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Sister Mary Joseph's nodule: the tip of an iceberg.

Sister Mary Joseph's nodule is a rare palpable umbilical cutaneous lesion as a result of an advanced intra-abdominal and/or pelvic malignancy. It may be the initial clinical manifestation of an underlying malignancy, originating mainly from the gastro-digestive or genito-urinary tract. We present here a rare case of a 67-year-old woman with a Sister Mary Joseph's nodule. On surgical exploration, a left ovarian mass with anterior abdominal wall metastasis, ascites and extensive intra-abdominal metastatic lesions were observed. Our case report shows the importance of a careful physical examination as an invaluable diagnostic tool in modern medicine. High index of suspicion and awareness of this clinical sign may lead to the detection of the primary source, to its diagnosis and more appropriate treatment options in order to achieve the best survival possibility.

KEY WORDS: Ovarian cancer, Sister Mary Joseph's nodule, Umbilical metastasis

Introduction

Sister Mary Joseph's nodule (SMJN) is an uncommon palpable umbilical cutaneous lesion as a result of metastasis of an intra-abdominal and/or pelvic malignancy ¹. It was named after Sister Mary Joseph, who was a surgical assistant of Dr. William James Mayo. She first noticed the association between advanced abdominal-pelvic malignancies and the presence of an umbilical nodule ^{2,3}. It may be the initial clinical manifestation of an underlying malignancy, originating mainly from the gastrointestinal and genitourinary tract ¹. The proposed possible mechanisms of tumor spread to the umbilicus may be through lymph ducts, blood vessels, contiguous extension, or via embryologic remnants in the abdominal wall ⁴⁻⁶. Herein is described and discussed a rare case of a 67-year-old female, where the presence of the umbilical metastatic nodule was the first and only clinical sign of an underlying ovarian cancer, along with a review of the literature.

Case Report

A 67-year-old female with a six-month history of a growing mass protruding through the umbilicus presented to the outpatient department for a surgical consultation. She was in a state of good general health with no particular medical or surgical history. Three months ago, the patient received 3-month antibiotic treatment for suspected omphalitis (diagnosis provided by another physician) with no improvement of her condition. On clinical examination, there was not observed any regio-

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ABBREVIATIONS

SMJN	Sister Mary Joseph's nodule
CT	computed tomography
CK	cytokeratin
MRI	magnetic resonance imaging
PET	positron emission tomography

nal lymphadenopathy. On inspection, there was a 2 cm firm protuberant ulcerated nodule in the umbilical region (Fig. 1). Auscultation and palpation of the abdomen did not reveal any abnormality. However, percussion of the abdomen revealed ascites with shifting dullness. The physical examination of the chest and the cardiovascular system were normal.

Hemoglobin and hematocrit in blood routine tests were also normal. Liver function tests revealed hypoalbuminemia. Blood sugar, electrolytes, kidney function tests and urine examination were within normal limits. Serum levels of cancer antigen 125 (in upper normal limits), cancer antigen 19-9 and carcinoembryonic antigen were within normal limits, as well.

Abdominal ultrasonography detected a small amount of ascites, para-aortic lymphadenopathy and a left ovarian mass. The umbilical metastasis appeared as solid hypoechoic mass with irregular margins and without any sonographic signs of inflammation of the surrounding tissues. With the suspicion of a metastatic umbilical nodule, computed tomography (CT) of the abdomen was performed. CT scan confirmed the presence of the left ovarian mass and revealed a hyperdense contrast-enhancing tumor in the umbilical region and intraperitoneal deposits.

An exploratory laparotomy was performed. A left ovarian mass with anterior abdominal wall metastasis, ascites and extensive intra-abdominal metastatic lesions were observed. Because of the extensive local spread, the primary tumor was judged to be inoperable and after radical excision of the umbilical tumor and omentectomy, the patient was put on chemotherapy for further treatment. The postoperative course was uncomplicated and the patient was discharged three days after surgery.

Histopathological examination of the umbilical lesion showed metastatic papillary serous adenocarcinoma. Immunohistochemistry studies revealed a strong positive staining for cytokeratin (CK) 7, 8/18 and for estrogen receptor in the nucleus (Fig. 2). These results are considered to be consistent with metastatic ovarian cancer. The patient is still alive 4 years after the diagnosis.



Fig. 1: Umbilical metastasis in a 67-year-old woman with ovarian cancer. A), B) Preoperative images showing an erythematous protruding nodule from the umbilicus, C) Gross picture of the umbilical mass, D) Resected and divided metastatic umbilical nodule (SMJN).



Fig. 2: A) Histology revealed a metastatic papillary adenocarcinoma from the ovary. The cytoplasm of the tumor cells is clear or eosinophilic and there is nuclear pleomorphism, B) Tumor cells are strongly positive for cytokeratin (CK) 7, 8/18 and for estrogen receptor.

