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Case report

Sister Mary Joseph's nodule: A rare metastasis of hilar cholangiocarcinoma: A new case report and review of the literature

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ABSTRACT

Introduction: Sister Mary Joseph's Nodule (SMJN) is a rare clinical sign of metastatic abdominal malignancies, particularly cholangiocarcinoma, with limited reported cases in the literature. SMJN is associated with poor prognosis, often indicating advanced disease with widespread metastasis.

Case presentation: we present a new case report of SMJN in a 46-year-old patient who presented with ten days of right upper quadrant pain, obstructive jaundice, and fever. Physical examination revealed obstructive jaundice with scratchy lesions in the trunk and tenderness in the right upper quadrant, along with a two-centimeter protuberant, tender ulcerated umbilical nodule. Despite previous management with antibiotics and local care, the nodule had been progressively growing over a month. Imaging studies revealed a hilar cholangiocarcinoma with extensive local invasion and multiple distant metastases, including cutaneous involvement at the umbilicus. Biopsies of the umbilical lesion confirmed metastatic adenocarcinoma of the biliary tree. Palliative measures, including biliary stent placement and chemotherapy, were initiated.

Discussion: SMJN is a rare but notable cutaneous manifestation associated with advanced intra-abdominal malignancies. Although often linked to gastric, pancreatic, and ovarian cancers, it is uncommonly reported with cholangiocarcinoma. SMJN typically signifies a late-stage, metastatic progression, with prognosis largely determined by the underlying primary cancer's aggressiveness and the extent of metastasis. In this case, SMJN presented alongside other symptoms of advanced disease, such as obstructive jaundice and extensive local invasion, underscoring its prognostic significance. Recognition of SMJN is essential for prompt diagnosis and initiation of palliative interventions in patients with suspected metastatic disease. This case adds to the limited literature on cholangiocarcinoma-associated SMJN and highlights the need for awareness among clinicians regarding atypical metastatic presentations, which may facilitate earlier diagnosis and tailored care strategies.

Conclusion: This case emphasizes the importance of recognizing SMJN as a rare but crucial indicator of advanced cholangiocarcinoma. It highlights the clinical challenges posed by metastatic cholangiocarcinoma and underscores the need for a comprehensive approach to palliative care in patients with SMJN.

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1. Introduction

Cholangiocarcinoma, a malignant tumor originating from the biliary epithelium, remains a significant challenge in hepatobiliary surgery due to its often insidious onset and poor prognosis. It accounts for approximately 3 % of all gastrointestinal cancers and is notorious for its aggressive nature and late-stage presentation [1]. The clinical manifestation of cholangiocarcinoma can vary widely, ranging from asymptomatic cases to severe obstructive jaundice. The majority of patients present with advanced disease, often complicated by metastasis to distant organs, which further complicates the therapeutic approach.

Umbilical metastasis, also known as Sister Mary Joseph nodule (SMJN), is a rare clinical finding indicative of advanced intra-abdominal malignancy [2]. While SMJN can arise from various primary tumors, including gastrointestinal, ovarian, and pancreatic cancers, its association with hilar cholangiocarcinoma is particularly uncommon. To the best of our knowledge, this is one of fewer than ten cases of hilar cholangiocarcinoma presenting with Sister Mary Joseph's Nodule reported in the literature. This underscores the rarity of this clinical manifestation and its potential diagnostic significance in advanced cholangiocarcinoma. This manuscript aims to explore the existing literature on umbilical metastasis specifically originating from hilar cholangiocarcinoma, focusing on its clinical significance, diagnostic considerations, management challenges, and prognosis.

By elucidating the nuanced clinical course of this patient and synthesizing insights from existing literature, this case report underscores the imperative for heightened vigilance and multidisciplinary engagement in the evaluation and management of umbilical metastases. Furthermore, it underscores the necessity for ongoing research efforts aimed at unraveling the underlying mechanisms driving such metastatic phenomena, thereby paving the way for more effective diagnostic modalities and therapeutic interventions in the realm of advanced malignancies.

