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Sister Mary Joseph's nodules as the presenting symptom of primary peritoneal carcinoma: a case report

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Summary

Sister Mary Joseph's nodule as the presenting symptom of primary peritoneal cancer is quite a rare finding. The authors report here an 82-year-old patient with Sister Mary Joseph's nodule. She was diagnosed with primary peritoneal cancer and treated with surgical excision. Histological examination showed a papillary as well as a tubular pattern in the tumor. Adjuvant chemotherapy was administered but was discontinued because of the occurrence of pancytopenia. Although she could not avail of combination therapy, no recurrence has been observed at until now.

Key words: Sister Mary Joseph's nodule; Peritoneal cancer; Surgical excision; Adjuvant chemotherapy.

Introduction

Sister Mary Joseph's nodule is one of the presenting symptoms of an internal malignancy [1]. It is estimated that between 1% and 3% of patients with abdominal disease present with an umbilical nodule [2, 3]. The majority of Sister Mary Joseph nodules are of gastrointestinal origin (52%); however, cases of female genital tract or genitourinary tract origin (28%), or non-specified origin (18-20%) have also been reported [2, 4, 5].

In women, ovarian cancer is the most common primary origin site for Sister Mary Joseph's nodules [3]. Although peritoneal and epithelial ovarian cancers are similar since the lining of the abdomen and the surfaces of the ovaries have the same embryonic origin, it is rare to have Sister Mary Joseph's nodule as the first manifestation of primary peritoneal cancer [6]. The present authors hereby present a patient with peritoneal cancer who had Sister Mary Joseph's nodule as the presenting symptom.

Case Report

The patient was an 82-year-old woman with no significant past medical or family history. She was referred to the present hospital for evaluation of an umbilical tumor and itching (Figure 1). She had no complaints of appetite loss, vomiting, or abdominal pain. In addition, there was no evidence of abdominal distention.

The patient's height, body weight, and body mass index were 140.0 cm, 35.5 kg, and 18.1, respectively. Her vital signs were as follows: blood pressure: 123/87 mmHg, pulse rate: 98 bpm, respiratory rate: 17 beats/minute, and body temperature: 35.8°C. Levels of serum tumor markers analyzed were as follows: carcinoembryonic antigen: 1.0 ng/dL, cancer antigen 19-9: 14.9 U/mL, and cancer antigen 125: 15.0 U/mL.

Transvaginal ultrasonography (TVUS) showed a 3×2 cm hypoechoic mass on the lateral side of the uterus. No significant ascites was observed in the pelvic cavity. Dynamic contrast-enhanced CT of the abdomen revealed an unclear mass under the umbilicus and three masses around the uterus.

A T2-weighted (T2W1) MRI of the pelvis revealed three unclear masses in the ventral uterus and left and right side of the dorsal uterus, with sizes approximately 3.0 cm, 2.6 cm, and 2.5 cm, respectively (Figures 2 and 3). These masses had the same imaging signal intensity as the umbilical tumor. The differential diagnosis included myoma, ovarian carcinoma, peritoneal carcinoma, leiomyosarcoma or metastasis of ovarian cancer. A biopsy of each mass was carried out under local anesthesia to assess the origin of the masses.

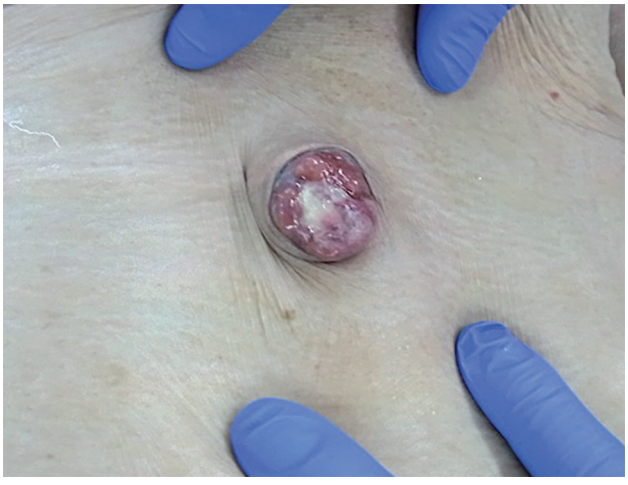

Figure 1. — Umbilical tumor.

