

# Large Necrotic Mass in the Small Bowel

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## ABSTRACT

Melanoma of unknown primary (MUP) is a melanoma found in sites other than the skin, mucosa, or eye. It is most commonly present in lymph nodes and least frequently in visceral organs. Diagnosis is difficult given its internal presentation and is often late stage with poor prognosis. We report an 89-year-old man who presented with weakness, a 27-kg weight loss, and gastrointestinal bleeding. He was found to have a large necrotic mass in the small bowel consistent with melanoma. Although he had extensive skin, anogenital, and ocular examinations, no cutaneous lesion was identified, therefore leading to a diagnosis of MUP.

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## INTRODUCTION

Melanoma of unknown primary (MUP) is defined as malignant melanoma present in sites other than the skin, mucosa, or eye. Most commonly, MUP is found in lymph nodes followed by subcutaneous tissues and visceral organs. Approximately 3% of all melanomas are present in distal locations with no known primary site.<sup>1,2</sup> Although the mechanism of MUP is unclear, various hypotheses have been proposed including spontaneous regression of the primary tumor or ectopic melanocytes existing within the lymph nodes and visceral organs.<sup>3,4</sup> It most commonly occurs in the fourth and fifth decades of life and affects men twice as often as women.<sup>1,2</sup> Visceral organs account for approximately 20% of MUP diagnoses. The most common organ system affected is the gastrointestinal tract, although it has also been described in the kidney, heart, brain, bone marrow, and seminal vesicles, in addition to other organs.<sup>5</sup> Gastrointestinal bleeding is often the initial presenting symptom of malignancy but other manifestations include intestinal obstruction, intussusception, and bowel perforation.<sup>5</sup>

## CASE REPORT

We report an 89-year-old white man with no significant medical history who presented to the hospital with weakness, fatigue, and a 27-kg weight loss over the past year. Physical examination was grossly unremarkable with the exception of trace lower extremity edema and dark maroon blood on rectal examination. Laboratory test results were significant for microcytic hypochromic anemia (hemoglobin of 5.7 g/dL) with low serum iron (17 µg/dL) and low transferrin saturation (6%). Abdominal computed tomography with intravenous contrast showed a 14.1 × 10.2 × 10.7 cm necrotic mass along the midline of the small bowel mesentery with invasion of the adjacent small bowel loop and 2 enlarged, necrotic mesenteric lymph nodes without evidence of additional abdominal or pelvic disease (Figure 1). Multidisciplinary evaluation was obtained, and 1 m of small bowel was removed with melanoma extending to involve the abdominal wall resection margin (R1 tumor classification). Microscopic examination showed cells with large nuclei, prominent nucleoli, and scattered cells with brown pigment. Immunostaining was positive for S100, HMB-45, and Melan-A and negative for cytokeratin AE1/AE3 (Figure 2). These findings were consistent with melanoma. Tumor profiling with BRAF and c-KIT was negative. He also had extensive skin and ocular examinations with a dermatologist and ophthalmologist, respectively. Given the patient's age and prognosis, conservative management was preferred by the patient and family members. However, approximately 9 months later, the patient's tumor recurred in the mesentery of the left lower quadrant abutting the sigmoid colon.



**Figure 1.** (A) Sagittal, (B) coronal, and (C) axial view of the abdominal computed tomography showing a large, heterogeneously enhancing and partially necrotic mass in the midline of the upper pelvis along the small bowel mesentery measuring  $14.1 \times 10.2 \times 10.7$  cm.

