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Two case reports of umbilical metastasis: the enigmatic Sister Mary Joseph nodule

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ABSTRACT

Background: Umbilical metastasis, also known as Sister Mary Joseph nodule, is a rare pathognomonic clinical sign suggesting the presence of an internal cancer.

Case Presentation: We describe two female patients with Sister Mary Joseph nodule. In one case, there was a relapse of cancer. In the other patient, the Sister Mary Joseph nodule was the first and only clinical sign of an abdominal malignancy. We will briefly discuss the association with various internal malignancies as well as the pathogenesis and differential diagnosis.

Conclusion: We conclude that Sister Mary Joseph nodule is a sign of intra-abdominal malignancy most frequently associated with gastro-intestinal or gynecological cancer.

It can be the first and only clinical sign of abdominal malignancy in an otherwise healthy appearing patient or it can be an indication of oncological progressive disease, tumor relapse.

Umbilical lesions should raise suspicion of a Sister Mary Joseph nodule, but a differential diagnosis must be made with other primary umbilical malignancies as well as with benign conditions involving the umbilicus.

Keywords: Sister Mary Joseph nodule, metastasis, umbilicus, gastric signet cell adenocarcinoma, ovarian serous papillary adenocarcinoma.

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Background

The first clinical description of umbilical metastasis was made in 1896 by the French surgeon Edouard Quenu [1]. It is also known as "Sister Mary Joseph nodule". This description was first used by Hamilton Bailey, an English surgeon, in his book "Demonstrations of physical signs in clinical surgery" in honor to Sister Mary Joseph [2]. Sister Mary Joseph (1856-1939), born as Julia Dempsey, was superintendent nurse of Dr William James Mayo at St. Mary's Hospital (nowadays Mayo Clinic) in Rochester. She observed that patients with an intra-abdominal malignancy sometimes presented an umbilical nodule. Dr William James Mayo described the phenomenon but did not mention Sister Mary Joseph [3]. A Sister Mary Joseph nodule can be the only sign of malignancy in an otherwise healthy appearing patient [4,5]. We describe two female patients with a Sister Mary Joseph nodule. The Sister Mary Joseph nodule was the first clinical sign of malignancy in one patient. In the other patient, the Sister Mary Joseph nodule was the first clinical sign of relapse of her primary tumor despite negative radiological findings.

Case Presentation Patient 1

A 71-year-old female consulted in February 2017 with complaints of dysphagia, loss of appetite, and weight loss. Peripheral blood values as well as biochemistry were within normal limits. computed tomography (CT)- imaging disclosed diffuse widening of the stomach wall without pathological lymph nodes. Endoscopy showed a suspect tumoral lesion at the greater curvature of the stomach at the proximal stomach corpus. Biopsy revealed a less differentiated adenocarcinoma with immunophenotype CK7+, MUC5AC+, and CDX2+, compatible with gastric signet cell adenocarcinoma. Additional staging with CT thorax- abdomen, echoendoscopy and diagnostic laparoscopy showed clinical stadium cT3N1M0. Preoperative platinum-based chemotherapy was given, followed by total gastrectomy with lymph node dissection. Viewing microscopically positive sectionplane, chemotherapy was intensified to (TCF) Taxol-Cisplatinum – 5 – Fluorouracil (TCF) scheme. Radiotherapy was not applied due to the risk of fistulation. Further follow-up was uneventful for more than 2 years. In September 2019 a routine abdominal CT scan did not show any tumoral recidive. Nevertheless, the physician observed a hard nodular umbilical plaque with a diameter of 1.5 cm and suspicious macroscopical features (Figure 1). Histopathological evaluation revealed metastasis of the gastric signet cell adenocarcinoma, suggesting a Sister Mary Joseph nodule (Figures 2 and 3). Because of proven tumor relapse, she went through several treatments with chemotherapy. The patient died in April 2021. The overall survival was 19 months after the diagnosis of the Sister Mary Joseph nodule.

