad Talha MD ⁴; Ali, Aman MD ³

1. The Wright Center for GME, Scranton, PA
2. Geisinger Wyoming Valley Medical Center, Wilkes-Barre, PA
3. Wilkes-Barre General Hospital, Wilkes-Barre, PA
4. University of Michigan Health-West Hospital, Wyoming, MI

Abstract:

Uveal melanomas are one of the most common primary malignancies of the eye [1]. Metastasis to solid organs has been documented, but very rarely has it been noted to occur in the stomach [2]. Symptoms can depend on the site of metastasis and can include, but are not limited to, nausea/vomiting, iron deficiency, malabsorption, obstruction, etc. We present a case of a patient with choroidal melanoma with associated development of esophageal, gastric, hepatic, and lung malignancies.

Case:

A 64-year-old male with a past medical history of intermittent palpitations, nicotine abuse, and choroidal melanoma of the left eye status post radiation (10/2022) presented due to sporadic episodes of dysphagia associated with occasional nausea and vomiting.

The patient proceeded to undergo EGD, for which findings of esophageal inflammation were observed; biopsy noted marked atypia, and high pan-cytokeratin/Ki-6,7, which was concerning for squamous cell carcinoma (SCC).

Repeat EGD showed dysplastic-looking epithelia between 34 cm - 37 cm from the incisors (Figure 1). Endoscopic mucosal resection was performed. PET-CT was unremarkable for any obvious areas of abnormal uptake or lymphadenopathy. The EMR scar site was observed upon follow-up EGD, as well as a pigmented gastric polyp (Figure 2). Chromoendoscopy of the esophagus was unremarkable, with scar tissue pathology biopsies noting benign esophageal squamous mucosa. Pathology of the polyp, however, was concerning for metastatic malignant melanoma.

The tumor was positive for SOX10, Mart-1, HMB45, and BRAF (+ cytoplasmic staining) and negative for pan-cytokeratin and CD68 immunostains, which supported the diagnosis.

Repeat CT showed interval development of liver and lung nodules concerning further metastasis. The patient is to follow up to discuss further management and goals of care.

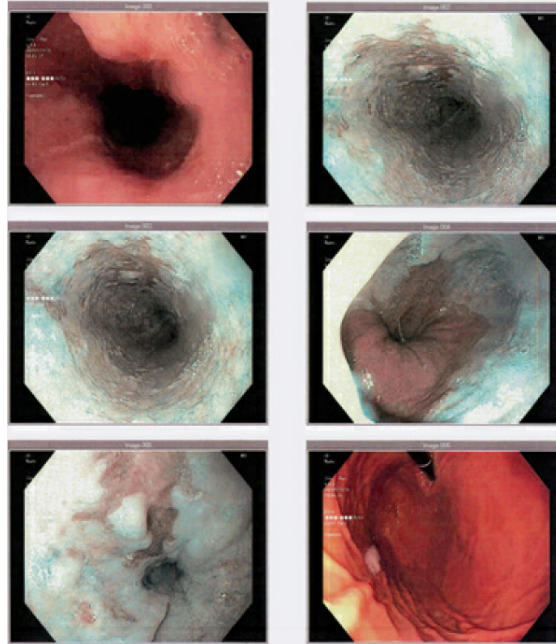


Figure 1: EGD findings showing dysplastic-appearing epithelia 34 cm - 37 cm from the incisor.

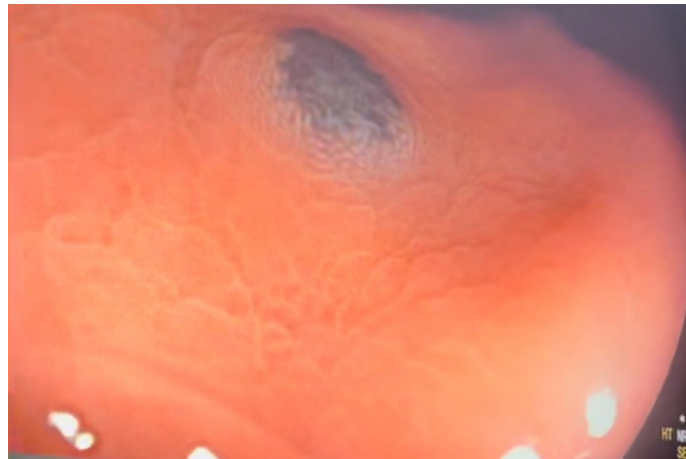


Figure 2: Pigmented gastric polyp.

Discussion:

Unlike cutaneous melanomas, known to metastasize to the GI tract, choroidal melanomas usually have a predilection for hematogenous spread to the liver [3]. Although there have been some cases detailing the possibility of esophageal carcinomas metastasizing to the eye in literature, no obvious reports have noted the opposite; this begs the question of whether the 2 cancers were somehow related or separate entities. Of the two, the latter is more likely, as melanoma and SCC have different histologies and, as far as we are aware, one type of cancer cannot turn into another. Of note, however, there have been cases reported of mixed-type tumors [4]. The patient was known to have a history of nicotine abuse, which is one of the most common risk factors for esophageal SCC [5].

