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Review Article

Sister Mary Joseph's Nodule - Clinical Aspests, Pathophysiology and Therapeutic Possibilities

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Abstract

Sister Mary Joseph's nodule (SMJN) is an uncommon but clinically important cutaneous sign of visceral malignancy, presenting as metastatic involvement of the umbilicus. It is reported in approximately 1-3% of patients with intra-abdominal or pelvic neoplasms, most frequently originating from adenocarcinomas of the stomach, ovary, colon, or pancreas. Less common primary sites include the endometrium, gallbladder, lung, and prostate. The metastatic spread to the umbilical region can occur via several mechanisms, including direct peritoneal extension, lymphatic and hematogenous dissemination, or through embryonic remnants such as the urachus, the umbilical vein, and the falciform ligament. Clinically, SMJN manifests as a firm, irregular, and sometimes painful umbilical nodule, which may ulcerate or discharge serous or sanguinous fluid. In many cases, it represents the first visible sign of an otherwise occult malignancy, making its recognition of critical diagnostic value for dermatologists and other clinicians. As a readily accessible cutaneous marker, SMJN provides an opportunity for early suspicion of advanced intra-abdominal cancer, which can lead to timely imaging studies, biopsy, and referral for oncological evaluation. The prognosis associated with SMJN remains poor, with median survival reported between 6 and 12 months, reflecting its association with late-stage disease and widespread metastasis. Treatment is primarily palliative and depends on the type and extent of the underlying malignancy. Therapeutic strategies may include systemic chemotherapy, targeted therapy, or limited surgical excision for symptomatic relief, all within the framework of a multidisciplinary approach involving oncology, surgery, radiology, and dermatology. For dermatologists, awareness of SMJN is essential, as it underscores the role of the skin as a window to systemic disease. Prompt recognition and biopsy of suspicious umbilical lesions may not only establish the diagnosis but also provide critical information guiding further management. Although rare, SMJN remains a valuable clinical indicator that bridges dermatology and oncology, highlighting the importance of cutaneous examination in systemic malignancy.

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1. Introduction

Sister Mary Joseph's node (SMJN) is a rare but clinically significant umbilical metastasis associated with advanced intra-abdominal or pelvic malignant tumors. It is found in 1-3% of patients with such neoplasias and most often originates from adenocarcinomas of the stomach, ovaries, colon, and pancreas. Metastasis to the umbilicus occurs by various mechanisms - direct invasion, lymphogenous and hematogenous routes, and through embryonic structures. SMJN is usually an indicator of an advanced process associated with an unfavorable prognosis and a median survival of about 10-11 months. Its timely recognition has important diagnostic and prognostic significance, since in some cases it is the first visible manifestation of occult malignancy.

2. Historical Facts

Sister Mary Joseph Dempsey (n é e Duffy; 1856-1939) was a Catholic nurse who worked as an operating assistant to Dr. William J. Mayo and Dr. Charles H. Mayo at St. Mary's Hospital in Rochester, Minnesota, from 1890 to 1915. The Mayo brothers later founded the world-famous Mayo Clinic [1]. During her practice, Sister Mary Joseph noticed that patients with advanced intra-abdominal malignancies often had skin changes in the umbilical region—papules, nodules, or infiltrates. The term "Sister Joseph's nodule" was coined in 1949 by the British surgeon Hamilton Bailey, who included it in his manual “Demonstrations of Physical Signs in Clinical Surgery” in honor of her clinical contributions to the recognition of this important prognostic sign [2].

3. Discussion

Umbilical metastases, known as SMJN, are rare but significant manifestation of advanced malignancies of intra-abdominal or pelvic origin. In men, the most common primary tumors metastasizing to the umbilicus are: gastric carcinoma (30%), colorectal (25%), and pancreatic (18%). In women, ovarian carcinoma is the leading cause (34%), followed by endometrial (12%) and colorectal (12%) [3]. Histologically, adenocarcinoma is the most common (about 75% of cases) [4]. Squamous cell carcinoma, undifferentiated tumors, carcinosarcomas, and malignant melanoma are rarely detected [5].

