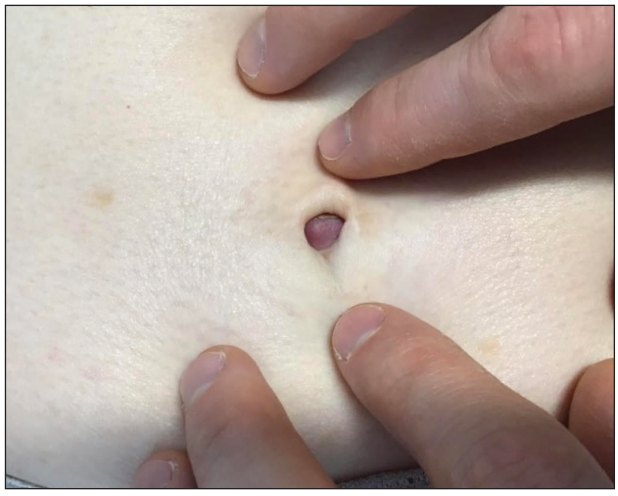
Asymptomatic Umbilical Nodule

David Walton Crasto, DO; Jennifer Wong, DO; Drew Taylor, MD; Eduardo Weiss, MD



A 64-year-old woman with no notable medical history was referred to our dermatology clinic with an intermittent eczematous rash around the eyelids of 3 months' duration. While performing a total-body skin examination, a firm pink nodule with a smooth surface incidentally was discovered on the umbilicus. The patient was uncertain when the lesion first appeared and denied any associated symptoms including pain and bleeding. Additionally, a lymph node examination revealed right inguinal lymphadenopathy. Upon further questioning, she reported worsening muscle weakness, fatigue, night sweats, and an unintentional weight loss of 10 pounds. A 6-mm punch biopsy of the umbilical lesion was obtained for routine histopathology.

WHAT'S YOUR **DIAGNOSIS?**

a. amelanotic melanoma
b. cutaneous endometriosis
c. dermoid cyst
d. Merkel cell carcinoma
e. Sister Mary Joseph nodule

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Drs. Crasto and Wong are from the Department of Dermatology, Larkin Community Hospital, South Miami, Florida. Dr. Taylor is from Aspen Dermatology, Colorado. Dr. Weiss is from the Miller School of Medicine, University of Miami, Florida, and the Florida International University, Miami.
The authors report no conflict of interest.
Correspondence: David Walton Crasto, DO, Larkin Community Hospital, South Miami, 7031 SW 62nd Ave, South Miami, FL 33143 (davecrastodo@gmail.com).
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THE **DIAGNOSIS:** Sister Mary Joseph Nodule

Histopathologic analysis of the biopsy specimen revealed a dense infiltrate of large, hyperchromatic, mucin-producing cells exhibiting varying degrees of nuclear pleomorphism (Figure 1). Immunohistochemical (IHC) staining was negative for cytokeratin (CK) 20; however, CK7 was found positive (Figure 2), which confirmed the presence of a metastatic adenocarcinoma, consistent with the clinical diagnosis of a Sister Mary Joseph nodule (SMJN). Subsequent IHC workup to determine the site of origin revealed densely positive expression of both cancer antigen 125 and paired homeobox gene 8 (PAX-8)(Figure 3), consistent with primary ovarian disease. Furthermore, expression of estrogen receptor and p53 both were positive within the nuclei, illustrating an aberrant expression pattern. On the other hand, cancer antigen 19-9, caudal-type homeobox 2, gross cystic disease fluid protein 15, and mammaglobin were all determined negative, thus leading to the pathologic diagnosis of a metastatic ovarian adenocarcinoma. Additional workup with computed tomography of the abdomen and pelvis highlighted a large left ovarian mass with multiple omental nodules as well as enlarged retroperitoneal and pelvic lymph nodes.

The SMJN is a rare presentation of internal malignancy that appears as a nodule that metastasizes to the umbilicus. It may be ulcerated or necrotic and is seen in up to 10% of patients with cutaneous metastases from internal malignancy.[1] These nodules are named after Sister Mary Joseph, the surgical assistant of Dr. William Mayo who first described the relationship between umbilical nodules seen in patients with gastrointestinal and genitourinary cancer. The most common underlying malignancies include primary gastrointestinal and gynecologic adenocarcinomas. In a retrospective study of 34 patients by Chalya et al,[2] the stomach was found to be the most common primary site (41.1%). The presence of an SMJN affords a poor prognosis, with a mean overall survival of 11 months from the time of diagnosis.[3] The mechanism of disease dissemination remains unknown but is thought to occur through lymphovascular invasion of tumor cells and spread via the umbilical ligament.[1,4]

Merkel cell carcinoma is a cutaneous neuroendocrine tumor that most commonly presents in elderly patients as red-violet nodules or plaques. Although Merkel cell carcinoma most frequently is encountered on sun-exposed skin, they also can arise on the trunk and abdomen. Positive IHC staining for CK20 would be expected; however, it was negative in our case.[5]

Cutaneous endometriosis is a rare disease presentation and most commonly occurs as a secondary process due to surgical inoculation of the abdominal wall. Primary cutaneous endometriosis in which there is no history of abdominal surgery less frequently is encountered. Patients typically will report pain and cyclical bleeding with menses. Pathology demonstrates ectopic endometrial tissue with glands and uterine myxoid stroma.[6]