As per the gastric polyp, very few cases in the literature have noted a primary choroidal melanoma metastasizing to the stomach. Pathology of the polyp did have markers that supported the evidence of choroidal melanoma metastasis. SOX10 is a transcription factor for which overexpression has been related to melanoma and prostate cancer [6]. Mart-1 is a normal transmembrane protein found in most melanocytes for which increased expression is associated with malignant melanoma [7]. Human Melanoma Black (HMB45) is a monoclonal antibody that reacts with gp100 proteins, which are expressed in immature and activated melanocytes [8]. BRAF belongs to the family of proto-oncogenes for which mutations can lead to unregulated cell signaling and growth [9].

The mean survival time has been noted to be as little as 4-6 months when there is evidence of metastasis [10]. However, there have been documented long-term disease-free periods in some who underwent early surgical resection with appropriate chemotherapy [11]. Ultimately, the management is a combination of immunotherapy and palliative interventions.

Conclusion:

A high index of suspicion should be taken with patients with previously known melanomas due to their vague metastatic symptoms. Regular mucosal inspections should be conducted with appropriate immunohistochemical biopsies for any suspicious changes [12]. Goals of care and management discussions, for chemotherapy and palliation, should be had abruptly as the signs of metastasis render a very poor prognosis.

References:

1. Ye Z, Yang Z, Zheng S, Wang W. Robot-assisted laparoscopic surgery for abdominal metastatic melanoma mimicking a gastrointestinal stromal tumor: A case report and review of the literature. *Medicine (Baltimore)*. 2018 Jun;97(26):e11207. doi: 10.1097/MD.00000000000011207. PMID: 29952974; PMCID: PMC6039597.
2. Baba S, Akiyama Y, Endo F, Nikai H, Sugimoto R, Umemura A, Katagiri H, Hasegawa Y, Iwaya T, Nitta H, Koeda K, Sugai T, Sasaki A. Laparoscopic distal pancreatectomy for metastatic melanoma originating from the choroidal membrane: a case report. *Surg Case Rep*. 2021 Dec 20;7(1):268. doi: 10.1186/s40792-021-01345-x. PMID: 34928463; PMCID: PMC8688594.
3. Kaila, Vishal MD1; Lager, Donna J. MD2; Jain, Rajeev MD, FACP3. Choroidal Melanoma Metastases to the Stomach and Duodenum: 2629. *American Journal of Gastroenterology* 113():p S1461-S1462, October 2018.
4. Kochoumian E, Kazlouskaya V, Mangold A, Lal K, Maia-Cohen S, Elston DM. Tumor with the features of both squamous cell carcinoma and melanoma (melanocarcinoma). *Indian Dermatol Online J*. 2015 May-Jun;6(3):217-9. doi: 10.4103/2229-5178.156422. PMID: 26009723; PMCID: PMC4439757.
5. Tarazi M, Chidambaram S, Markar SR. Risk Factors of Esophageal Squamous Cell Carcinoma beyond Alcohol and Smoking. *Cancers (Basel)*. 2021 Feb 28;13(5):1009. doi: 10.3390/cancers13051009. PMID: 33671026; PMCID: PMC7957519.
6. Mohamed A, Gonzalez RS, Lawson D, Wang J, Cohen C. SOX10 expression in malignant melanoma, carcinoma, and normal tissues. *Appl Immunohistochem Mol Morphol*. 2013 Dec;21(6):506-10. doi: 10.1097/PAI.0b013e318279bc0a. PMID: 23197006.
7. Fetsch PA, Marincola FM, Filie A, Hijazi YM, Kleiner DE, Abati A. Melanoma-associated antigen recognized by T cells (MART-1): the advent of a preferred immunocytochemical antibody for the diagnosis of metastatic malignant melanoma with fine-needle aspiration. *Cancer*. 1999 Feb 25;87(1):37-42. PMID: 10096358.

8. Rothberg BE, Moeder CB, Kluger H, Halaban R, Elder DE, Murphy GF, Lazar A, Prieto V, Duncan LM, Rimm DL. Nuclear to non-nuclear Pmel17/gp100 expression (HMB45 staining) as a discriminator between benign and malignant melanocytic lesions. *Mod Pathol*. 2008 Sep;21(9):1121-9. doi: 10.1038/modpathol.2008.100. Epub 2008 Jun 13. PMID: 18552823; PMCID: PMC2570478.
9. Aksenenko MB, Kirichenko AK, Ruksha TG. Russian study of morphological prognostic factors characterization in BRAF-mutant cutaneous melanoma. *Pathol Res Pract*. 2015 Jul;211(7):521-7. doi: 10.1016/j.prp.2015.03.005. Epub 2015 Apr 2. PMID: 25888143.
10. Chamoun, Romy MD1; Lander, Jared DO2; Collazzo, Jack A. MD3. S3649 Choroidal Melanoma: A Rare Cause of Gastric/Duodenal Pigmented Macules. *The American Journal of Gastroenterology* 117(10S):p e2288-e2289, October 2022. | DOI: 10.14309/01.ajg.0000871236.78470.89
11. Lin S, Wan D, Chen H, Chen K, Zheng S. Complete resection of isolated hepatic metastatic uveal melanoma with a notably long disease-free period: A case report and review of the literature. *Oncol Lett*. 2015 Jul;10(1):196-200. doi: 10.3892/ol.2015.3217. Epub 2015 May 18. PMID: 26170998; PMCID: PMC4487100.
12. Liang KV, Sanderson SO, Nowakowski GS, Arora AS. Metastatic malignant melanoma of the gastrointestinal tract. *Mayo Clin Proc*. 2006 Apr;81(4):511-6. doi: 10.4065/81.4.511. PMID: 16610571.