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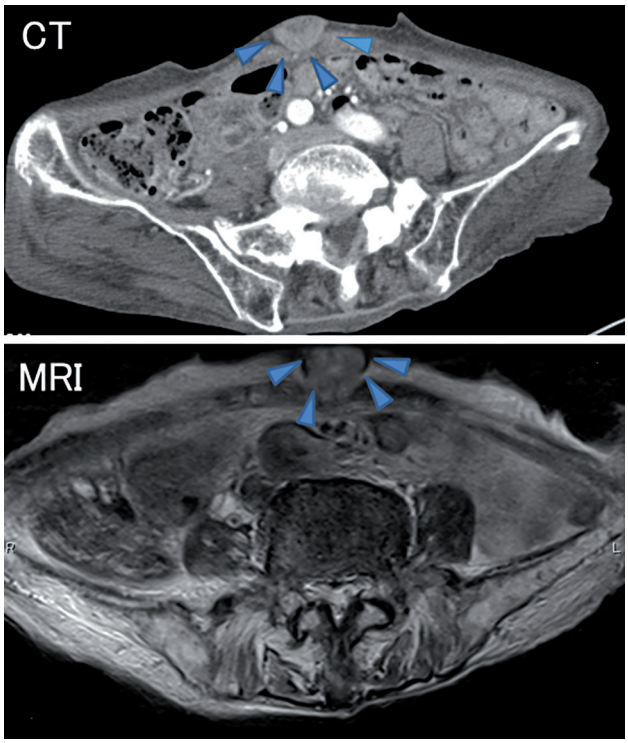

Figure 2. — Contrast-enhanced CT and T2-weighted MRI of the abdomen showing an umbilical mass (blue triangles).

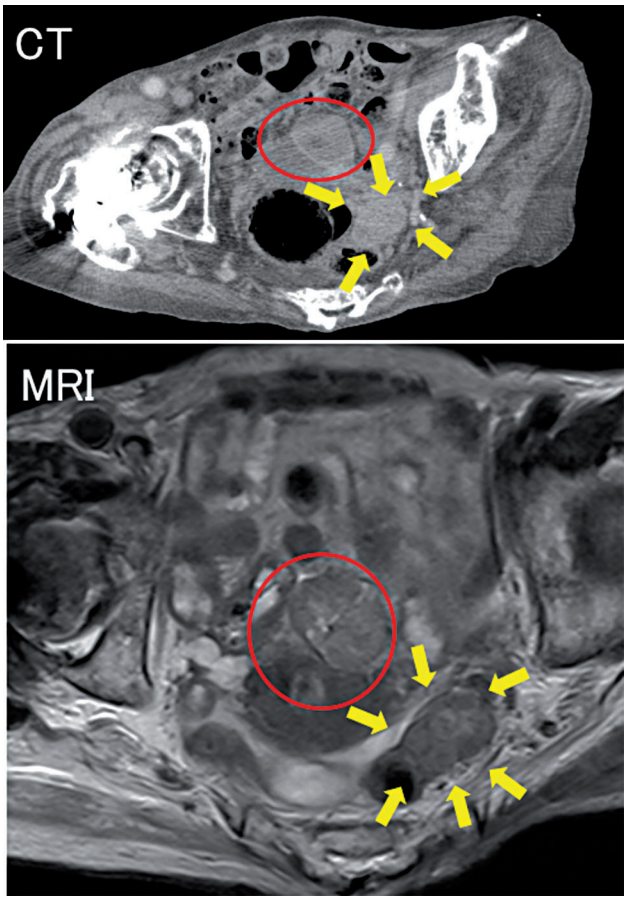

Figure 3. — Contrast-enhanced CT and T2-weighted MRI showing two tumors, one of 30.0 mm and the other of 26 mm in the ventral uterus (red circle) and left dorsal uterus, respectively (yellow arrows). Each tumor corresponds to the gross findings shown in Figure 3 (red circle: d, yellow arrow: e).

