



Case report

Primary peritoneal carcinoma presenting as a Sister Mary Joseph's nodule: A case report and review of the literature

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ABSTRACT

Sister Mary Joseph's nodule is sometimes the first sign of an internal malignancy, including gastrointestinal, gynecological, or malignancy of unknown primary. It is rarely the sole presentation of a primary peritoneal cancer. In this report, we present the case of a 70-year-old female with umbilical drainage and a computed tomography scan consistent with solitary umbilical nodule. Excision of the nodule revealed adenocarcinoma of likely müllerian origin. Surgical staging did not show any evidence of malignancy with the exception of pelvic washings. She was considered to have primary peritoneal adenocarcinoma and was treated with adjuvant chemotherapy.

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1. Introduction

Metastatic tumors of the umbilicus are a rare occurrence, first described by Sister Mary Joseph Dempsey in the early 1900s during her work with Dr. William James Mayo (Dubreuil et al., 1998). The often termed Sister Mary Joseph's nodule could be the first sign of an internal malignancy at an advanced stage. It usually presents as a small, firm nodule, sometimes with exudates, or as a diffuse induration of the subcutaneous tissue. Differential diagnosis may include metastasis from internal malignancy, endometriosis, benign tumors, or primary umbilical carcinoma. Gastrointestinal malignancy is found in 52% of the metastatic cases and gynecologic and genitourinary origin in 28%, with gastric and ovarian cancers being the most common (Dubreuil et al., 1998). Although rare, other tumors can also manifest with umbilical metastasis, including breast and lung cancers, mesothelioma, and multiple myeloma (Dubreuil et al., 1998). However, a primary malignancy is undetermined in approximately 15% of the cases (Dubreuil et al., 1998; Galvan, 1998; Papalas & Selim, 2011). Metastasis to the umbilicus is thought to occur via lymphatic channels, venous network, arterial spread, direct extension from the anterior peritoneal surface, via embryologic remnants, or in an umbilical hernia, and iatrogenic after laparoscopy (Dubreuil et al., 1998). However, the exact mode of spread is not well understood, and direct extension from the anterior peritoneal surface is thought to be the main route.

2. Case

A 70-year-old female patient initially presented with umbilical drainage. Computed tomography scan of the abdomen and pelvis was only relevant for a small umbilical fluid collection. An excision of the umbilical lesion was performed, and pathology showed metastatic serous carcinoma of müllerian origin. Immunoreactivity stains are shown in Table 1. PET scan, colonoscopy, esogastroduodenoscopy, and tumor markers were within normal limits (Table 2).

The patient's past medical history was relevant for an abnormal mammogram for which she underwent a right breast stereotactic core biopsy showing intraductal papilloma with florid ductal hyperplasia arising in the background of proliferative fibrocystic changes, without any evidence of malignancy. In addition, she had two episodes of postmenopausal bleeding with negative hysteroscopy and negative endometrial biopsy.

After referral to our institution, the patient underwent a thorough physical examination, with normal findings. A Papanicolaou test showed rare atypical glandular cells of undetermined significance, and endometrial biopsy was negative for malignancy. Pathology slides from the Sister Mary Joseph's nodule were reviewed by a pathologist with expertise in gynecological cancers (Fig. 1). Immunohistochemistry stains were positive for estrogen receptor, WT-1, PAX-8, CK-7, pancytokeratins, and had patchy positivity for progesterone receptor. This was consistent with a tumor of müllerian origin.

Her case was presented at our institutional tumor board, and it was recommended to proceed with surgery to rule out primary ovarian or primary peritoneal carcinoma. She underwent an examination under anesthesia, exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, complete omentectomy, and pelvic

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Table 1
Immunoreactivity of final pathology of umbilical lesion biopsy.

Marker	Immunoreactivity
Pancytokeratin AE1/AE3	Positive
CK7	Positive
Progesterone receptor	Patchy positivity
Estrogen receptor	Strong diffusely immunoreactive
WT-1	Strong diffusely immunoreactive
PAX8	Positive
TTF-1	Negative
CDX-2	Negative
CK-20	Negative

Table 2
Serum levels of tumor markers.

Tumor marker	Serum level in patient	Reference range
CA-125	15.7 U/mL	0–35.0 U/mL
CEA	0.8 ng/mL	0–5.2 ng/mL
CA 27-29	27.9 U/mL	0–38.0 U/mL
AFP	4.4 ng/mL	0–8.3 ng/mL
CA 19-9	9.8 U/mL	0–36.9 U/mL

and para-aortic lymph node dissection. Surgical pathology was significant only for focal serous tubal intraepithelial carcinoma, with no evidence of invasive carcinoma. However, pelvic washings were positive for adenocarcinoma. The presumed final diagnosis was primary peritoneal carcinoma presenting at the umbilicus, and the recommendation was for adjuvant chemotherapy with carboplatin and paclitaxel.

3. Discussion

The case outlined in this study demonstrates a rare presentation of primary peritoneal carcinoma as an umbilical lesion, or Sister Mary Joseph's nodule. Cases of ovarian and endometrial cancers presenting

initially as a Sister Mary Joseph's nodule have been previously reported, but there have been very few cases of a Sister Mary Joseph's nodule as the initial presentation of primary peritoneal cancer (Galvan, 1998; Iavazzo et al., 2012).

