



Beyond the Surface: Sister Mary Joseph's Nodule in Metastatic Gallbladder Cancer: A Case Report and Review of Literature

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Ind J Med Paediatr Oncol

Abstract

Sister Mary Joseph's nodule (SMJN) is an umbilical nodule occurring because of metastasis of the abdomen and pelvic malignancies. It is a rare physical finding, reported in nearly 3% of patients with gastrointestinal or gynecological cancers. The majority of cases presents at a very advanced stage of the disease, and often results in dismal prognosis. Here, we report the case of a 54-year-old woman with metastatic gallbladder cancer, presenting with SMJN. The patient declined chemotherapeutic intervention following the cancer diagnosis and later arrived with an umbilical nodule, which was identified as SMJN. The patient was advised to take a gemcitabine-cisplatin regimen, but opted solely for palliative care and passed away within a few weeks of SMJN diagnosis. This case report emphasizes how an untreated malignancy can advance quickly and present as an unusual clinical sign. Drawing the attention of health care professionals to this clinical sign will eventually help in the early detection of disease progression and its management to improve survival outcomes.

Keywords

- Sister Mary Joseph's nodule
- gallbladder carcinoma
- umbilical mass

Introduction

Sister Mary Joseph's nodule (SMJN) refers to the umbilical manifestation of metastatic carcinoma of intra-abdominal and/or pelvic origin. It is a palpable nodule, bulging into the umbilicus, representing an advanced malignancy leading to unfortunate prognostic outcomes.¹ This peculiar physical finding was named in honor of Sister Mary Joseph, a surgical assistant at Mayo Clinic, who first pointed out that these cutaneous nodules might indicate the spread of intra-abdominal malignancies. It is highly uncommon and only found in 1 to 3% of cancer patients. In nearly 20% of the cases, it is the primary sign of malignancy. It is most commonly found in cancer of the stomach (30%), colon (25%), and pancreas (18%) in men, and ovarian (34%), endometrial (12%), and colon (12%) in women. The source of primary neoplasm remains

unknown in nearly 30% of the cases.² These nodules are often overlooked during physical examinations.

The review of the available literature reveals that the Gangetic belt is endemic for gallbladder carcinoma (GBC), accounting for a higher prevalence of this disease in India. Despite this, the occurrence of metastasis to the umbilicus from the gallbladder is only 2.4%.³ Furthermore, numerous epidemiological studies have shown a higher incidence of SMJN in females compared with males.⁴ The management mainly relies on gemcitabine with/without platinum compounds-based palliative chemotherapy. Apart from palliative chemotherapy, surgical resection of SMJN followed by radiotherapy is preferred in cases of isolated umbilical metastasis.⁴ Nonetheless, these nodules usually present in the advanced stages of the disease, which ultimately limits the

DOI <https://doi.org/10.1055/s-0045-1804501>.
ISSN 0971-5851.

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available treatment options. The overall survival (OS) of the patient usually depends upon the extent of metastasis and the treatment received. It has been demonstrated that the average survival is better with primary surgery followed by adjuvant chemotherapy (OS: 17.6–21 months) compared with surgery (OS: 7.4 months) or chemotherapy alone (OS: 10.3 months).⁵

In this case report, we present a case of SMJN in a patient diagnosed with metastatic carcinoma of the gallbladder. It is an atypical presentation of GBC that requires widespread awareness. Informed consent was obtained from the patient, and the patient's confidentiality was maintained.

Case Report

Here, we present a case of a 54-year-old woman, presenting with right upper quadrant pain, and dyspepsia for the past 10 days. Subsequently, the patient was diagnosed with cholelithiasis and underwent laparoscopic open cholecystectomy on June 2, 2023. Following the surgery, the patient was diagnosed with GBC metastasized to the liver and peritoneum. The patient was referred to a medical oncologist for further management of the malignancy and was advised to take a gemcitabine-cisplatin regimen. However, she refused to receive any chemotherapeutic interventions. The patient inconsistently visited the outpatient clinic for supportive treatment and pain management alone. On February 10, 2024, the patient presented with complaints of pain and itching in the umbilical region. On physical examination, the patient was icteric and SMJN was observed inferior to the umbilicus, nearly 2 cm in diameter (►Fig. 1). The patient was counseled regarding the cause behind the appearance of this nodule and prescribed sever-



Fig. 1 A Sister Mary Joseph's nodule inferior to the umbilicus, in a patient with metastatic gall bladder carcinoma.

al medications for symptomatic relief. The patient passed away on February 28, 2024.

Discussion

Gallbladder cancer is an aggressive malignancy that accounts for nearly two-thirds cases of biliary tract cancers. Owing to the deep-seated anatomical location of the gallbladder and nonspecific early-stage symptoms, most patients are diagnosed at an advanced stage of the disease. This limits the treatment options, resulting in poor prognostic outcomes.⁶ Nearly 50% of the patients present with regional lymph node metastasis at the time of diagnosis. The other most frequent sites for metastasis of gallbladder cancer include the liver, peritoneum, and nonabdominal sites such as the lung and brain.⁷ Cutaneous metastasis is extremely rare in this malignancy. This case report discussed skin metastasis of GBC in the form of SMJN, which is noteworthy in this patient population.