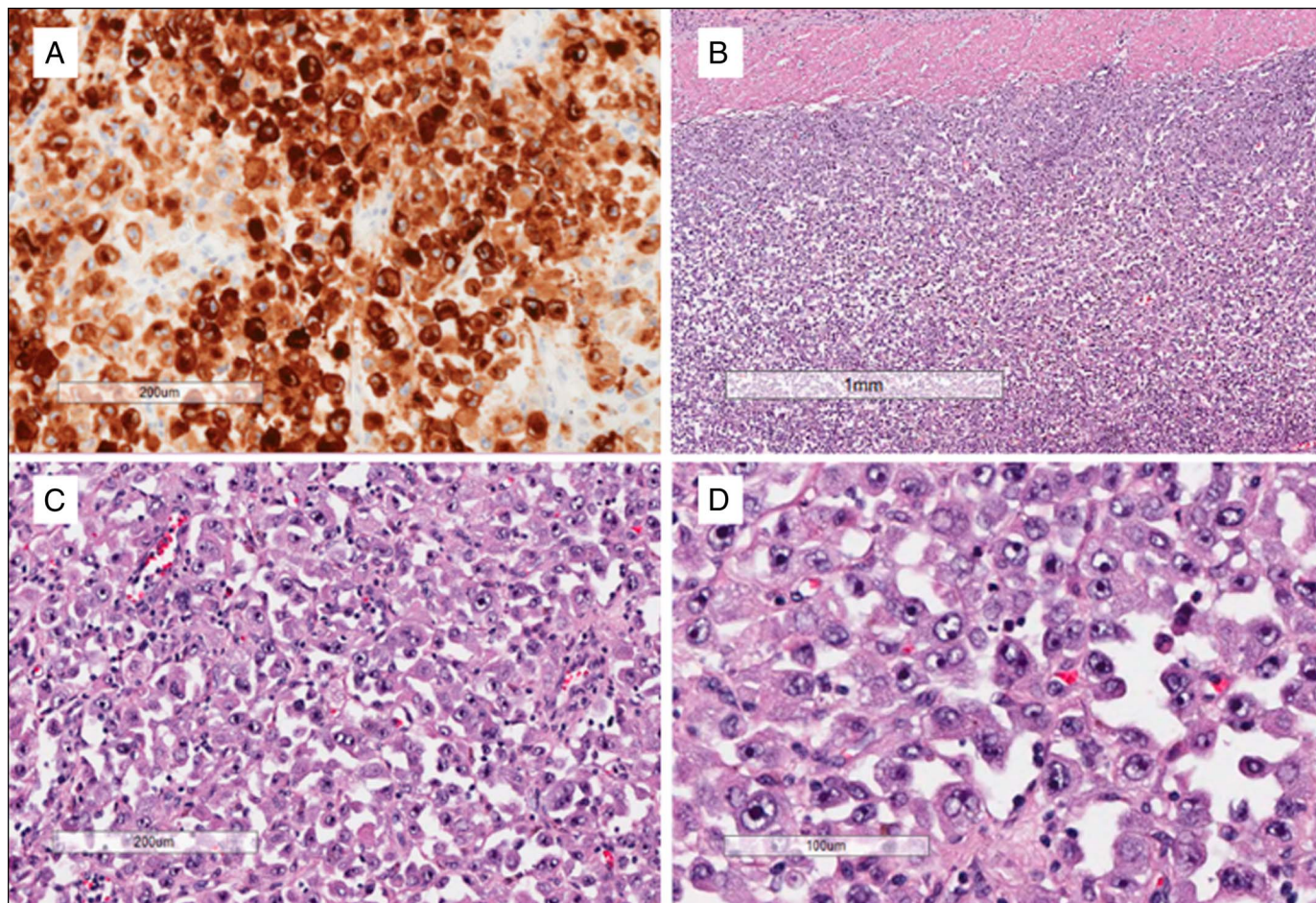
## DISCUSSION

In clinical practice, MUP is a challenging diagnosis given its internal presentation in lymph nodes and visceral organs unlike its cutaneous counterpart, melanoma of known primary. A thorough workup of the patient's symptoms including laboratory testing and imaging is warranted; however, MUP is often not included in the differential diagnosis of suspected internal malignancies. The necrotic mass in our patient's small bowel showed a high-grade malignant neoplasm with nuclear pleomorphism and mitotic activity. Further staining was performed given the invasive and poorly differentiated features, and Melan-A, HMB-45, and S100 were strongly positive, consistent with malignant melanoma. Mutational analysis of tissue samples can also assist in the diagnosis of MUP. The most common mutation is BRAF, followed by NRAS, although they are not present in all melanomas as exhibited in this case.<sup>5</sup>