Case Presentation Patient 2

A 62-year-old female visited the outpatient department of surgery in November 2020 for a hard painless umbilical nodule with diameter of 2.5 cm. In another hospital, a diagnosis of umbilical hernia had been made. Biopsy was performed and showed an epithelial high-grade malignant serous papillary tumor with immunoreactivity

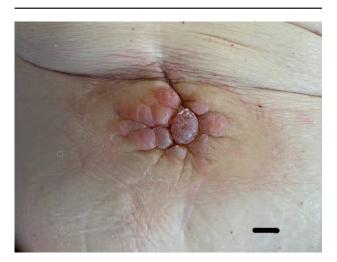


Figure 1. Umbilical skin with bluish black Sister Mary Joseph nodule of patient invaded by neoplastic cells from gastric less differentiated adenocarcinoma (Scale bar: 1 cm).

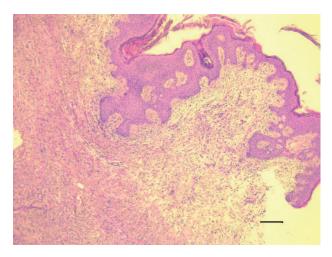


Figure 2. Umbilical skin (Sister Mary Joseph nodule) infiltrated by diffuse proliferation of malignant epithelial cells of gastric less differentiated adenocarcinoma (magnification 10×. Scale bar :200 μm. Hematoxylin/Eosin stain).

for estrogen receptor, p53, and PAX-8, highly suggestive for an umbilical metastasis (Sister Mary Joseph nodule) of an ovarian serous papillary adenocarcinoma (Figures 4 and 5). Magnetic resonance imaging (MRI) followed by laparoscopy and subsequent debulking revealed a high grade serous papillary ovarian adenocarcinoma (FIGO grade IIIB) with omental and peritoneal metastasis (TNM: pT3b N0 G3). Adjuvant chemotherapy was started with six cycli of Carboplatinum-Taxol. The patient is alive and disease free.

Discussion

Umbilical metastasis is found in 1%-3% of abdominal malignancies most frequently with gastric and ovarian carcinoma. Sister Mary Joseph nodule presents as an umbilical nodule that may be painful and discharge fluid. The size can range between 0.5 and 15 cm. It is very important to

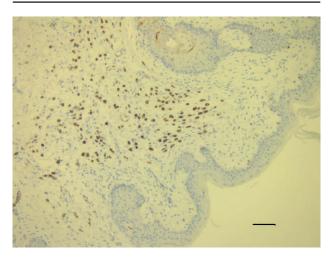


Figure 3. Umbilical skin (Sister Mary Joseph nodule) infiltrated by diffuse proliferation of malignant epithelial cells of gastric less differentiated adenocarcinoma displaying strong cytoplasmic immunoreactivity for cytokeratin 7 (immunohistochemistry for mouse anti-human monoclonal antibody CK7 with peroxidase/ DAB visualization magnification 40×. Scale bar :50 μm)

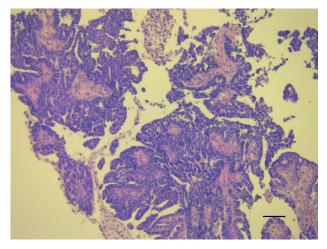


Figure 4. Biopsy of Umbilical skin (Sister Mary Joseph nodule) displaying neoplastic tissue consisting of serous papillary high grade malignant epithelial tumor (magnification 40×. Scale bar: 50 µm. Hematoxylin/Eosin stain).



Figure5. Biopsy of umbilical skin (Sister Mary Joseph nodule) displaying neoplastic tissue consisting of serous papillary high grade malignant adenocarcinoma with strong nuclear immunoreactivity for PAX-8 suggesting ovarian origin (magnification 40x. Immunohistochemistry for mouse anti-human monoclonal antibody PAX8 with peroxidase/DAB visualization magnification 40x. Scale bar: 50 µm).

bear in mind that a Sister Mary Joseph nodule can be the only sign of malignancy in an otherwise well patient [4,5]. This was the case in the second patient. Metastasis to the umbilicus is quite rare and accounts for only 10% of all cutaneous metastases.