Metastatic involvement of the umbilicus may be the initial manifestation of malignancy or a marker of recurrence. In approximately 59% of cases, umbilical metastasis is detected after the diagnosis of the primary tumor, while in 40% it is the first clinical manifestation [6].

SMJN is a rare clinical finding, observed in approximately 1-3% of intra-abdominal and pelvic malignancies [6]. Its incidence varies depending on the location and type of the primary tumor. Although overall it appears to be slightly more common in men, SMJN is also diagnosed frequently in women, likely due to the predominance of ovarian carcinoma among the primary neoplasms [7]. Regardless of the time of onset, its presence indicates advanced disease and is associated with an unfavorable prognosis. Median survival after diagnosis ranges from 7.9 to 11 months and is even shorter in cases of undifferentiated tumors or additional metastatic spread [7].

These data emphasize the need for careful examination of the umbilical region in patients with known or suspected neoplasia. Recognition of umbilical metastasis may facilitate localization of the primary tumor and guide personalized therapeutic management, even in cases with poor prognosis.

4. Pathophysiology

The umbilical region is prone to metastatic involvement due to [5]:

1) rich arterial blood supply;
2) complex lymphatic network;
3) proximity to the peritoneal cavity;
4) presence of embryonic remnants.

The main mechanisms of metastasis are [8-13]:

1) Lymphogenous dissemination - most likely. It occurs through the umbilical and periumbilical lymphatic vessels, connected to the lymphatic network of the abdominal cavity;
2) Hematogenous dissemination - through the rich vascularization of the umbilical area;
3) Direct invasion - from peritoneal metastases or adjacent tumors. The umbilicus is separated from the peritoneum only by the transversalis fascia, which is not a barrier to direct invasion;
4) Embryonic remnants - urachus, umbilical vein or omphalomesenteric canal. They create an anatomical route, but are rarely a guiding mechanism.

Embryonic and vascular structures associated with the umbilicus:

1) Meckel's diverticulum (remnant of the vitelline duct);
2) Falciform ligament (associated with the v. portae);
3) Urachus (remnant of the allantois connecting the umbilicus to the urinary bladder);
4) Medial umbilical ligaments (remnant of the umbilical arteries) [9].

Vascular and lymphatic anatomy:

1) Arterial blood supply: a. epigastrica inferior (from a. iliaca externa) and a. epigastrica superior (from a. thoracica interna);
2) Venous drainage: v. epigastrica inferior → *v. femoralis; v. thoracica interna → v. axillaris;*
3) Lymphatic circulation:
   1) Superficial - to axillary and inguinal nodes;
   2) Deep - to paraaortic, internal thoracic and iliac nodes [11].

5. Primary Neoplasia in Sister Mary Joseph's Nodule

The most common primary tumors in Sister Mary Joseph's nodule are:

1) Gastrointestinal tract (GIT) (35-65%) - stomach, colon, pancreas [8];
2) Gynecological tumors (12-35%) - especially ovarian carcinoma [9];
3) Urogenital tract (UGT) and others - including prostate carcinoma, renal cell carcinoma, cholangiocarcinoma [10].

In about 15-30% of cases, the primary tumor cannot be identified at the time of diagnosis [6, 11].

6. Clinical Findings

SMJN presents as a single umbilical lesion, usually 0.5-2 cm in diameter, but can be up to 10 cm in diameter [5]. It is usually a firm, painless or slightly painful nodule, with a variable consistency - from elastic to firm. The color may be erythematous, bluish, brownish or pearly, and the surface - smooth, nodular, ulcerated or with excretion of serous, bloody or purulent secretion [12].

In about 30-40% of cases, it is the first visible sign of a malignant process, which emphasizes the importance of clinical vigilance [3, 6].

In advanced cases, systemic symptoms - weight loss, abdominal pain, anorexia, anemia, ascites, gastrointestinal or urogenital symptoms - are observed, depending on the localization of the primary tumor [13].

Clinical variants

There are four main types of SMJN according to the localization and mechanism of development [14]:

Type 1 - Typical form

Located in the navel itself. Most common. Main mechanism - direct tumor invasion through peritoneal spread [15].

