

# Beyond the surface: The primary care diagnostic challenge of Sister Mary Joseph nodule

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## ABSTRACT

Sister Mary Joseph nodule is a rare manifestation of metastatic umbilical malignancy, most commonly associated with gastrointestinal and genitourinary cancers. It often signifies advanced disease and carries a poor prognosis. Early recognition is critical, yet diagnostic delays may occur due to nonspecific presentations in primary care. We report a case of a 63-year-old Malay woman with a history of diabetes mellitus, hypertension, and hyperlipidemia, presented with an 8-month history of progressive umbilical skin growth, mild abdominal discomfort, and constitutional symptoms, such as loss of weight and loss of appetite over two months. Retrospectively, she noticed an erythematous nodular skin lesion over the umbilicus, which had slowly increased in size over the last 8 months. She visited health clinics four times, where the lesion was treated as eczema, and she was prescribed steroid creams. However, her symptoms persisted. One month before referral, she developed significant weight loss, prompting her doctor to refer her to a dermatology clinic for suspected skin cancer. We aim to enhance clinical awareness among primary care providers about recognizing and promptly treating the disease to prevent further deterioration.

**Keywords:** Sister Mary Joseph nodule, delayed diagnosis, umbilical metastasis, gastric carcinoma

## INTRODUCTION

The term Sister Mary Joseph (SMJ) nodule was coined by British surgeon Sir Hamilton Bailey in 1949 in honor of Sister Mary Joseph Dempsey, a nurse superintendent and first surgical assistant to Dr. William J. Mayo at St. Mary's Hospital in Rochester, Minnesota. Sister Mary Joseph was the first to observe the association between umbilical nodules and intra-abdominal malignancies [1].

SMJ nodule is a rare clinical finding, occurring in approximately 1-3% of all intra-abdominal malignancies and accounting for 10% of all cutaneous metastases. Among cases of umbilical metastasis, two-thirds originate from gastrointestinal (GI) tract malignancies, with the stomach and colon being the most common primary sites. Pancreatic cancer accounts for approximately 6% of cases, and gynecological malignancies (ovarian and uterine cancers) constitute about 20% [1].

The presence of an SMJ nodule is usually indicative of advanced disease and carries a poor prognosis, with a median survival of less than one year, ranging from approximately 7.9 months to 14.6 months following diagnosis [2]. Diagnosing an SMJ nodule in primary care can be challenging due to its rarity

and the potential for misidentification as benign umbilical conditions, such as umbilical hernias, keloids, or dermatologic lesions such as eczema. This can lead to delays in recognizing the underlying malignancy [3].

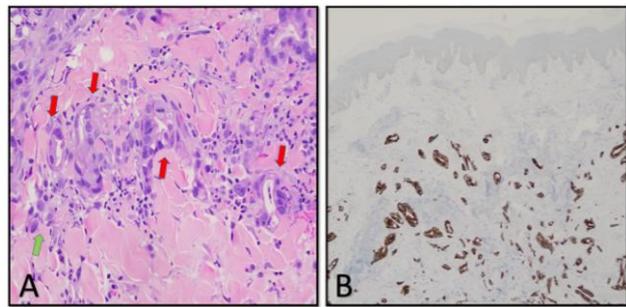
A comprehensive patient history, meticulous physical examination, and biopsy are essential for early detection of an SMJ nodule. Identifying this clinical sign and symptom promptly can lead to earlier diagnosis and treatment of the underlying malignancy, potentially improving patient outcomes [3].