Most Sister Mary Joseph's nodules are umbilical metastases from adenocarcinoma followed by squamous cell carcinoma and undifferentiated tumors. Gastrointestinal malignancy is the most common etiology in men, whereas gynecological malignancy is the most common etiology in women, especially ovarian and endometrial malignancies. However, the primary etiology remains unknown in about 15% to 30% of cases (Dubreuil et al., 1998; Papalas & Selim, 2011). In a review of 77 umbilical tumors identified over 20 years, Papalas et al. found that 68 (88%) were metastatic adenocarcinoma, and of these, 58 (85%) were identified in the setting of a known primary tumor (Papalas & Selim, 2011). Among the 10 patients without an assigned primary tumor, 5 had other sites of metastatic disease, and for 5 the umbilical nodule was the only site of malignancy identified. Equally of interest, there were 9 total patients who presented with an umbilical nodule as the only known site of disease, of these 3 were ultimately found to have ovarian cancer, and 1 pancreatic cancer, whereas the remaining 5 were designated as unknown primary (2 poorly differentiated carcinomas, 2 well differentiated carcinomas, and 1 neuroendocrine tumor). From these data, the authors conclude that the likelihood of identifying a primary lesion when presenting with an isolated metastasis to the umbilicus is less than 50% (Papalas & Selim, 2011).

In the absence of a known primary tumor, diagnosis of Sister Mary Joseph's nodule is based on histopathological assessment, which can be followed by targeted physical exam, imaging and biopsies to identify the primary site. Immunohistochemistry can aid in the diagnosis of tumor origin in cases of unclear etiology. In this case, the tumor stained positive for estrogen receptor, progesterone receptor, CK-7, PAX-8, and WT-1. The ovarian epithelium expresses cytokeratins, including CK-7, as well as Wilms' tumor gene product (WT1) (Marjoniemi, 2004). Mucinous tumors of müllerian origin tend to express estrogen and progesterone receptors (McCluggage, 2012) and PAX-8 is highly expressed in primary peritoneal serous carcinomas (Kawai et al., 2016). Carcinoma

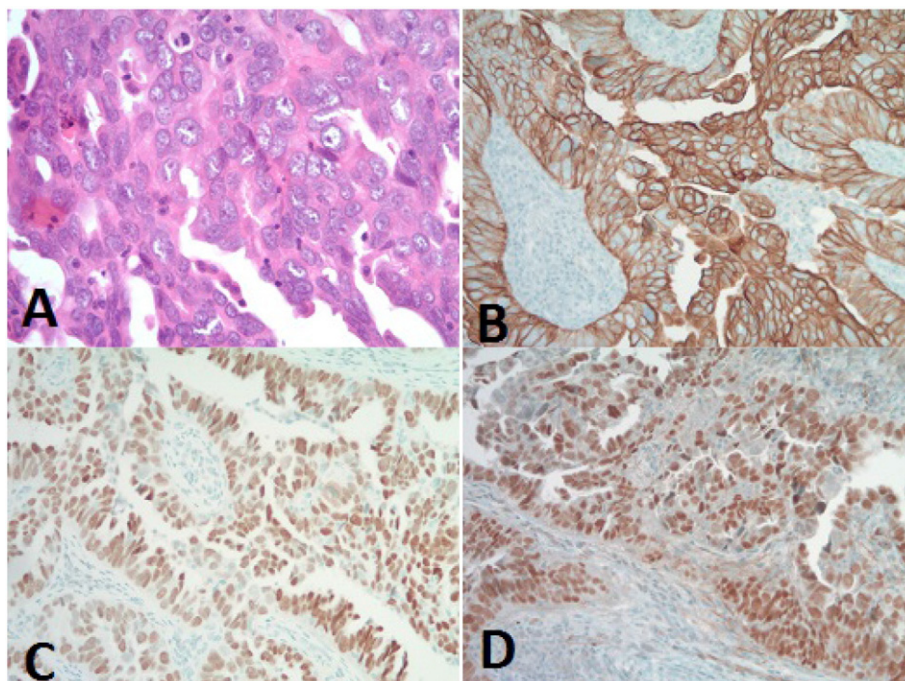


Fig. 1. (A) $\times 20$ magnification of serous adenocarcinoma found from umbilical nodule. (B) Immunostaining positive for CK-7. (C) Immunostaining positive for ER. (D) Immunostaining positive for WT-1.

of urachal origin may express the markers CDX-2 and CK-20 (Gladell et al., 2011), which were negative in the case pathology.

The presence of umbilical metastasis usually indicates a poor prognosis. Survival without treatment ranges from 2 to 11 months from the time of diagnosis. Data have shown improved survival for patients in whom the umbilical lesion is found before the primary malignancy in contrast to patients in whom the umbilical lesion is discovered after treatment for primary malignancy (mean survival of 9.7 months versus 7.6 months, respectively). Some studies have additionally shown improved survival for patients who are treated with a combination of surgery and chemotherapy as opposed to surgery or chemotherapy alone (Gabriele et al., 2005). Patients who present with isolated umbilical involvement may experience prolonged survival after surgical resection and appropriate chemotherapy (Galvan, 1998).

Of the cases reviewed in the literature, only one involving malignancy of primary peritoneal origin has been recently reported, by lavazzo and associates (lavazzo et al., 2012); another case was reported by Steck and colleagues in 1965 (Steck & Helwig, 1965), making this an extremely rare occurrence. In contrast to the other cases presented in the literature, the case outlined above describes an umbilical nodule as the sole site of a primary peritoneal cancer. In cases where histopathology of an umbilical nodule indicates a serous müllerian tumor, but there is no definite evidence of a gynecologic primary, we suggest imaging of the chest, abdomen and pelvis to evaluate for any other sites of disease, evaluation of tumor markers including Ca 125, and surgical exploration for both diagnosis and cytoreduction. Adjuvant treatment platinum/taxane based chemotherapy is a reasonable approach and may improve survival.

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