

Umbilicus as the Only Site of Metastasis in Recurrent Ovarian Cancer

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We present 2 rare cases of umbilical metastases (Sister Mary Joseph's nodule) as the first sign of late recurrent ovarian cancer. Two patients with ovarian cancer treated with optimal debulking surgery plus chemotherapy were regularly followed up postoperatively. An isolated umbilical nodule was noted accidentally 8 years and 3 years, respectively, after the initial operation. Abdominal computed tomography (CT) for both patients showed a 1.8-cm mass and a 2.3-cm mass with negative peritoneal tumor seeding. Other tumor surveys, including CA125, showed negative findings. Both patients had exploratory laparotomy and complete excision of the umbilical tumor. The pathology showed an isolated metastatic adenocarcinoma without evidence of other metastases. Both patients were treated with 4-course postoperative adjuvant chemotherapy of carboplatin and paclitaxel. Both patients have been in complete clinical remission for 22 months and 12 months, respectively. In addition to tumor marker CA125, a careful and thorough physical examination, assisted by modern imaging evaluation, is the best method for detecting early recurrence in patients with previously treated ovarian cancer. Although an umbilical metastasis usually indicates advanced disease with disseminating peritoneal spread, it does not always imply inoperable or incurable disease. Intensive treatment can improve the outcome. [*J Chin Med Assoc* 2006;69(5):233–235]

Key Words: recurrent ovarian cancer, Sister Mary Joseph's nodule, umbilical metastasis

Introduction

The umbilical region is a rare site to be metastasized by intra-abdominal malignancies. Metastasis to the umbilicus, or Sister Mary Joseph's nodule (in recognition of the superintendent at St Mary's Hospital, Mayo Clinic, who identified the clinical significance of these nodules), has been described in a variety of tumor types.¹ From its initial description,² more than 400 cases have been reported in the English literature.³ The vast majority of cases involve intra-abdominal carcinomas from the gastrointestinal tract and female genital tract,^{4–6} and the majority of metastatic cases are adenocarcinoma. Other less common primary malignancies include carcinomas from the lung, breast, liver, gall bladder, peritoneum, kidney, bladder,

prostate, and cervix, as well as leiomyosarcoma from the uterus.³ Isolated cases of umbilical metastases from intestinal carcinoid, multiple myeloma, and non-Hodgkin's lymphoma have also been reported.^{3,6} Regardless of the primary disease, the finding of umbilical metastases is generally considered to be an ominous sign because it usually represents tumor recurrences or widespread dissemination. In fact, many patients die from their malignancy within a year.³

Hence, we present 2 cases with the Sister Mary Joseph nodule noted as the only site of recurrent ovarian cancer without widespread dissemination, which is a reminder of the importance of careful and thorough physical examination during follow-up and the value of intensive and active treatment in managing such patients.

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Case Reports

Case 1

A 72-year-old woman, G4P4, with serous ovarian cystadenocarcinoma, stage IIIC, was treated with optimal debulking surgery followed by 6 courses of multi-agent chemotherapy (cisplatin, adriamycin, and cyclophosphamide — PAC). Postoperative follow-up was uneventful. Eight years after the initial operation, a palpable umbilical nodule was accidentally found. The patient did not report any other symptom or sign, such as abdominal pain, body weight loss, or poor appetite. Physical examination showed a firm, nontender 1.5-cm nodule just in the umbilical area. The nodule was smooth without ulceration or discharge. Abdominal computed tomography (CT) showed a 1.8-cm soft tissue mass just below the umbilical area without intraperitoneal tumor seeding. Other tumor surveys, including CA125, was unremarkable. Fine-needle biopsy showed metastatic adenocarcinoma. Exploratory laparotomy and umbilical mass excision was performed. A thorough intra-abdominal examination was negative. Final pathology revealed an isolated metastatic adenocarcinoma in the umbilical area with negative results for all the other random biopsies. The patient received 4 courses of postoperative adjuvant chemotherapy with carboplatin and paclitaxel. She has been free of disease for 22 months.

Case 2

A 44-year-old woman, P2, with endometrioid ovarian cystadenocarcinoma, stage IIC, was treated with optimal debulking surgery and 6-course multi-agent chemotherapy (PAC). Postoperative follow-up was unremarkable. Three years after the initial operation, a 3-cm umbilical mass was noted. She was admitted to the hospital for a thorough evaluation. The surface of the nodule was not ulcerated and there was no discharge or sinus. The nodule was painless.

The tumor marker CA125 was unremarkable. Other tumor surveys also failed to detect any other abnormal findings. Fine-needle biopsy showed metastatic adenocarcinoma. Exploratory laparotomy and tumor excision showed an isolated umbilical tumor without evidence of the tumor spreading within the abdominal cavity. The pathology proved an isolated metastatic adenocarcinoma on the skin with negative random biopsies. Four courses of adjuvant chemotherapy with carboplatin and paclitaxel were administered. She has been free of disease for 12 months.