Discussion

Sister Mary Joseph's nodule (SMJN) refers to a palpable nodule bulging into the umbilicus usually indicative of an underlying advanced metastatic disease ¹. This malignant metastatic umbilical nodule is a rare occurrence but may represent the first sign of intra-abdominal or pelvic malignant disease and its presence implies dismal prognosis¹. In 1949, the British surgeon Sir Hamilton Bailey coined this term after Sister Mary Joseph (1856-1939), who was a superintendent nurse and a surgical assistant of Dr. William James Mayo at St. Mary's Hospital (at present the Mayo Clinic) in Rochester, Minnesota, USA. She was the first person who noticed and suggested an association between the presence of an umbilical nodule and advanced abdominal-pelvic malignancy ^{2,3}. Until now, over 400 cases of SMJN have been reported in the literature 7.

The exact mechanism of tumor spread to the umbilical region remains unclear. However, most authors support the idea that the metastatic infiltration of the umbilicus may be the result of direct extension from a contiguous tumor, hematogenous (arterial and venous network) or lymphatic spread and/or direct extension via the vestigial remnants of embryonal ligaments including the round ligament, the urachus, the vitellointestinal duct remnant and the obliterated vitelline artery 4-6. Ching et al. 8 suggested that the rich vascular and lymphatic supply of the periumbilical region along with the connection of the umbilicus with multiple embryologic remnants facilitate the migration and the implantation of neoplastic cells to the umbilicus. In addition, due to the incomplete fascial structure of the umbilicus and lack of a muscular layer, the transversalis fascia constitutes the only barrier to direct extension of peritoneal metastases in this region of the abdominal wall. Despite the fact that there is a rich vascular supply to the umbilical region ^{8,9}, direct spread of the tumor seems to be the most common form of umbilical involvement ¹⁰.

Sugarbaker¹¹ suggested that the proper mechanism of a cancerous umbilical nodule may be the result of transcoelomic dissemination of the tumor eventually owing to the fact that neoplastic cells detach from the primary gastrointestinal or gynecologic malignancy and disseminate throughout the peritoneal cavity by the flow of peritoneal fluid. He also suggested that gravity causes large volumes of tumor to accumulate within the cul-de-sac. Iatrogenic metastases at the umbilical port site following laparoscopic surgery have been reported in the literature. The possible mechanisms of spread of tumors to the umbilicus may include direct or indirect contamination and implantation of malignant cells because of excessive manipulation, unprotected retraction of the surgical specimen (tumor tissue), leakage of insufflation gas along the trocars leading to the tumor cell deposition at port sites, replacement of trocars and the CO₂ pneumoperitoneum which leads to diffuse damage to the entire mesothelial cell layer 12.

In our case, since this patient had peritoneal metastatic deposits and no other metastatic lesions, direct infiltration of the tumor from peritoneal dissemination was assumed to be the most possible mode of tumor spread to the umbilicus.

The SMJN represents 1-3% of patients with abdominalpelvic malignancy 13,14 . The most frequent primary sites of SMJN are the gastrointestinal (35-65%) and genitourinary tract (12-35%) ¹. Carcinomas of the stomach can be found as cause of the 25% of the SMJN, followed by primary tumors from colon and rectum (10%) and pancreas (7%) ^{1,15}. In men, umbilical metastases usually derive from the gastrointestinal tract, with gastric cancer being the most common origin ¹⁶. However, in females, most of the primaries are from ovary, of which serous papillary cystadenocarcinoma is the most common (34%) ^{1,17}. Adenocarcinoma is considered to be the most common histopathological type described in umbilical metastatic lesions. Other reported primary sites of the tumor include gallbladder, liver, breast, lungs, lymphoma, prostate, penis, kidney, endometrium, cervix and fallopian tube ^{15,17}. Furthermore, in 15 to 30% of the patients, the primary tumor may not be found ¹. The SMJN seems to be slightly more frequent in females ^{18,19}. Al-Mashat et al. ¹⁵ reported that the mean age of patients at diagnosis was approximately 50 years with

a range of 18-87 years. In contrast, other authors reported older age at the time of diagnosis 15,18 .

The potential differential diagnosis of an umbilical lesion is extensive and includes primary malignancy, metastatic umbilical nodule (SMJN) and many benign causes such as umbilical hernia, endometriosis, omphalitis, pyoderma gangrenosum, abscess, eczema, keloid, foreign body, epithelial inclusion cyst, congenital polyps, melanocytic nevi and fibroepithelial papillomas (Table I) ^{4,17,20}. Primary and metastatic umbilical malignancies constitute 10% and 30% of all umbilical tumors, respectively ^{8,21}.