The histological examination indicated adenocarcinomas of a female genital organ or peritoneal carcinoma as the probable diagnosis. Approximately four weeks after admission, the patient was in poor physical condition because of a high fever and malnutrition. Blood and urine cultures ruled out the presence of infection. The authors suspected that the fever was causing a lack of appetite and that a malignancy could be the underlying cause for the fever. Although they initiated treatment with nonsteroidal anti-inflammatory medication to stabilize her condition, they reasoned that a tumor resection was the treatment of choice. Prior to surgery, an esophagogastroduodenoscopy was performed to assess the possibility of gastric cancer, but there were no significant findings.

Two months after admission, the patient's physical condition improved and subsequently, a total hysterectomy, oophorectomy, and a small intestine and umbilical nodule resection were performed. Gross examination of the surgical specimens revealed that the uterine and bilateral uterine adnexa ware intact. No abnormalities were observed in the uterine adnexa, but a small soft nodule measuring 40.0 mm was found in the lower uterine body (Figure 4).

All mass tissue samples, including the sample taken from the lower uterine body, had a papillary morphology as indicated by a central core of fibrovascular tissue lined by layers of cells with crowded oval nuclei (Figure 5a). The final histological diagnosis was peritoneal carcinoma. Immunostaining results revealed that all masses were positive for several markers including, estrogen receptors (ER) (Figure 5b), paired-box gene 8 (PAX8) transcription factor (Figure 5c), and diffusely positive for p53 (Figure 5d). The tumor nuclei were also positive for Wilm's tumor-1 protein (WT-1) (Figure 5e). The final histological diagnosis was primary peritoneal carcinoma. The patient's overall condition stabilized gradually after the operation. For adjuvant chemotherapy, the authors followed the Japanese ovarian cancer treatment guidelines [1] and planned a dose-dense combination therapy with paclitaxel and carboplatin (TC). The regimen was as follows: the dose on the first day included 96 mg of paclitaxel (80 mg/m^2) and 540 mg/m^2 of carboplatin; the patient also received 96 mg of paclitaxel on days 8 and 15.

Eight days after medication administration, the patient's platelet count dropped to below 30,000/mm^3 and therefore the authors discontinued the day 8 dosage. Instead, a transfusion with ten units of platelets was performed. However, on day 13, the neutrophil count was found to be below 500/mm^3. Therefore, due to grade 4 adverse events, the authors discontinued chemotherapy. The patient was discharged on the 62nd postoperative day. They have been monitoring the patient on a monthly basis and to date, seven months after surgery, no recurrence has been reported.

Discussion

The incidence of Sister Mary Joseph's nodule in primary peritoneal carcinoma is quite low. To the best of the present authors' knowledge, cases in the literature that have re-

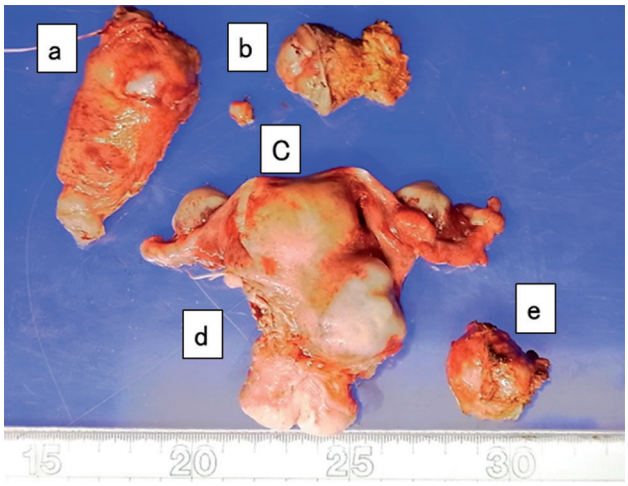

Figure 4. — Gross findings of the surgical specimens. (a) Tumor including a part of the small intestine. (b) Umbilical nodule. (c) Mesenteric lymph node. (d) Uterus and bilateral uterus adnexa. A soft tumor is found in the lower, left uterine body. (e) Tumor in the left dorsal uterus.