Type 2 - Periumbilical metastases

Located in the subcutaneous tissue around the navel. Usually responds well to local treatment. The risk of perforation or GIT complications is low [16].

Type 3 - Metastases in the hernial sac

The tumor tissue is localized in the umbilical or paraumbilical hernia. Surgical treatment is often required [17].

Type 4 - Iatrogenic metastases

After surgical intervention - in the area of a previous surgical scar. May resemble type 1 or 2. Treatment approach requires personalization [18].

7. Diagnosis

Accurate diagnosis is essential to determine the origin of the umbilical lesion, its malignant nature and the choice of an adequate therapeutic approach. The diagnosis is supported by imaging (CT/MRI) as well as fine-needle aspiration cytology (FNAC), which allow both differentiation between primary and metastatic lesions and targeting of the primary tumor process. The combination of multidetector computed tomography (MDCT) and FNAC is considered the gold standard in establishing the nature of the lesion and localizing the primary tumor [14, 15]. MDCT provides both a detailed anatomical assessment of the abdominal cavity, peritoneum and retroperitoneal space and a detection of the primary malignant process, regional and distant metastases. FNAC allows for a rapid, minimally invasive and highly specific cytological assessment of the umbilical lesion.

If SMJN is suspected, the following diagnostic algorithm is recommended:

Physical examination

1) Assessment of the umbilical lesion: shape, consistency, firmness, pain, secretion
2) History of previous malignancies or surgical interventions

Main Imaging diagnostic tools

1) Abdominal wall and umbilicus ultrasound - initial screening for solid or cystic structure
2) MDCT of abdomen and pelvis with contrast - to detect the primary tumor and metastases

Cytological and histological evaluation

1) FNAC of the umbilical lesion
2) In case of unclear results - core biopsy for histological confirmation and immunohistochemical profiling

Additional imaging studies (in case of unknown primary neoplastic process)

1) CT or PET-CT scan is used to look for the primary tumor and assess the spread of the disease
2) MRI - if pelvic pathology is suspected, especially in women

3) Mammography, colonoscopy, gastroscopy, gynecological ultrasound - according to gender and clinical guidelines

Laboratory findins and tumor markers

CEA, CA-125, CA 19-9, CA 15-3, PSA, CK7, CK20, AFP, β-hCG и др., depending of the primary neoplastic process [16].

The etiology of the primary malignancy is a key prognostic factor. Tumors with peritoneal involvement or abdominal carcinomatosis usually have a worse prognosis. Timely use of the described algorithm supports not only early diagnosis, but also the proper therapeutic management.

8. Differential Diagnosis

About 90% of neoplastic lesions in the umbilical and periumbilical region are metastases from internal malignant tumors [8, 9]. Only about 10% are primary neoplasms originating from local embryonic remnants (vitelline duct, urachus), skin or soft tissue structures [13]. The most common among the primary tumors are adenocarcinomas [4]. Benign umbilical lesions are extremely rare (less than 1%) [18]. Table 1 demontarates a differential diagnosis of periumbilical skin nodules.

Table 1. *Differential diagnosis of periumbilical skin nodules.*

Category	Possible diagnosis
Metastatic tumors (COPS)	C - colorectal, stomach, pancreatic carcinomas
	O - ovarial, endometrial
	P - pertitoneal mesothelioma
	S - sarcoma, melanoma
Primary malignancies	Urachus and vitelline duct adenocarcinomas
	Melanoma
	Basal and squamous cell carcinomas
	Leiomyosarcoma
Benign tumors	Umbilical endometriosis (Villar nodule)
	Epithelial cysts (dermoid, epidermal)
	Fibromas, benign fibrous proliferations
	Umbilical granuloma, omphalitis
	Hernia
	Urinary and biliary fistula (urachus fistula)

9. Therapy

Umbilical metastases treatment depends on the characteristics of the primary tumor, the extent of metastatic disease, and the patient's general condition. The approach should be individualized, involving a multidisciplinary team, taking into account the patient's will, expected survival, and quality of life. In most cases, umbilical metastasis is a sign of advanced disseminated disease, and treatment is primarily palliative [19].