Clinically, SMJN usually presents as an umbilical or periumbilical irregular indurated plaque or nodule frequently with vascular appearance. The nodule may be occasionally painful with skin ulcerations and sometimes serous, purulent discharge or bleeding. Its size usually ranges from 0.5 to 2 cm; however, some nodules can be larger and reach up to 15 cm in size ²². SMJN may be the initial clinical manifestation of an underlying malignant tumor. In contrast, other patients may pre-

sent in poor clinical status with epigastric pain, nausea, weight loss, abdominal distension, ascites, pleural effusion and bleeding per rectum 3 .

Imaging with ultrasonography, Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) can contribute to establish the diagnosis and the extent of the malignancy. However, once SMJN is discovered, a biopsy from the umbilical nodule, either excisional or fine needle aspiration cytology, is considered to be an invaluable tool in the diagnosis and recognition of the possible primary source.

Overall, SMJN has been associated with advance malignancies and is considered as a poor prognostic indicator with an average life expectancy of 2-11 months without treatment ²³. Early detection of the primary tumor may improve the prognosis. For the therapeutic approach of the disease, we should take into account the clinical status of the patient, the cell type and the primary source of the tumor. The presence of the umbilical metastatic nodule usually indicates widespread metastases and treatment in commonly palliative. However, in carefully selected cases surgical excision, radiotherapy and chemotherapy could prolong survival. Majmudar et al. ⁶ reported that the average survival of the patients was 17.6 months for those treated aggressively with surgery and adjuvant therapy, 7.4 months for those treated with surgery alone and 10.3 months for those treated with adjuvant therapy alone. A combination of aggressive surgical approach and chemotherapy may prolong survival ¹.

Differential diagnosis	Characteristics
Primary umbilical malignancy	An irregular lump on the umbilical or periumbilical region. It may be indistinguishable from a SMJN
SMJN	Occasionally the umbilical skin is ulcerated or necrotic with discharges (blood, serous)
Umbilical hernia	It may be congenital or acquired (multiple pregnancies, obesity, coughing). Surgery is usually recommended for adults to prevent the complications
Endometriosis	Usually symptomatic (tenderness, bleeding). A solitary nodule which may change in size during menstruation
Omphalitis	Infection of the umbilicus and/or the surrounding tissues. It is characterized by erythema, tenderness and induration of the umbilicus
Pyoderma gangrenosum	It is a rare ulcerative cutaneous condition usually associated with systemic diseases
Abscess	It may be presented with abdominal pain and mild redness of the periumbilical and umbilical region. Drainage and antibiotics
Eczema	It is a common skin condition. It may cause swelling, dark colored patches, crusting and oozing
Keloid	It is abnormal proliferation of scar tissue. It usually forms at the site of cutaneous injury
Foreign body	Identification of the foreign body
Epithelial inclusion cysts	They are the most common cutaneous cysts. They appear as small hard lumps
Fibromas	Benign tumors which are composed of fibrous or connective tissue
Congenital polyps	A congenital lesion as a result of an intestinal mucosal remnant at the umbilicus
Melanocytic nevi	Benign tumors composed of melanocytes
Fibroepithelial papillomas	They are usually soft, pigmented exophytic benign lesions

TABLE I - The differential diagnosis of an umbilical lesion.

Conclusion

Sister Mary Joseph's nodule is an uncommon but poor prognostic sign of an advanced disseminated malignancy. It can be present for several months before the diagnosis of a tumor is finally established. Our case report shows the importance of a careful physical examination as an invaluable diagnostic tool in modern medicine. High index of suspicion and awareness of this clinical sign may lead to prompt detection of the primary source, earlier diagnosis and more appropriate treatment options in order to achieve the best survival probability.

Riassunto

Il nodulo noto come "sister Mary Joseph" è una rara lesione cutanea palpabile che si evidenzia a livello dell'ombelico, quale segno dell'esistenza di una neoplasia endoaddominale dell'apparato digerente o pelvica dell'apparato genito-urinario in stato avanzato, di cui però può rappresentare la sola manifestazione clinica iniziale. Presentiamo qui un raro caso di una donna di 67 anni con un nodulo di sister Mary Joseph. Durante l'esplorazione chirurgica, sono state osservate una massa ovarica sinistra con metastasi della parete addominale anteriore, ascite ed estese lesioni metastatiche intra-addominali. Il nostro caso clinico mostra l'importanza di un attento esame fisico come strumento diagnostico irrinunciabile nella medicina moderna. Un alto indice di sospetto e consapevolezza nel rilevare questo segno clinico può portare all'individuazione della causa primitiva, alla sua diagnosi e all'adozione del trattamento più appropriato al fine di ottenere la migliore possibilità di sopravvivenza.