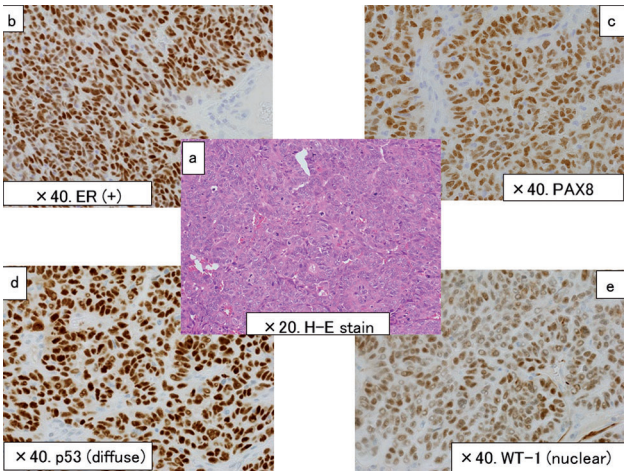

Figure 5. — Hematoxylin-eosin-stained specimens. A papillary as well as a tubular pattern is seen in the tumor (×40) (a), positivity for ER (×40) (b), positivity for PAX8 (×40) (c), diffuse positivity for p53 (×40) (d), and nuclear positivity for WT-1 (×40) (e).

ported Sister Mary Joseph's nodule as the first manifestation of primary peritoneal cancer are limited. A review of the literature revealed four other case reports and one review article [1, 4, 6, 7].

Patients with primary peritoneal cancer usually show abdominal symptoms such as abdominal pain and distension [4, 6]. However, Sister Mary Joseph's nodule could be the first sign of an advanced stage internal malignancy [1]. The present patient did not have any abdominal symptoms except the umbilical tumor. In order to identify the origin of the umbilical tumor, the authors used different methods, including imaging techniques such as TVU, CT, T2W1 MRI, and biopsy, a well-established and easy method for early diagnosis [5, 7, 8]. A biopsy confirmed that the umbilical tumor was a papillary adenocarcinoma, positive for ER and PAX-8. ER is a regularly used predictive biomarker for primary carcinomas of unknown origin [8]. PAX-8, a marker for carcinomas of ovarian origin, showed membranous and nuclear positivity in all tumors of primary peritoneal carcinomas, with very high sensitivity (100%) and specificity (95%) [1, 9]. The present patient was older and had poor general health, therefore the authors reasoned that surgery would only worsen the patient's general status. Nonetheless, as the patient had a recurrent fever of approximately 38°C, the authors speculated that the underlying cause could be the existence of a malignancy. Therefore, to improve the patient's condition and to make the final diagnosis, they decided to perform a surgical excision of the tumor mass. The presence of Sister Mary Joseph's nodule usually indicates a poor prognosis [2, 3, 10]. Aggressive treatment with surgical excision, radiotherapy, and chemotherapy is usually recommended in most cases. [3, 4, 10, 11]. Studies have reported that in the absence of treatment, survival in these patients is mostly in the range of two to 11 months [1, 7, 10]. However, recent studies have revealed a better survival (21 months) for patients treated with combination therapy such as surgery and chemotherapy rather than surgery (7.4 months) or chemotherapy (10.3 months) [4, 5, 10, 11]. The authors initiated combination chemotherapy but withdrew the treatment because of severe pancytopenia. Despite the drawbacks and challenges associated with combination therapy, the patient currently, after eight months of her initial diagnosis, has survived without any recurrence after initial treatment. Thus, the success of an aggressive treatment approach is largely dependent on the clinical status of the patient [10]. Sister Mary Joseph's nodule is usually associated with a poor prognosis and some authors recommend only palliative treatment [4, 10]. However, in the present authors' experience, timely and appropriate treatment approaches are key factors for an improved prognosis in patients with Sister Mary Joseph's nodule.

Conclusion

Although rare, Sister Mary Joseph's nodule can be a presenting sign of primary peritoneal cancer. In addition to the careful physical examination, biopsy results and a histological examination can help significantly with making an accurate diagnosis and for selecting suitable treatment modalities. Although aggressive surgical treatment, combined with chemotherapy or radiotherapy is usually recommended, the present authors believe that a treatment regimen that takes into account the physical condition of the patient can have a large impact on the patient's prognosis.

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