The main therapeutic strategies are:

A. Curative approach, which aims to achieve a cure for the patient or long-term remission, and not just to relieve symptoms. Patients with a single metastatic lesion and in good general health require intensive multimodal therapy, which includes:

1) Systemic chemotherapy directed at the primary tumor. This is the most commonly used approach, especially for ovarian, gastrointestinal, and pancreatic carcinomas. It may lead to regression of the umbilical mass but rarely achieves complete remission [20].
2) Surgical removal of the umbilical metastasis. In carefully selected patients with limited metastatic disease and good overall status, cytoreductive surgery with radical excision of the umbilical leision is considered. In some cases, it is combined with chemotherapy [21].

B. Palliative approach - in patients with multiple metastases and/or poor functional status, therapy is primarily palliative. The goal is to control symptoms and maintain quality of life through:

1) Maintenance therapy;
2) Systemic chemotherapy. Mainstay of treatment. The choice depends on the histology of the primary tumor (e.g. FOLFOX for colorectal carcinoma, aclitaxel/carboplatin for ovarian carcinoma).
3) Radiotherapy or local application of chemotherapeutic agents for painful, bleeding, or infected lesions [22]. Radiotherapy for Value Stream Map (VSM) is based on single clinical reports due to the lack of standardized protocols. Different regimens are used:
   1) 16 Gy in 2 fractions, combined with hormonal therapy (tamoxifen), with survival over 18 months;
   2) 30 Gy in 10-15 fractions, with good pain control;
   3) 45-56 Gy in 25-28 fractions in advanced cases, without significant side effects;
   4) Combined external beam radiotherapy and interstitial brachytherapy - 30 Gy + 12 Gy.

Targeted and immunotherapy, which is included in some histological subtypes with proven expression of specific molecules. For example, in HER2-positive gastric tumors (trastuzumab), in MSI-H or PD-L1-positive tumors - immunotherapeutic regimens (pembrolizumab) [23].

Treatment remains challenging due to the advanced stage of the disease at diagnosis. Surgical resection and chemotherapy can prolong survival in selected patients. Radiotherapy plays an increasing role in palliative symptom control, especially in the aging population and the increasing number of patients with cancer. The lack of large clinical trials re-

quires personalized intervention with a multidisciplinary approach.

10. Prognosis

SMJN is associated with advanced stage of the disease and a poor prognosis. The mean survival rate is 7-11 months as:

1) Patients with ovarian origin have a relatively better prognosis;
2) Longer survival is observed in cases with isolated umbilical metastasis and on cytoreduction combined chemotherapy;
3) The worst prognosis is observed with metastases with an unknown primary source [7].

11. Conclusions

Any umbilical lesion, regardless of its clinical appearance, requires careful assessment due to the possibility of metastasis. SMJN is usually associated with an unfavorable prognosis and an advanced stage of the primary focus, and in some cases it can be the first clinical manifestation of an underlying oncological process. Its timely recognition can facilitate the identification of the primary tumor and guide the diagnostic and treatment strategy.

Multidetector computed tomography (MDCT) and fine needle aspiration cytology (FNAC) play a key role in localizing and staging the primary process.

Modern treatment aims not only to control the primary disease, but also to improve the patient's quality of life. It should be multidisciplinary — with the participation of oncologists, surgeons, dermatologists and palliative specialists — and individualized, according to the patient's condition. In the case of solitary metastases and preserved general condition, a curative multimodal approach (surgery and chemotherapy) is possible, while in advanced disease, primarily palliative methods, including radiotherapy, are applied.

Abbreviations

SMJN	Sister Mary Joseph’s Nodule
GIT	Gastrointestinal Tract
UGT	Urogenital Tract
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
FNAC	Fine-needle Aspiration Cytology
MDCT	Multidetector Computed Tomography
PET-CT	Positron Emission Tomography-Computed Tomography
FOLFOX	Chemotherapy Regimen for the Treatment of Colorectal Cancer, Consisting of Folinic Acid, Fluorouracil, and Oxaliplatin
VSM	Value stream Map

Conflicts of Interest

The authors declare no conflicts of interest.

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