Amelanotic melanoma is an uncommon subtype of malignant melanoma that presents as nonpigmented nodules that have a propensity to ulcerate and bleed. Furthermore, the umbilicus is an exceedingly rare location for primary melanoma. However, one report does exist, and amelanotic melanoma should be considered in the differential for patients with umbilical nodules.[7]

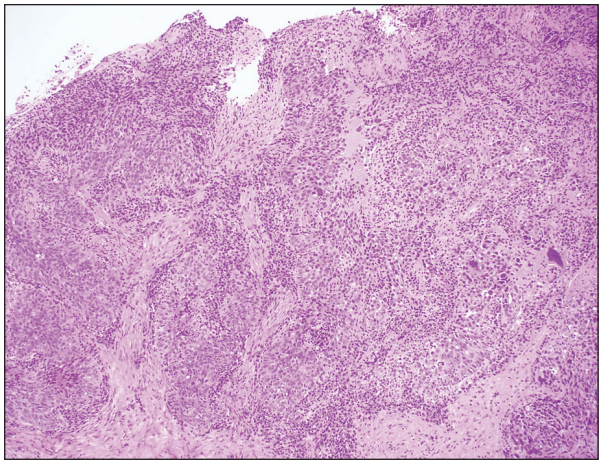

FIGURE 1. Invasive mucin-producing population of pleomorphic cells with prominent nuclear hyperchromasia (H&E, original magnification ×10).

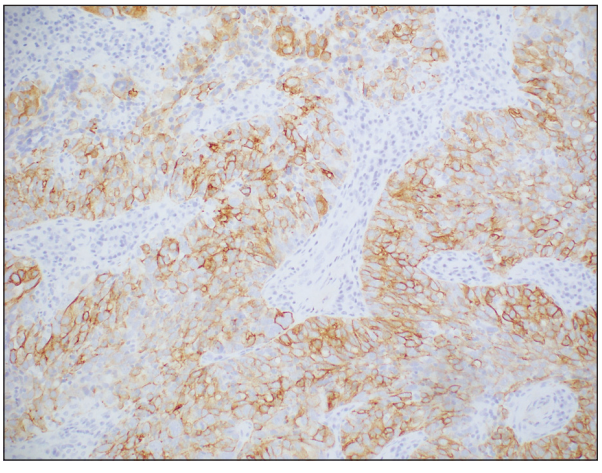

FIGURE 2. Positive cytokeratin 7 immunohistochemical staining prompted further immunophenotyping (original magnification ×20).

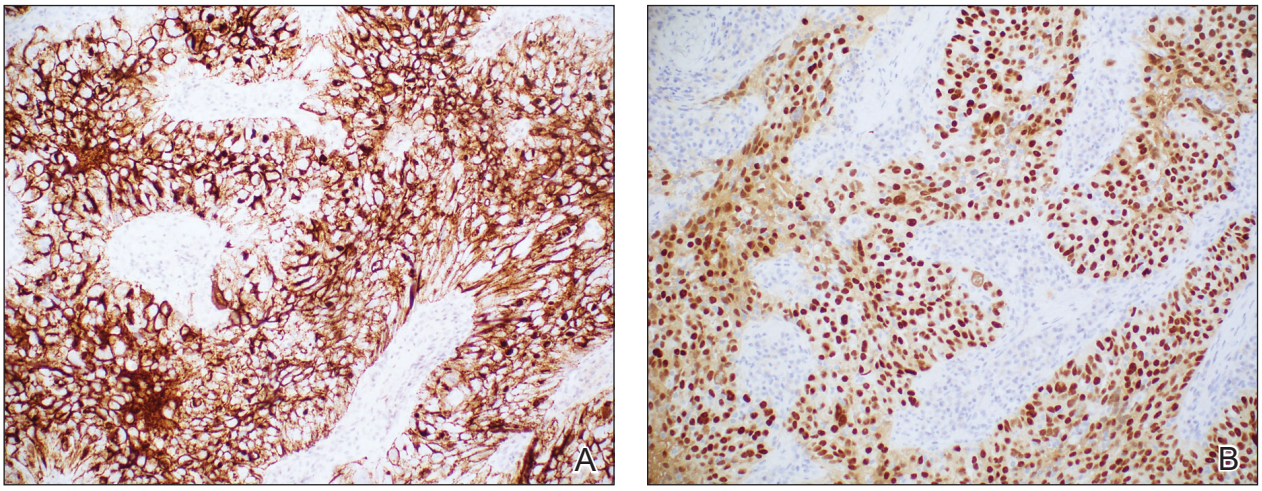

FIGURE 3. A, Densely positive cancer antigen 125 immunohistochemical staining rendered the diagnosis of primary ovarian carcinoma (original magnification ×20). B, Paired homeobox gene 8 (PAX-8) immunohistochemical staining displayed the uptake in the tumor cells, providing further evidence for ovarian origin of the primary neoplasm (original magnification ×20).

Dermoid cysts are benign congenital lesions that typically present as a painless, slow-growing, and well-circumscribed nodule, as similarly experienced by our patient. They most commonly are found on the testicles and ovaries but also are known to arise in embryologic fusion planes, and reports of umbilical lesions exist.[8] Dermoid cysts are diagnosed based on histopathology, supporting the need for a biopsy to distinguish a malignant process from benign lesions.[9]

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