Sister Mary Joseph Nodule (SMJN) – A Review

Sajad Ahmad Salati* and Lamees Sulaiman Alsulaim

Unaizah College of Medicine and Medical Sciences, Qassim University, Unaizah, Kingdom of Saudi Arabia

Abstract: Sister Mary Joseph Nodule is an eponymous term referring to an umbilical nodule harbouring malignant metastatic cancer. It is a physical finding that is uncommon yet significant since it indicates the late manifestation of a variety of deep-seated abdominopelvic malignancies. This review article briefly revisits the historical background, epidemiology, anatomical routes of metastasis, clinical presentation, differential diagnosis, diagnostic work-up, clinical significance and prognosis of Sister Mary Joseph's nodule.

Keywords: Sister Mary Joseph's Nodule (SMJN), Umbilical metastasis, Cutaneous metastasis, Abdominopelvic cancer, Eponymous sign.

INTRODUCTION

A medical eponym is a term for a disease or condition that is derived from the name of a person or location. Eponyms also make it convenient to refer to groups of pleomorphic conditions whose detailed descriptions are otherwise hard to recall and describe. Additionally, eponyms frequently provide a historical backdrop and a connection to the advancement of medical knowledge in relation to a particular disease [1]. For the description of the advanced metastatic diseases, various medical eponyms are in use including Sister Mary Joseph Nodule (SMJN), Troisier's sign, Virchow's node and Blumer's shelf [1-4]. This review article has been drafted to revisit the historical background, epidemiology, anatomical routes of metastasis, clinical presentation, differential diagnosis, diagnostic work-up, clinical significance and prognosis of SMJN.

METHODS AND MATERIALS

Systematic literature search was conducted through electronic databases, including PubMed, Research Gate, SEMANTIC SCHOLAR and Scopus using the key-words "Sister Mary Joseph Nodule" and "Umbilical metastasis ". The search was carried out by using individual keywords with a combination of Boolean Logics (AND). Studies published in English language were used and the studies in the time frame of 2002-2022 were preferred and only those earlier references were used that had concepts that have not been revalidated in recent years.

HISTORICAL BACKGROUND

In 1846, the first case of umbilical metastasis originating from the stomach was published when Store described a circumscribed tumor of the umbilicus that closely simulated an umbilical hernia. Baluff in 1854 and Nelaton in 1860 also reported cases of umbilical metastases [3,6]. William James Mayo (1861-1939) of the Mayo Clinic in 1928, referred to umbilical metastasis as "trouser button navel" and in 1949, Sir Hamilton Bailey coined phrase "Sister Mary Joseph's nodule" to describe all the metastatic lesions of the umbilicus, in his book '*Demonstrations of Physical Signs in Clinical Surgery', to* honour Sister Mary Joseph (1856-1939), a nurse who first observed the nodule at the St. Mary's Hospital (now Mayo Clinic) of Rochester, Minnesota. Sister Mary (born as Julia Dempsey), worked as the first surgical assistant of the Dr. William J. Mayo and was responsible for prepping patients scheduled for surgery [7-9]. It was while performing this task she first noted that some patients discovered to have advanced intraabdominal malignancy at surgery had unusual nodules located around the umbilicus. This observation even allowed her to "choose" the patients who might be suitable candidates for surgery with the Mayo brothers' full approval [7-10].

Anatomy of the Umbilical Region & Routes of Metastasis

The umbilicus is a complex invaginated scar like structure located on the abdominal wall between the peritoneum and transversalis fascia. The fetal umbilical cord structures get obliterated and change into peritoneum folds or ligaments after birth. Urachus forms the median umbilical ligament, the left umbilical vein becomes the ligamentum teres, which continues to produce the falciform ligament in the liver, while the umbilical arteries form the medial umbilical ligaments. Inferior epigastric vessels and, sometimes, an obliterated vitello-intestinal duct connecting the umbilicus to the ileum can be recognized in the lateral umbilical folds [3,11].

*Address correspondence to this author at the Unaizah College of Medicine & Medical Sciences, Qassim University, Saudi Arabia; Mob: 00966530435652; E-mail: docsajad@yahoo.co.in, docsajad@gmail.com

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Arterial Circulation

The umbilical region is richly supplied by arteries that includes the paired inferior epigastric and deep circumflex iliac arteries arising from the external iliac artery, as well as the superior epigastric arteries branching from the internal mammary artery [7,11].

Venous Circulation

Venous drainage from the umbilical region takes three main routes: (a) superficial epigastric vein draining caudally into the femoral vein, (b) internal mammary veins continue cranially, emptying into the axillary vein, (c) small veins that are connected to the portal system by way of the ligamentum teres [7,11].