## CASE REPORT

A 63-year-old Malay housewife presented with a progressively enlarging umbilical lesion over the past eight months. It was painless and non-itchy. The onset was insidious, and the lesion gradually increased in size. She initially sought medical attention at four different primary care centres, where the lesion was misdiagnosed as an eczematous skin condition based solely on its clinical appearance of the lesion. The nodule was crusted and associated with a plaque like lesion for which she was prescribed topical steroid creams. However, her symptoms persisted, and the lesion showed no improvement



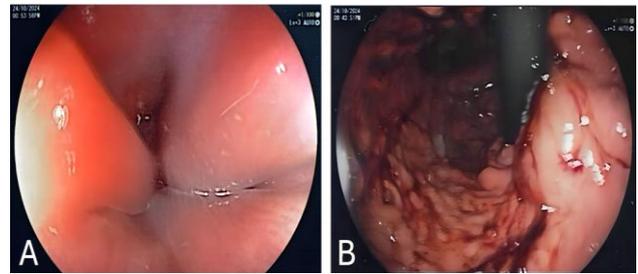
**Figure 1.** An SMJ nodule (Reprinted with permission of the patient)



**Figure 2.** Photomicrograph shows (A) infiltrative malignant epithelial tumor arranged in irregular glands (red arrow) and groups (green arrow) & the tumor cells show immunoreactivity to (B) CK7 (A: Hematoxylin-eosin stain; original magnification,  $\times 200$  & B: Original magnification  $\times 40$ ) (Reprinted with permission of the patient)

despite adherence to the treatment and regular follow-ups at primary care clinics. Over time, she experienced significant weight loss of approximately 4 kg and was noted to have a firm mass in the lower abdomen. She subsequently returned to the nearest health clinic for further evaluation. This prompted the attending primary care doctor to refer her to the dermatology clinic for assessment of a suspected skin malignancy.

Upon physical examination at the dermatology clinic, she was found to have a lobulated, nodular umbilical lesion measuring approximately  $2 \times 2$  cm, with a brownish-grey appearance, an erythematous periphery, and a dry, mildly tender surface (Figure 1). A firm, non-mobile periumbilical mass measuring around  $5 \times 5$  cm was palpated and fixed to the underlying structures. No discharge or ulceration was observed. The abdomen was soft and non-distended, with no organomegaly. No other cutaneous lesion was seen with normal lymph nodes and per rectal examination. A systemic review did not indicate signs of jaundice, ascites, or pedal edema. Laboratory investigations taken by the dermatology team revealed elevated tumor markers, with carcinoembryonic antigen (CEA) of  $21.2 \mu\text{g/L}$  and cancer antigen 125 of  $343.4 \text{ U/mL}$ . Routine blood tests, including full blood count, liver function tests, and renal profile, were largely



**Figure 3.** (A) OGDS revealed a tumor at the gastroesophageal junction (white arrow), approximately 40 cm from the upper incisors, extending distally about 2 cm & (B) An area of raised, suspicious-appearing mucosa was observed at the proximal body and posterior wall of the stomach (red arrow) (no definite ulcerative or polypoidal growth was identified) (Reprinted with permission of the patient)

unremarkable except for mild anemia with hemoglobin at  $10.5 \text{ g/dL}$  and low sodium levels of  $132 \text{ mmol/L}$ .

A biopsy of the umbilical lesion was performed. Histopathological examination revealed skin tissue with an infiltrative malignant epithelial tumor arranged in irregular glands and solid groups within the dermis and subcutaneous tissue (part A in Figure 2). No evidence of keratinization is seen. The tumor cells exhibit moderate to markedly pleomorphic vesicular nuclei with conspicuous nucleoli, and abundant eosinophilic to clear cytoplasm. A panel of immunohistochemical tests are helpful as a guide for the identification and classification of carcinoma of unknown primary site. The staining patterns of cytokeratin 7 (CK7) and CK20 help in defining subsets of carcinomas. The likely primary sites based on morphology of adenocarcinoma and pattern of CK7 positive (part B in Figure 2)/CK20 negative include the upper GI tract, pancreaticobiliary tract, breast, salivary gland, lung, thyroid and female genitalia tract. The possibility of primary site is narrowed down with negative TTF1 stain that exclude lung and thyroid, and negative PAX8 stain that exclude female genitalia tract. However, no single antibody is fully sensitive and specific for a particular tumor. Therefore, to determine the possible primary origin, it requires multidisciplinary approach including clinical findings and radiological imaging.