2. Case presentation

A 46-year-old patient, without past medical history, presented to the emergency department with ten days of right upper quadrant pain, obstructive jaundice (dark-colored urine, light-colored stool, and yellowing of his skin), and fever. Physical examination revealed an obstructive jaundice with scratchy lesions in the trunk and tenderness in the right upper quadrant. It also found a two-centimetre protuberant, tender ulcerated umbilical nodule (Fig. 1A) that had been growing for a month and had been managed with antibiotics and local care without any improvement. Biological findings included leukocytosis at 19000 elements/mm3 with high CRP at 153 mg/L, hyperbilirubinemia (299 μmol/L) with direct predominance (158 μmol/L) and transaminases five times higher than the normal range. The diagnosis of Tokyo II acute cholangitis was then made. Abdominal ultrasonography showed a non-distended acalculous gallbladder with a 4.5mm thickened wall. The intrahepatic bile ducts were dilated and the common bile duct (CBD) was measured at 8mm. Computed tomography (CT) scans showed a hilar cholangiocarcinoma extending to the superior biliary convergence (Fig. 2A) and the right hepatic duct, invading the hepatic artery and the right portal branch with multiple secondary localizations: hepatic, peritoneal (Fig. 2C and D), adrenal, pulmonary, and cutaneous at the umbilicus (Fig. 2 B). Biopsies of the umbilical lesion were performed. The histopathologic analysis of the specimen showed the presence of cords of large tumor cells with atypical nuclei in the dermis suggestive of metastatic adenocarcinoma of the biliary tree (Fig. 1B). The biliary origin of the umbilical metastasis was confirmed by immunochemistry. Once the diagnosis of metastatic cholangiocarcinoma was established, a palliative biliary stent was placed and the patient was subsequently referred for palliative chemotherapy. After biliary stent placement, the patient experienced rapid relief from jaundice, confirmed by improved liver function tests. He began palliative chemotherapy with a gemcitabine-cisplatin regimen, adhering to the regimen, though he reported fatigue, nausea, and anorexia as side effects. These symptoms were managed with supportive medications and dietary advice. No complications from the stent or unanticipated adverse events were noted. A follow-up CT scan performed after these interventions showed stable disease, with the biliary stent in situ, evidence of aerobilia, and newly developed ascites (Fig. 3A and B). The umbilical nodule was no longer visible, indicating a partial response to treatment. To

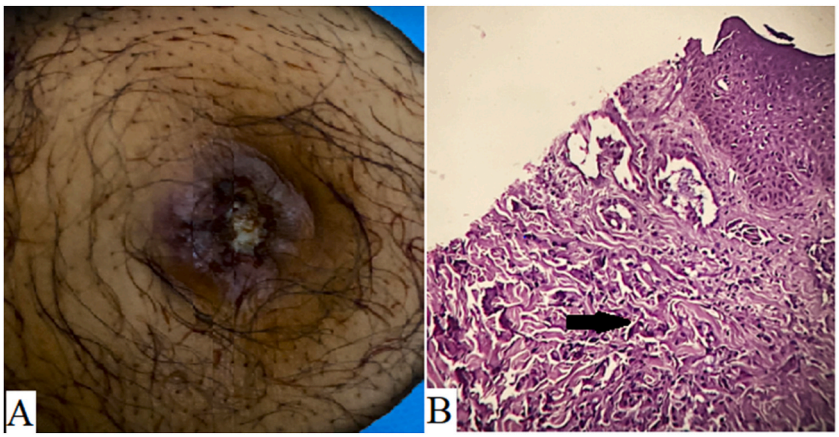

Fig. 1. Ulcerated umbilical nodule (A). Umbilical biopsy showing cords of large tumor cells with atypical nuclei in the dermis (Black arrow) (B).

further elucidate the anatomical and pathological findings, multiplanar reconstructed images in the coronal and sagittal planes were obtained from this follow-up CT scan and are presented in Fig. 3. However, due to the advanced stage of his disease, the patient's overall condition declined. Further imaging or clinician-assessed outcomes were unavailable to document his long-term response to treatment.

3. Discussion

The presented case of Sister Mary Joseph's nodule underscores several key clinical and diagnostic considerations that warrant comprehensive discussion. Umbilical metastases, though rare, serve as poignant indicators of advanced intra-abdominal malignancies, often heralding a grim prognosis. Here, we delve into the multifaceted aspects of this case, exploring its diagnostic challenges, therapeutic implications, and broader implications for clinical practice.

Sister Mary Joseph's nodule, characterized by umbilical metastasis, is a rare clinical manifestation often indicative of advanced intra-abdominal malignancies. The eponymous term pays homage to Sister Mary Joseph Dempsey, a surgical assistant of Dr. William Mayo, recognized for her astute observations of umbilical nodules in patients with undiagnosed abdominal cancers. These nodules serve as a poignant reminder of the intricate interplay between systemic disease and cutaneous manifestations.

SMJN is a rare umbilical lesion resulting from the metastasis of neoplasms in the pelvic and/or abdominal cavity [2]. It may be the earliest sign of an undiagnosed neoplasm. It can also indicate a recurrence or progression of a known tumor.

The most common sites of these cutaneous metastatic lesions are gastrointestinal tumors (predominantly the stomach) followed by genitourinary tract neoplasms (especially ovaries in females) [2].