Lymphatic System

Lymphatics of the umbilical region follows the venous system and drain into the axillary, inguinal, and para-aortic lymph nodes. Lymphatics follows the veins and drain after forming two systems: superficial and deep. The superficial system from above the umbilicus drains into the axillary nodes and the inguinal nodes from below the umbilicus. The deep lymphatic system drains into the internal thoracic nodes and courses to the nodes around the external iliac arteries and/ or abdominal para-aortic nodes [7,12].

Certain lymphatics pass along the falciform ligament and pierce the diaphragm to enter the anterior mediastinum [13-15]. It is these extensive connections to intraabdominal spaces through a vast network of arterial, venous, lymphatic vessels as well as ligamental attachments that have been linked to the spread of intraabdominal malignancy to umbilicus. Even though the precise mechanism remains unclear, however, various hypotheses point towards these possible dissemination pathways: direct extension from a contiguous tumor (the most important), hematogenous (arterial, venous), lymphatic and direct extension along the vestigial remnants of embryonal ligaments [15-16]. For gastrointestinal tumors, direct extension through the peritoneum is thought to be the preferred route [11] and for the female reproductive systems, however, hematogenous, venous, and lymphatic spread represent the routes of metastasis [15, 17]. In addition, direct implantation following laparoscopy is another mode of spread of tumors to the umbilicus [8].

Epidemiology

Umbilical metastasis is rare in clinical practice and represents only 10% of all cutaneous metastasis in cancer [11]. The age of diagnosis of cases with SMJN ranges from 18–87 years with a mean of 50.6 years [18] and there is a predominance of females with male to female ratio of 0.69 [8]. In about 14–33% of patients, the discovery of umbilical metastasis is the first manifestation of an otherwise unknown neoplasia [19-21].

Piura *et al*. have reported a 51-year-old woman, in whom a SMJN coexisting with a large fibroid uterus was incidentally detected during operation for suspected strangulated umbilical hernia. Subsequent laparotomy had confirmed endometrial carcinoma metastasizing to the umbilical region [22]. Caulo *et al*. have reported a case of an 82-year-old woman who presented with an ulcerated umbilical nodule which on evaluation was identified as a SMJN, representing the only distant metastasis from a silent caecal adenocarcinoma [23]. Munoz *et al*. reported a 44-year-old female with poorly differentiated malignant neoplasm involving ovaries, whose clinical presentation was progressive abdominal distension which she had attributed to pregnancy and a tumour protruding through her umbilical area that was oozing serosanguinous fluid [24]. Salemis has reported an extremely rare case where the SMJN was the first sign of a caecal adenocarcinoma and became evident 8 months before the onset of the disease [25].

In contrast, among those patients with known neoplasia, the umbilical nodules are an early sign of recurrence in about 40% and in about 59% of cases, the umbilical metastases occur after discovery of the primary tumor [19, 26]. The primary sources for metastasis to the umbilicus are as depicted in Table **1**. About two-third of primary lesions arise from the gastrointestinal tract, stomach, and colon being the more common sites. The origin of the primary tumor is unknown in 15%–30% patients. The gastrointestinal tract (GIT) is the most common site of the primary neoplasm (35 to 65%) in males and the organs in decreasing order of frequency are: stomach (25%), colorectal (10%), and pancreas (7%) [11, 27-32]. Gynaecological neoplasms, on the other hand, are the most prevalent primary site in females, with ovarian serous papillary cystadenocarcinoma being the most common (34%), followed by endometrial and cervical carcinoma [7, 33].

Primary thoracic malignancies from lungs, pleura and esophagus are rarely associated with SMJN and only a few cases have been reported so far [28,29, 35-37].

Table 1: Primary Sources for Metastasis to the Umbilicus

Digestive system	Genitourinary system	Female reproductive system	Miscellaneous
Stomach	Prostate	Ovary	Respiratory
Colon	Kidney	Uterus	System
Pancreas	Penis	Fallopain tube	Breast
Small bowel		Cervix	Mesothelioma
Vermiform			Hematological
Gallbladder			

Clinical Significance

The presence of SMJN has traditionally been considered a sign of advanced, inoperable primary malignancy and hence is analogous to “a tip of an iceberg" [38-40]. Prognosis is poor and the average survival time has been reported to be 11-12 months with less than 15% of the patients surviving beyond 2 years [41-43]. In some patients, however, depending on the state of the primary neoplasm and the patient's general condition, surgery and/or chemotherapy may improve survival [1, 30, 42].

Clinical Features

The most common physical finding of SMJN is a firm, irregular and painless nodule. The size can vary between 0.5–15 cm [43-45] though it is typically less than 5 cm in diameter.