In many reports, the most common cause is gastro-intestinal cancer (35%-65%) and genito-urinary cancer (12%-35%) among which gastric cancer and ovarian cancer are often mentioned [4,5]. In one of the two patients, the umbilical metastasis was the first sign of ovarian neoplasia, more specifically papillary serous adenocarcinoma. It is worth mentioning that the patient's umbilical nodule was first diagnosed in another hospital as a benign umbilical hernia. A biopsy performed in our hospital disclosed the malignant nature of the nodule and suggested the possibility of a gynecological tumor. In the other patient, the appearance of a Sister Mary Joseph nodule was the first sign of relapse of her gastric signet cell adenocarcinoma, although the clinical imaging (CT scan) was not conclusive for malignancy. ¹⁸F-FDG PET/MRI or ¹⁸F-FDG PET/CT can be of value not only for highlighting Sister Mary Joseph nodule but also for detecting the primary malignant tumor and staging [6,7]. It is, therefore, very important to be clinically aware of the possibility of malignancy when exploring an umbilical nodule. The finding of a Sister Mary Joseph nodule bears an ominous prognosis for the patient. Median survival time ranges from 2 to 11 months for a known primary tumor and 10 months for an unknown primary tumor [8]. Review of the literature shows very few cases of gastric signet ring cell adenocarcinoma presenting as a Sister Mary Joseph nodule [4,9,10].

Differential diagnosis must be made with primary umbilical tumors (38% of cases) such as primary umbilical adenocarcinoma and malignant skin tumors as melanoma, basal and squamous cell carcinoma [11]. Benign lesions include endometriosis (32% of all cases), omphalit, keloid tissue, hernia, urachal duct cysts, abscesses, pyogenic granuloma, epidermoid cysts, pyoderma gangrenosum, and foreign body reaction (piercing material). We reviewed the archives of our pathology department in Lier from 2010 to 2021 and found one case of a primary umbilical malignant tumor consisting of a basal cell carcinoma.

The exact genesis of Sister Mary Joseph nodule is not very well known. Some authors hypothesize hematogenous spread by arteries or veins, lymphatic spread, direct infiltration by peritoneal dissemination and direct extension along the embryonic ligaments [12]. These fetal structures develop into ligaments or peritoneal folds after birth. The fetal umbilical structures become four ligaments: median umbilical ligament (urachus), median umbilical ligament (umbilical arteries) ligamentum teres and falciform ligament (umbilical vein). The umbilical region is connected by the lymphatic system to the axillary, inguinal and para-aortic lymph nodes. There is a rich arterial, as well as venous blood supply connecting the umbilical region with the inferior epigastric and deep circumflex iliac vessels as well as several anastomoses from the internal mammary vein, or from the portal system of the liver. Dissemination of malignant cells can occur by the fibrotic embryonal remnants or by the rich periumbilical lymphatic, arterial and venous network.

We conclude that Sister Mary Joseph nodule is a rare but pathognomonic sign of malignancy. It is important that physicians pay attention to this sign because it can lead to a rapid diagnosis. Differential diagnosis must be made with primary malignant umbilical lesions, as well as with benign umbilical lesions such as umbilical hernia as was the case in one of our patients. Biopsy can elucidate the exact nature of an umbilical nodule and suggest a possible origin in case of malignancy.

List of Abbreviations

CDX2 Caudal related homeobox gene 2

CK 7 Cytokeratin 7

CT computed tomography DAB 3,3' diaminobenzidine

FIGO Federation Internationale de Gynécologie

et d' Obstétrique

MRI Magnetic Resonance Imaging
MUC5AC Gel forming/secreted mucin 5AC
P53 Tumor suppressor gene protein 53

PAX8 Paired box gene 8

PET Positron Emission Tomography
TCF Taxol-cisplatinum- 5-Fluorouracil

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Written informed consent was obtained for the clinical picture from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	Patient (gender, age)	Females: 71 and 62 years
2	Final diagnosis	Metastasis gastric adenocarcinoma, metastasis ovarian serous papillary adenocarcinoma
3	Symptoms	Dysphagia, weight loss, umbilical plaque
4	Medications	Chemotherapy
5	Clinical procedure	Imaging, biopsy, gastrectomy, hysterectomy + bilateral ovarectomy
6	Specialty	Oncology