To the best of our knowledge, only a few reports described SMJN as skin metastasis of cholangiocarcinomas which usually had a lymphatic spread. The aetiological mechanism of SMJN is not fully understood. The first hypothesis is a direct invasion from the peritoneum through lymphatic or blood vessels. The second hypothesis is extension along ligaments of embryonic origin (round ligament of liver, urachus) [3]. The presence of umbilical metastasis denotes an advanced stage of the primary tumor and is typically associated with a poor prognosis with an average survival time of 11 months [4]. The diagnosis of Sister Mary Joseph's nodule poses a significant challenge due to its nonspecific clinical presentation and rarity. They are commonly described as firm and irregular nodules measuring 1–2cm. These lesions can sometimes ulcerate or fistulise, with a serous, purulent, or bloody discharge [4]. In the case described, the patient initially presented with symptoms suggestive of obstructive jaundice, prompting an investigation into the underlying etiology. However, it was the incidental discovery of the umbilical nodule that ultimately led to the diagnosis of metastatic cholangiocarcinoma. This highlights the importance of a thorough physical examination and considering atypical metastatic presentations when evaluating umbilical lesions. Recognition of this rare manifestation can aid in early diagnosis and management of advanced abdominal malignancies. The diagnosis is classically confirmed by the anatomopathologic examination of the biopsy of the umbilical lesion. The use of positron emission tomography (PET)-CT has been described in one patient [5]. Furthermore, the presence

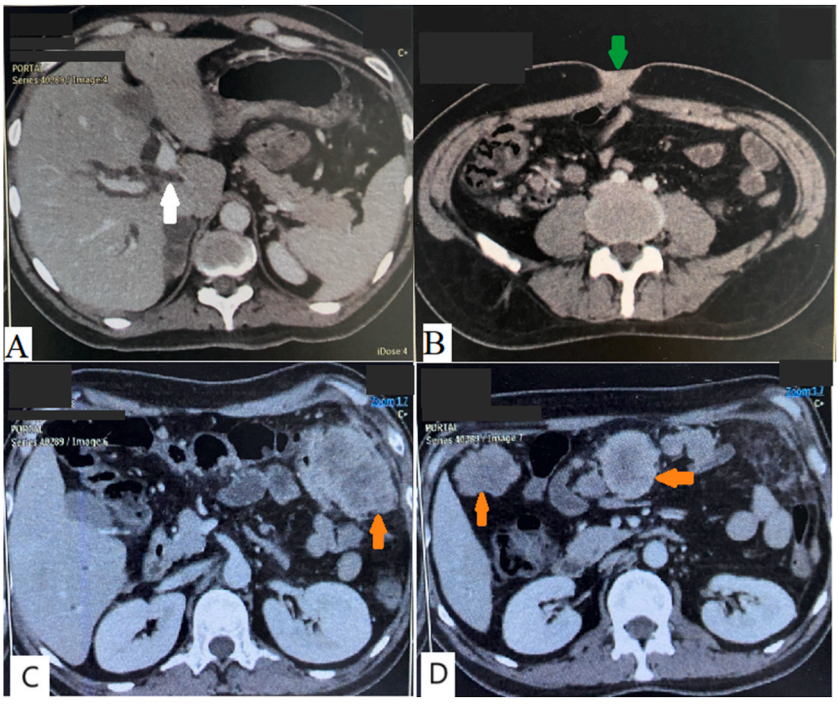

Fig. 2. CT of the abdomen showing hilar cholangiocarcinoma extending to the superior biliary convergence (White arrow) (A). Umbilical nodule (Green arrow) (B). Peritoneal metastasis (Orange arrows) (C and D).