Figure 1: Sister Mary Joseph’s Nodule (SMJN) with erythematous surface. Source: 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; DOI: https://doi.org/10.3399/bjgp13X673900

The nodule may appear normal skin coloured, whitish, bluish violet, darkish or brownish red [46] as shown in Figures **1** and **2**. The surface of the nodule may appear fissured and ulcerated (Figure **2**) and a sanguineous, mucinous, serous, or purulent secretions may also be discharged [47].

Figure 2: Sister Mary Joseph’s Nodule (SMJN) with multiple inflamed ulcers. Source: Mouna Kouira, Imen Bannour, Mohammed Raouf Ben Abdesslem, Nihed Abdessayed, Badra Bannour, "Ovarian Cancer Was Discovered in Sister Mary Joseph’s Nodule", Case Reports in Medicine, vol. 2022, Article ID 5131705, 3 pages, 2022. https://www.hindawi.com/journals/crim/2022/5131705/

SMJN is generally solitary but there are rare reports of multiple lesions. Ehmann *et al*. reported ten firm, umbilicated, erythematous, polygonal SMJNs (size up to 7 mm), partly covered with central haemorrhagic

Table 2:

Differential diagnosis	Associated features
Primary malignant umbilical tumor (melanoma, basal cell carcinoma, squamous cell carcinomas, myosarcoma, and adenocarcinoma)	Clinically may be indistinguishable from a Sister Mary Joseph's nodule.
Umbilical and paraumbilical hernia	May be congenital or acquired; uncomplicated hernias are reducible and associated with a visible /palpable cough impulse
Umbilical endometriosis	Occurs specifically in females of reproductive age; presents with a bleeding umbilical nodule especially during menstruation.
Keloid	History of skin trauma or navel piercing.
Omphalolith	Poor personal hygiene leading to hardening of exfoliated skin and sebum accumulated within the umbilicus.
Benign cutaneous lesions (epidermal cyst, dermatofibroma, verrucae, lipoma, polyp, angioma, etc)	Dermoscopic findings of Sister Mary Joseph nodules showed a polymorphous vascular pattern and a white or milky-red, amorphous area. Benign lesions showed different dermoscopic patterns: pigment networks with white areas (dermatofibromas), thrombosed capillaries (verrucae), and the "pore sign" (epidermal cysts).
Pyogenic granuloma	Often associated with pregnancy, medications and injury to the skin; The lesions break and bleed easily.
Pyoderma gangrenosum	Typically associated with an underlying chronic disorder, e.g., inflammatory bowel disease, rheumatoid arthritis, and myeloproliferative disorder
Urachal duct cyst	Usually asymptomatic preperitoneal lump; becomes painful when infected.
Pilonidal sinus	Pain and swelling, as well as a purulent umbilical discharge; usually in young active hairy males with deep umbilicus.
Foreign body	May present as discharge; identification of a foreign body.

crusts or scales in a 52-year-old previously diagnosed case of advanced stage of an adenocarcinoma of the stomach [48].

Differential Diagnosis

Various benign and malignant cutaneous disorders that develop on the umbilicus can be confused with the SMJN; the clinical, imaging, dermoscopic and histopathological differences may be useful for establishing a differential diagnosis [49-50] as depicted in Table **2**.

Diagnostic Work-Up

To determine the root cause of an umbilical mass, a thorough history and physical examination supplemented with imaging and histopathology is required. Imaging modalities include sonograms (USG), computerized tomography (CT), and magnetic resonance imaging (MRI). CT scan is often the first modality adopted in clinical practice, as it offers a global look within the body (Figures **3**, **4**). However, an increased radiation exposure to the patient is the disadvantage of this tool. In resource rich settings, MRI is being used for the purpose but the undeveloped and the developing world, the high cost and limited availability may prohibit its routine use [51].

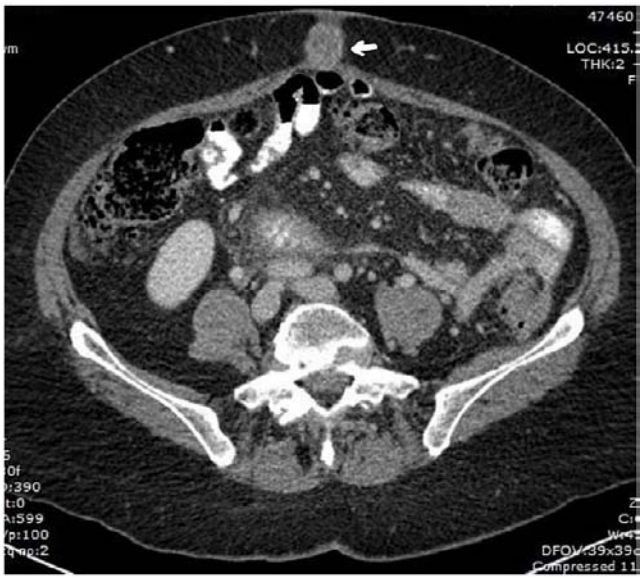

Figure 3: CT scan showing umbilical lesion (SMJN). Source: Dharan M, Ryan-Fisher C. Sister Mary Joseph Nodule and Concomitant Pancreatitis as Initial Presentation of Pancreatic Adenocarcinoma – Case Report and Review of the Literature. Cureus 13(12): e20069. doi:10.7759/cureus.20069