Numerous reports suggest that nearly 57% of umbilical nodules might be benign, including umbilical hernia, umbilical cyst, umbilical endometriosis, congenital lesions, umbilical polyps, and umbilical abscess. A careful differential diagnosis of a patient presenting with umbilical nodules can be difficult in some cases. A thorough examination of these lesions is essential as they might indicate potentially lethal malignancies.⁸

The precise mechanism of umbilical spread of neoplastic cells remains unidentified. However, several hypotheses have been put forward. Owing to its anatomical vicinity to the peritoneum, rich vascularization, and connections to embryological remains, the umbilicus is prone to being a location of metastasis. The proposed mechanisms for the umbilical seeding from primary tumors include hematogenous spread, lymphatic pathways, or contiguous extension. However, hematogenous spread to the umbilicus is rare in the absence of other sites of metastasis. Lymphatic drainage pathways in the para-aortic and pelvic nodes play crucial roles in the immediate transperitoneal spread of neoplasms. The contiguous spread occurs when the tumor cells that fall off are carried throughout the peritoneal cavity and adhere to the nearby organs, the umbilicus being one of them due to gravitational pull. This is considered to be the most common mechanism for the occurrence of SMJN.⁹

SMJN presents as a firm, irregular paraumbilical or umbilical nodule ranging from 1.5 to 10 cm in diameter. These nodules are occasionally painful and pruritic with mucinous, serous, or bloody discharge. They are identified at the time of diagnosis, at disease recurrence, or as a sign of disease progression as observed in our case. Moreover, the most common histology of umbilical skin metastases is adenocarcinoma (accounting for ~75% of cases), although it can also be rarely related to squamous cell carcinoma or undifferentiated cancer.¹⁰ These nodules are associated with a poor prognosis, with an average survival of 11 months. The management of these patients largely relies on palliative chemotherapy as surgery cannot be performed owing to the advanced stage of the disease.¹¹ Additionally, the review of

available literature regarding the various primaries, treatment received, and OS of SMJN are discussed in ►Table 1.

Gupta et al reported a case of a 32-year-old female diagnosed with GBC following laparoscopic cholecystectomy. The patient quickly progressed and was further presented with an umbilical metastasis within 1 month of the diagnosis. The patient received external beam radiotherapy followed by four cycles of fluorouracil-based palliative chemotherapy. Subsequently, after the treatment, the patient's symptoms subsided, and the nodule regressed by 90%. Moreover, abdominal ultrasonography revealed stable disease in the liver. The patient continued to receive palliative chemotherapy for 8 months following the diagnosis, which accounts for further clinical improvement in her symptoms. However, the OS in this case was not documented. This case highlights the significance of palliative chemotherapy and its impact on the patient's disease and quality of life. Furthermore, this case also presents a unique management strategy for SMJN originating from GBC. The external beam radiotherapy to the nodule and palliative chemotherapy demonstrated better survival outcomes and quality of life than other

SMJN cases. Despite this, further clinical studies and case reports are required to ascertain the benefits of this unique treatment approach.⁴

Another case reported by Karayiannakis and Knight describes a 59-year-old female patient who was diagnosed with cholelithiasis and subsequently underwent laparoscopic cholecystectomy. The surgery was uneventful and there were no signs of an underlying malignancy. However, a histological examination of the gallbladder revealed well-differentiated adenocarcinoma. Furthermore, there was no evidence of lymphatic or vascular invasion and the resection margins were clear. After 3 months of the surgery, the patient complained of periumbilical swelling and pain. The lesion was thoroughly examined and the biopsy revealed adenocarcinoma metastasized from the gallbladder. Furthermore, the computed tomography scan revealed that the umbilical region was the only site of recurrence. This case highlights laparoscopic cholecystectomy as a risk factor for umbilical metastasis. Moreover, the occurrence of SMJN in the absence of extensive metastasis so early after the surgery suggests tumor seeding secondary to it. However, this phenomenon is

Table 1 A literature review of SMJN cases from different primaries, treatment received, and overall survival