She was referred to the surgical team for further evaluation due to a suspected SMJ nodule, which raised concern for an underlying intra-abdominal malignancy. A diagnostic oesophagogastroduodenoscopy was subsequently performed, revealing a tumor at the gastroesophageal junction (GOJ) extending approximately 2 cm distally (part A in Figure 3). Additionally, an area of raised, suspicious-appearing mucosa was also noted at the proximal body and posterior wall of the stomach (part B in Figure 3). No definite ulcerative or polypoidal growth was identified, and there was no evidence of luminal obstruction. Biopsies were obtained, confirming the diagnosis of gastric adenocarcinoma.

Subsequently, a contrast-enhanced computed tomography (CT) of the abdomen and pelvis was performed, revealing an infiltrative mass centered at the GOJ with pancreatic involvement, multiple abdominal wall nodules with intraperitoneal extension, and suspicious pulmonary metastases. Based on endoscopic findings, histopathological results from the umbilical lesion, imaging studies, and tumor marker levels, a diagnosis of locally advanced gastric

adenocarcinoma with metastatic disease was established. These findings confirm metastatic adenocarcinoma, with the SMJ nodule representing the first clinical manifestation of the advanced malignancy.

The patient started chemotherapy by the surgical oncology team. However, she later presented herself with worsening abdominal pain and persistent vomiting. X-ray imaging revealed free intra-abdominal fluid and air under the diaphragm, raising concerns for gastric perforation. Despite aggressive resuscitation, fluid replacement, and supportive care, her condition continued to deteriorate. Given the extent of her disease and her clinical decline, palliative care was initiated.

She was subsequently discharged with symptomatic management, including oral morphine for pain relief, and scheduled for follow-up care to monitor symptom progression and optimize comfort-focused treatment before eventually passing away at her home 4 months following the diagnosis of SMJ nodule.

## DISCUSSION

The SMJ nodule is a rare but significant physical finding representing cutaneous metastasis of intra-abdominal or pelvic malignancies, often associated with gastric, pancreatic, ovarian, or colorectal cancer [4]. It is presented as a firm, irregular, and often umbilical mass, sometimes with ulceration, discharge, or induration. Although it serves as an external manifestation of advanced malignancy, its diagnosis remains challenging in primary care due to its rarity, non-specific presentation, and resemblance to benign dermatological conditions [5]. Many primary care doctors lack familiarity with SMJ nodules, leading to misdiagnosis or delayed referrals, which can significantly impact prognosis. Similar to our case, it was also reported that a patient with SMJ nodules presented with no GI disturbance despite underlying advanced GI malignancy [3]. This is likely due to the early peritoneal metastasis, minimal intraluminal tumor growth, and tumor location, as reported in [6]. Although SMJ nodules are almost always indicative of advanced, inoperable GI malignancy, an accurate diagnosis and timely referral can significantly reduce the emotional and financial burden on patients [7].

Since most umbilical lesions encountered in primary care are benign, such as umbilical hernias, epidermoid cysts, lipomas, or infections, doctors may not immediately suspect malignancy. Misdiagnosis as a benign skin condition delays further investigation, leading to an undiagnosed metastatic cancer until later stages. Unlike other cutaneous metastases, which often affect multiple sites, the SMJ nodule is uniquely confined to the umbilicus, making it easily overlooked if physicians are unaware of its clinical significance. The nodule typically presents as a painful, firm mass with irregular borders and a hard consistency. Its surface may exhibit ulceration and necrosis, often accompanied by bloody, serous, purulent, or mucous discharge. While its size generally falls between 0.5 and 2 cm, some nodules can enlarge to as much as 10 cm [1, 2]. In our case, the nodule exhibited these characteristic features, except for the absence of ulceration and any discharge.