Sonography is economical imaging modality with no problem of radiation exposure and its widespread availability makes it a good choice for initial evaluation of suspected SMJN. High-resolution sonographic

Figure 4: CT scan showing pancreatic tumor in the tail. Source: Dharan M, Ryan-Fisher C. Sister Mary Joseph Nodule and Concomitant Pancreatitis as Initial Presentation of Pancreatic Adenocarcinoma – Case Report and Review of the Literature. Cureus 13(12): e20069. doi:10.7759/cureus.20069

imaging is able to demonstrate the nature of the solid umbilical nodules even when clinical diagnosis is difficult [11]. USG further offers an advantage of dynamically observing and guiding the needle throughout any biopsy process. In recent years, Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography FDG PET/CT and FDG PET/MRI have been reported as an innovative imaging tools in the identification of Sister Mary Joseph nodule by display of intense FDG uptake [52-54].

After imaging suggests an umbilical metastasis, for a definitive diagnosis, a histopathological analysis of specimen retrieved under imaging guidance through a fine-needle aspiration cytology (FNAC) or core biopsy is conducted [55]. Immunohistochemical staining may be required to identify the primary lesion (Figure **5**). FNAC has been suggested as an initial diagnostic procedure as it is simple, fast, accurate and inexpensive but can also spare the patient from other invasive diagnostic procedures [56-57]. There were no reported complications even when the needle penetrates the intestinal wall [58]. Handa *et al*. reported the achievement of diagnosis of six cases of Sister Mary Joseph's nodule by FNAC [59]. In all the cases, FNAC was the first modality and subsequently the patients were investigated for the primary tumor.

Management

The aetiology of the primary malignancy, patient preference, and the patient's clinical condition should all be considered when managing the disease. For some patients, palliative care may be the sole option as disease is usually advanced, although in carefully chosen circumstances, patients may benefit from more aggressive therapies such surgery, chemotherapy, and radiotherapy [11,60-62]. The patients where SMJN is detected before definitive treatment of the primary tumor rather than as a recurrence of it also have been found to have better outcome [63-64].

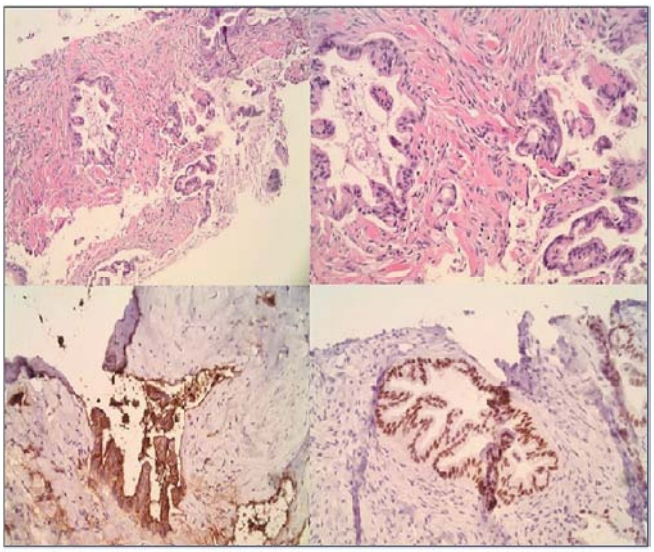

Figure 5: Core biopsy of the umbilical nodule depicting immunohistochemistry (IHC) positive for pankeratin, CK 7, CA 19-9, CEA, CDX2, CK 19 and negative for CK 20, TTF-1, Napsin A, PAX8. Source: Dharan M, Ryan-Fisher C. Sister Mary Joseph Nodule and Concomitant Pancreatitis as Initial Presentation of Pancreatic Adenocarcinoma – Case Report and Review of the Literature. Cureus 13(12): e20069. doi:10.7759/cureus.20069

CONCLUSION

Sister Mary Joseph's nodule is an uncommon but an important differential diagnosis to be considered in patients presenting with umbilical lumps. The presence of SMJN generally signifies an advanced, metastasizing cancer with a poor prognosis but in certain situations, an aggressive surgical approach combined with adjuvant therapy may improve the outcomes.

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