Discussion

Sister Mary Joseph's nodule represents only a small portion of cases with cutaneous metastases from intra-abdominal malignancies, and the frequency for occurrence in association with epithelial tumors at different primary sites varies greatly.⁷ In the majority of cases, the finding of an umbilical nodule represents recurrence or dissemination of known malignancies. Occasionally, however, this may be the initial presentation of the primary disease.⁶ In rare situations, the primary site remains unknown, even after an extensive search. In general, the interval between the primary tumor diagnosis and the detected umbilical metastasis is from 1 month to 10 years, with an average of 22 months.³ In our presented cases, the interval from the original diagnoses of ovarian cancers to the proved umbilical metastasis was 8 years and 3 years, respectively.

A full understanding of the mechanisms whereby the tumor spreads to the umbilicus remains unclear.⁸ However, several anatomic criteria and several hypotheses have been proposed,⁹⁻¹³ including direct extension from adjacent peritoneal implants, lymphatic spread, vascular spread, and, rarely, after laparoscopy (iatrogenic). The umbilical ring is a scar invaginated on the abdominal wall between the transversalis fascia and peritoneum. The venous drainage includes several anastomotic branches, cranially, coming from the axillary vein through the internal mammary vein, and, caudally, from the femoral vein through the superficial epigastric vein. The umbilicus can also be connected with the portal system, through small umbilical veins. The lymphatic drainage of the umbilical region follows the venous systems. The cross-connection of the umbilicus with multiple embryologic remnants and its extensive vascular and lymphatic communications represent possible routes by which metastatic tumor cells could implant into the umbilical region. Furthermore, the common association between hepatic and umbilical metastases may suggest that the tumor spreads from the primary tumor to the liver, through the portal system and the lymphatic and/or venous channels, then to the umbilicus. However, whether the nodule causes spread to the liver or vice versa would be difficult to prove, especially since the liver is so commonly involved during systemic spreading of the tumor. In our presented cases, the liver had no tumor metastasis; therefore, another possibility should be considered. The most simple theory is direct extension from adjacent peritoneal implants, which shows contiguous spread from intraperitoneal metastasis to the umbilicus, the thinnest part of the abdominal wall. This theory is based on the clinical

observation that umbilical metastases are frequently associated with intraperitoneal carcinomatosis. Although direct extension from adjacent peritoneal implants is a rational explanation, it cannot clearly explain our cases because both of them showed only an isolated umbilical metastasis even after a series of examinations, including exploratory laparotomy, but we failed to identify any microscopic or macroscopic tumors within the abdominal cavity or peritoneal area. In our cases, iatrogenic tumor implantation is most unlikely since the original exploratory laparotomy did not involve the umbilical area.

The finding of umbilical metastases is usually considered an ominous sign because it represents tumor recurrences or advanced neoplastic diseases with widespread disseminations that are not amenable to surgery. The survival of the patients left untreated has been reported to range from 2 to 11 months from the time of initial diagnosis; even after treatment, many patients will die of disease within 1 year.⁸ Several factors have been shown in recent studies to influence the prognosis, including the detection time before or after definitive treatment of the primary tumor, the etiology of the primary tumor, and the type of treatment. There are data to show a better survival (mean 9.7 months) in patients who had an umbilical metastasis detected before definitive treatment of the primary tumor, compared with those who had an umbilical metastasis detected after definitive treatment of the primary tumor.⁹ Certain data have shown a better survival rate for patients with primary ovarian carcinoma.⁴ Although some authors prefer palliative and supportive treatment because they anticipate poor outcomes of these patients,¹⁴ recent studies have demonstrated an improved survival (21 months) for patients treated with a combination of surgery and adjuvant therapy instead of surgery alone (7.4 months) or chemotherapy alone (10.3 months).^{4,9,15} Obviously, the appropriateness of such an aggressive treatment approach is determined by the clinical state of the patient. In our presented cases, the aggressive treatment in order to get promising results seemed to support the above observation.

In fact, recurrent ovarian cancer is still a major issue. A tumor marker such as CA125 may be the best monitor so far. An elevated serum level of CA125 without any presenting symptom is the most common and earliest sign predating the development of a clinically obvious tumor, although the serum CA125 level is neither sufficiently sensitive nor specific enough to diagnose recurrence. In this report, we further support the limited value of serum CA12 level. A

careful evaluation of the umbilical area and a definitive physical examination is highly recommended in all cancer patients.

We conclude that, although umbilical metastasis usually indicates advanced disease with peritoneal spread, it does not always imply inoperable or incurable disease. In addition to tumor markers, a careful and thorough physical examination, aided by modern imaging scanning is the best method for detecting early recurrence in those with known malignancies. Treatment should be individualized to the primary tumor, cell type, and clinical condition of the patient. Intensive treatment, including surgery, chemotherapy, and/or radiation could be applied in these highly selected patients, since the prognosis may be significantly improved.

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