Given its strong association with metastatic disease, the management of SMJ nodules primarily focuses on identifying the underlying malignancy and determining the extent of

disease spread. A thorough clinical evaluation, supplemented by imaging modalities such as CT scan, MRI, and PET-CT, is crucial for staging. Ultrasound-guided fine-needle aspiration biopsy or core biopsy provides histopathological confirmation, while tumor markers (CEA, CA 19-9, and CA-125) assist in identifying the primary tumor site. However, the diagnostic approach can vary depending on the healthcare provider's familiarity with cutaneous metastases. While primary care physicians often rely on clinical examination—which may not be definitive—dermatologists and oncologists, who are more experienced with skin metastases, may recognize SMJ nodules earlier and initiate advanced diagnostic testing without delay. While histopathological examination and diagnostic imaging are essential for confirming metastatic origin, these investigations are often not readily available in primary care settings [4]. In a study comparing biopsy efficiency among clinicians, dermatologists required fewer biopsies to diagnose one skin cancer compared to primary care physicians and other non-dermatology clinicians [8]. As seen in our case, limited access to biopsy and imaging forces primary care physicians to rely on external referrals, which can extend the diagnostic timeline, particularly in healthcare systems with specialist shortages or long waiting lists.

Misdiagnosis and delayed referrals further complicate the recognition of SMJ nodules. Since early symptoms can be mild or absent, patients often ignore the lesion, leading to advanced disease at presentation. Many primary care doctors may attempt empirical treatments such as antibiotics for suspected infection, topical steroids for eczema, or watchful waiting, further delaying the necessary oncological evaluation. In a retrospective study in [9], delayed diagnosis of SMJ nodule was frequently attributed to its initial misinterpretation as benign umbilical lesions, including hernias or cysts. This diagnostic delay contributed to late-stage presentations, limited therapeutic options, and consequently poor patient outcomes. Consistently, it was reported that SMJ nodules are particularly deceptive and may mimic conditions such as umbilical endometriosis (Villar's nodule) or post-surgical scars, especially in women and patients with prior abdominal surgeries [3]. This highlights the importance of increased awareness among primary care doctors regarding the differential diagnosis of umbilical lesions.

The treatment of SMJ nodules is primarily palliative, reflecting its association with advanced malignancy and poor prognosis. As reported in [10], systemic chemotherapy remains the cornerstone for GI and gynecologic cancers. In selected cases, targeted therapies or immunotherapy may be considered based on molecular profiling and tumor origin, although such approaches are rarely reported due to the advanced disease stage at presentation.

Surgical resection is rarely an option, except in select cases of oligometastatic disease, and radiotherapy is used for symptomatic relief, particularly in cases of pain or bleeding [6]. A multidisciplinary approach is crucial for optimizing treatment. Palliative and supportive care are essential in symptom management, focusing on pain relief (NSAIDs, opioids, and nerve blocks), wound care for ulcerated nodules, and ascites management through paracentesis. Nutritional support, psychological counselling, and hospice care further enhance patient well-being. In our case, systemic chemotherapy and palliative pain management were particularly relevant in preventing discomfort and complications.

Given the median survival of approximately 7.9 months following diagnosis, treatment of SMJ nodule often focuses on maximizing comfort and quality of life [2]. In our case, a shorter survival period (4 months) was seen due to the delay of recognition and referral by the primary care team, similar to a case that has been reported earlier [4]. Highly suspicion and early specialist referral is crucial to prevent delays in initiating care, especially in resource-limited settings. Ensuring timely access to palliative interventions aligns treatment with patient-centered goals, emphasizing symptom relief and dignity in end-of-life care.

## CONCLUSION

In conclusion diagnosing an SMJ nodule in a primary care setting is fraught with challenges, including clinical unfamiliarity, misdiagnosis, limited access to advanced diagnostics, and delayed referrals. Since primary care doctors rarely encounter SMJ nodules, they are often mistaken for benign umbilical lesions, causing critical delays in recognizing underlying advanced malignancy. Furthermore, the absence of on-site biopsy capabilities and limited access to imaging prolong the diagnostic process. To improve outcomes, it is crucial to enhance primary care education on rare cutaneous metastases, streamline referral pathways, and facilitate multidisciplinary care for prompt cancer diagnosis and treatment.

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