Author's name and year of publishing	Gender	Age	Primary tumor	Treatment received	Overall survival	References
Leyrat et al, 2021	Male	58 years	Metastatic pancreatic adenocarcinoma	1st line: fluorouracil, oxaliplatin, irinotecan; 2nd line: gemcitabine; 3rd line: fluorouracil, irinotecan	11 months 24 days	⁸
Menzies et al, 2015	Female	72 years	Metastatic pancreatic adenocarcinoma	Palliative supportive care and pain management	< 4 weeks	¹⁴
Nolan and Semer, 2012	Female	61 years	Metastatic papillary-serous endometrial carcinoma	Supracervical hysterectomy, bilateral salpingo-oophorectomy, omentectomy, small bowel resection, and generalized debulking with umbilical resection + palliative chemotherapy: 4 doses of paclitaxel + carboplatin	4 months	¹⁵
De Angeli et al, 2019	Female	80 years	Metastatic endometrial endometrioid carcinoma	Robotic single-site total hysterectomy and bilateral salpingo-oophorectomy + pelvic radiotherapy	35 months	¹⁶
Sina and Deng, 2007	Male	65 years	Poorly differentiated, epithelioid morphology metastatic prostate carcinoma	Palliative chemotherapy + radiotherapy	4 months	¹⁷
Rahman et al, 2012	Female	30 years	Poorly differentiated, squamous cell metastatic endometrial carcinoma	Endometrial curettage followed by exploratory laparotomy and herniotomy and para-aortic lymph node resection + palliative chemotherapy: 6 cycles of paclitaxel + carboplatin followed by 5 cycles of docetaxel + carboplatin	13 months	¹⁸

(Continued)

Table 1 (Continued)

Author's name and year of publishing	Gender	Age	Primary tumor	Treatment received	Overall survival	References
Aditi et al, 2021	Male	49 years	Metastatic adenocarcinoma of the gallbladder	Palliative chemotherapy	2 months	³
Ramia et al, 2016	Male	76 years	Poorly differentiated adenocarcinoma of gallbladder	Two layer gastrojejunostomy	Died during the postoperative period due to respiratory failure	¹⁹
Dodiuk-Gad et al, 2006	Female	64 years	Metastatic occult colon carcinoma	Surgical resection of colorectal tumor	3 months	²⁰
Dodiuk-Gad et al, 2006	Female	73 years	Undetected primary tumor	Surgical resection of the umbilical nodule followed by diagnostic laparoscopy, however, surgery was refused by the patient	4 months	²⁰
Dodiuk-Gad et al, 2006	Male	51 years	Metastatic adenocarcinoma of the lung	Palliative chemotherapy: 4 cycles of carboplatin + gemcitabine followed by addition of paclitaxel	9 months	²⁰
Kanayama et al, 2023	Female	58 years	Hormone receptor-positive metastatic breast cancer	Umbilical nodule excision followed by adjuvant hormonal therapy (toremifene) and radiation	5 years	²¹

Abbreviation: SMJN, Sister Mary Joseph's nodule.

not specific to laparoscopic cholecystectomy and cases of umbilical seeding have also been described in diagnostic laparoscopy and fine-needle aspiration.¹² Umbilical metastasis has been reported as early as 3 weeks and may even take up to 8 months after surgery to develop. The most plausible explanation of this phenomenon is that tumor seeding to the umbilicus occurs via rupture or significant manipulation of the gallbladder during the surgery. This may lead to increased spilling of tumor cells into the peritoneal cavity. Tumor seeding in incision sites can also occur due to frequent changes of tools and their transit via other ports, as well as the trapping of exfoliated tumor cells during deflation. Despite these shreds of evidence more case reports and clinical studies are required to provide a better understanding of this phenomenon.¹³

The aforementioned cases of SMJN originated from the gallbladder as observed in our case. The patient's survival could have been improved if the patient had received palliative chemotherapy. Moreover, alternate treatment recommendations such as the combination of chemotherapy with radiation should be given to the patient to offer them a better survival outcome. The case reported by Gupta et al highlights a unique treatment option for this disease. The provision of palliative chemoradiotherapy aided the patient in attaining a stable disease and hence significantly improved the survival outcomes and the quality of life. In the second case reported by Karayiannakis and Knight, laparoscopic cholecystectomy aided as a risk factor and led to the umbilical metastasis of

GBC. Similarly, in our case, the patient presented with SMJN 7 months postsurgery, which might indicate umbilical seeding of the tumor because of it. However, further case reports and novel, large multicentered studies of SMJN in different malignancies are required to spread awareness and improve the understanding of this distinctive clinical sign.

Conclusion

A rapidly developing umbilical mass should not be ignored, especially in patients with abdominal malignancies. To avoid such presentations, especially in cases of aggressive intra-abdominal malignancies necessary examinations, diagnostic modalities, and treatment according to the patient's needs should be exercised without delay. Moreover, clinicians should emphasize patient education and awareness regarding the severity of the disease and highlight the importance of palliative chemotherapy in such cases. Additionally, this case highlights the impact of poor socioeconomic background on treatment outcomes and patient quality of life. As every case report is unique, it can offer valuable insights into the mechanism and treatment approaches for this disease and ultimately improve the quality of health care provided.

Authors' Contributions

A.K., R.K. contributed to the conceptualization and design of the data. S.S. contributed to the acquisition of the data.

S.S., V.B.S. contributed to writing original draft of the manuscript. A.K., R.K. contributed to the review and editing of the manuscript.

Patient Consent

Informed consent was obtained from the individual who participated in this study.

Funding

None.

Conflict of Interest

None declared.

Acknowledgments

We are grateful to the patient and all the staff members of Oncowin Cancer Centre, Ahmedabad, for their kind support.

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