At present, there is no gold standard for the diagnosis of MUP, and different cases require individualized evaluation. In 1963, Das Gupta et al originally proposed the 4 following exclusion criteria for MUP: (i) evidence of previous orbital exenteration or

enucleation; (ii) evidence of previous skin excision, electro-dessication, cauterization, or other surgical manipulation of a mole, freckle, birthmark, paronychia, or skin blemish; (iii) evidence of metastatic melanoma in a draining lymph node with a scar in the area of skin supplying that lymph node basin; and (iv) lack of a thorough physical examination, including the absence of ophthalmologic, anal, and genital examinations.<sup>6</sup> If any of these exclusion criteria are present, a diagnosis of MUP cannot be definitively made.

Several hypotheses since the 1960s have been proposed to explain cases which do not satisfy the exclusion criteria. One more widely accepted theory is immune-mediated regression of the primary lesion after metastasis has occurred.<sup>4</sup> Others have argued that the tumor actually represents malignant transformation of ectopic nests of melanocytes within the involved tissue or that the primary lesion falls below the threshold for detection, although still present.<sup>3,5</sup> Of note, the incidence of histopathologic regression within melanoma is 6-fold higher than that of many other cancers. Partial regression is recognized in 10% to 35% of all cutaneous melanoma specimens indicating that this phenomenon could explain cases where there is no



**Figure 2.** (A) Strong Melan-A immunoreactivity by neoplastic target cells (Melan-A immunohistochemical stain, 10× magnification). (B) Low power microscopic view of the small bowel showing expansion of the subserosa by a diffuse neoplastic process (hematoxylin and eosin stain, 2× magnification). (C) Microscopic small intestine showing diffuse infiltration by an invasive neoplastic process (hematoxylin and eosin stain, 10× magnification). (D) High-grade malignant neoplasm with nuclear pleomorphism and mitotic activity (hematoxylin and eosin stain, 20× magnification).

visible primary cutaneous lesion, although complete regression is extremely rare.<sup>7,8</sup>

Once melanoma is discovered in a lymph node or visceral organ, a thorough history including previous skin biopsies, cutaneous surgical procedures, or trauma to the skin should be obtained. Previous biopsies of cutaneous lesions reported as benign should also be reviewed by a pathologist. A comprehensive physical examination with a detailed review of systems should be performed, including oral, anogenital, and ophthalmologic examinations. Referrals to specialists for more extensive ocular and anogenital examinations are warranted in cases where no primary lesion is identified. Imaging studies are helpful for staging purposes, and routine skin examinations every 4–6 months by a dermatologist can help identify cases in which there may be delayed presentation of the primary site.

Regarding treatment, wide local excision or lymph node dissection, either radical or modified, is the current standard of care for surgical management of Stage III MUP, whereas Stage IV (in

visceral organs) is treated more aggressively with a combination of surgery, chemotherapy, immunotherapy, and radiotherapy.<sup>5</sup> One systematic review of the literature found that patients with visceral disease had median survival times between 3 and 16 months, and 5-year survival rates between 5.9% and 18%.<sup>2</sup>

This case highlights the anomalous and rare presentation of malignant melanoma in the gastrointestinal tract. A thorough physical examination including a complete skin and ocular examination is of utmost importance; however, if clinical suspicion of malignancy is high, MUP should be considered in the differential diagnosis. Future studies are needed to better elucidate the etiology of MUP, especially in the new era of targeted treatment and immunotherapy.

## DISCLOSURES

Author contributions: R. Singh and K. Torre wrote the manuscript. H. Farooq and V. Chang wrote and edited the manuscript. R Singh is the article guarantor.

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