References

1. Gabriele R, Conte M, Egidi F, Borghese M: Umbilical metastases: Current viewpoint. World J Surg Oncol, 2005; 3(1):13.

2. Trebing D, Göring HD: The umbilical metastasis. Sister Mary Joseph and her time. Hautarzt, 2004; 55:186-89.

3. Dar IH, Kamili MA, Dar SH, Kuchaai FA: Sister Mary Joseph nodule. A case report with review of literature. J Res Med Sci, 2009; 14(6):385-87.

4. Powell FC, Cooper AJ, Massa MC, Goellner JR, Daniel WP: *Sister Joseph's nodule: a clinical and histologic study.* J Am Acad Derm, 1984; 11:610-15.

5. Goodheart RS, Cooke CT, Tan E, Matz LR: Sister Mary Joseph's nodule. Med J Aust, 1986; 11:477-78.

6. Majmudar B, Wiskind AK, Croft BN, Dudley AG: *The Sister Mary Joseph nodule: Its significance in gynecology.* Gynecol Oncol, 1991; 11:152-59.

7. Piura B: *Umbilical metastasis: Sister Mary Joseph's nodule*. Harefuah, 2006; 11:505-509.

8. Ching AS, Lai CW: Sonography of umbilical metastasis (Sister Mary Joseph's nodule): From embryology to imaging. Abdom Imaging, 2002; 27:746-49.

9. Coll DM, Meyer JM, Mader M, Smith RC: Imaging appearances of Sister Mary Joseph nodule. Br J Radiol, 1999; 72:1230-33.

10. Masmoudi A, Boudaya S, Charfeddine A, Dammak A, Amouri M, Khabir A, Marrekchi S, Bouassida S, Sallemi T, Krichen MS, Turki H, Zahaf A: Sister Mary Joseph's nodule: Report of five cases. Int J Dermatol, 2008; 47:134-36.

11. Sugarbaker PH: Sister Mary Joseph's sign. J Am Coll Surg, 2001; 193:339-40.

12. Martinez-Palones JM, Gil-Moreno A, Perez-Benavente MA, Garcia-Gimenez A, Xercavins J: Umbilical metastasis after laparoscopic retroperitoneal paraaortic lymphadenectomy for cervical cancer: A true port-site metastasis? Gynecol Oncol, 2005; 97(1):292-95.

13. Tso S, Brockley J, Recica H, Ilchyshyn A: Sister Mary Joseph's nodule: an unusual but important physical finding characteristic of widespread internal malignancy. Br J Gen Pract, 2013; 63:551-52.

14. Safini F, Naqos N, Sahraoui S, Benider A: Sister Mary Joseph's nodule: Unusual case. J Cancer Res Ther, 2016; 12(1):428.

15. Al-Mashat F, Sibiany AM: Sister Mary Joseph's nodule of the umbilicus: is it always of gastric origin? A review of eight cases at different sites of origin. Indian J Cancer, 2010; 11:65-69.

16. Piura B, Meirovitz M, Bayme M, et al: Sister Mary Joseph's nodule originating from endometrial carcinoma incidentally detected during surgery for an umbilical hernia: A case report. Arch Gynecol Obstet, 2006; 274: 385-88.

17. Panaro F, Andorno E, Di Domenico S, Morelli N, Bottino G, Mondello R: Sister Joseph's nodule in a liver transplant recipient: Case report and mini-review of literature. World J Surg Oncol, 2005; 11:4.

18. Touraud JP, Lentz N, Dutronc Y, Mercier E, Sagot P, Lambert D: *Umbilical cutaneous metastasis (or Sister Mary Joseph nodule) disclosing an ovarian adenocarcinoma.* Gynecol Obstet Fertil, 2000; 11:719-21.

19. Kolwijck E, Boss EA, van Altena AM, Beex LV, Massuger F: Stage IV epithelial ovarian carcinoma in an 18 year old patient presenting with a Sister Mary Joseph's nodule and metastasis in both breasts: A case report and review of the literature. Gynecol Oncol, 2007; 11:583-85.

20. Steck WD, Helwig EB: *Tumors of the umbilicus*. Cancer, 1965; 11:907-11.

21. Barrow MV: *Metastatic tumors of the umbilicus*. J Chronic Dis, 1966; 19:1113-17.

22. Salemis NS: *Umbilical metastasis or Sister Mary Joseph's Nodule as a very early sign of an occult cecal adenocarcinoma*. J Gastrointest Canc, 2007; 38(2-4):131-34.

23. Palaniappan M, Jose WM, Mehta A, Kumar K, Pavithran K: Umbilical metastasis: A case series of four sister Joseph nodules from four different visceral malignancies. Current Oncology, 2010; 17(6):78-81.