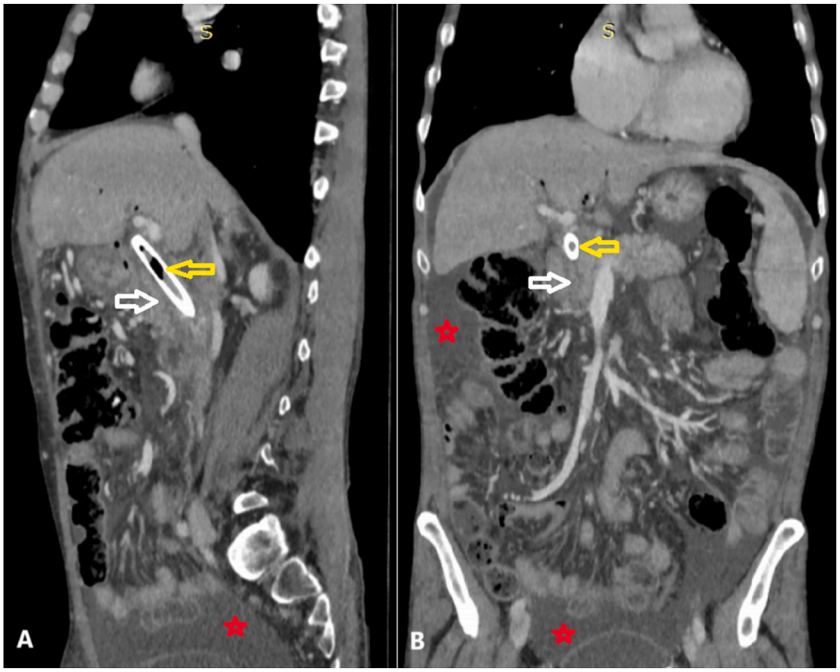

Fig. 3. Multiplanar reconstructed CT images demonstrating a thickened wall of the common bile duct consistent with cholangiocarcinoma (white arrow), the presence of a biliary stent (yellow arrow) with associated aerobilia, and ascites (red star).

of metastatic lesions at the umbilicus often signifies advanced disease with widespread dissemination. In this case, the identification of metastases to the peritoneum, adrenal glands, lungs, and skin underscores the aggressive nature of hilar cholangiocarcinoma and its propensity for hematogenous and lymphatic spread. Such extensive metastatic burden carries significant prognostic implications, correlating with poorer overall survival and limited treatment options. If it is a solitary metastasis, surgical excision is recommended [6], otherwise, palliative care including biliary stenting is often needed. Given the advanced stage of the disease at presentation, the therapeutic approach, in this case, was palliative, focusing on symptom management and quality of life optimization. Placement of a palliative biliary stent aimed to alleviate symptoms of obstructive jaundice, thereby improving the patient's comfort and facilitating the delivery of subsequent chemotherapy. However, it is important to recognize the limited efficacy of palliative interventions in the setting of advanced metastatic disease, with treatment goals shifting towards palliation rather than cure.

Moreover, the selection of chemotherapy regimens in metastatic cholangiocarcinoma remains a topic of ongoing debate, with no consensus on optimal first-line or salvage therapies. Current standard-of-care regimens typically involve combinations of gemcitabine

Table 1
Reported cases of umbilical metastasis (SMJN) of cholangiocarcinoma in the Literature.

Year of publication	Age	sex	Tumor characteristics	Management	Survival (weeks)
2010 [7]	48	female	cholangiocarcinoma	n/a	15
2011 [5]	69	female	Klatskin carcinoma type IV, stage IIIA	n/a	n/a
2012 [8]	17	female	cholangiocarcinoma in the mid-common bile duct	The patient did not consent to undergo endoscopic retrograde cholangiopancreatography for brush cytology and biliary stenting.	n/a
2013 [9]	77	male	Hilar cholangiocarcinoma	Palliative biliary stenting	3
2014 [10]	71	female	intrahepatic cholangiocarcinoma	n/a	n/a
2016 [11]	49	female	Klatskin tumor	palliative stenting of the biliary tree	
2018 [12]	59	male	extra-hepatic cholangiocarcinoma	palliative biliary stent	12
2020 [13]	53	male	hilar cholangiocarcinoma	excision of the Sister Mary Joseph nodule + palliative chemotherapy (capecitabine)	12
2022 [14]	61	male	hilar cholangiocarcinoma Bismuth Corlette type II	The patient refused chemotherapy	8
2024 (our case)	46	male	Klatskin tumor	Palliative chemotherapy	8

n/a = not available.

and cisplatin or oxaliplatin-based chemotherapy, although response rates are often modest, and disease progression is inevitable in the majority of cases. As such, there is a critical need for the development of novel therapeutic strategies targeting the unique molecular pathways driving cholangiocarcinogenesis and metastasis.

Only ten cases (including ours) of SMJN due to cholangiocarcinoma have been described in PubMed. Table 1 shows the demographic and clinicopathological details of all reported cases in the literature [5,7–14].

The case of Sister Mary Joseph's nodule serves as a poignant reminder of the intricate interplay between systemic malignancy and cutaneous manifestations. It underscores the importance of a holistic approach to patient care, encompassing thorough physical examination, interdisciplinary collaboration, and judicious utilization of diagnostic modalities. Moreover, it highlights the significance of early detection and prompt intervention in improving patient outcomes and mitigating disease progression.

4. Conclusion

The presented case exemplifies the diagnostic and therapeutic challenges associated with Sister Mary Joseph's nodules in the context of advanced intra-abdominal malignancies. By elucidating the clinical course of this patient and synthesizing insights from existing literature, we underscore the imperative for heightened vigilance, multidisciplinary engagement, and ongoing research efforts aimed at unraveling the complexities of metastatic disease. By sharing this case, we aim to enhance clinician awareness and promote earlier recognition of advanced malignancies.

CRediT authorship contribution statement

Imen Ben Ismail: Writing – original draft, Investigation, Data curation, Conceptualization. **Mouna Mlika:** Investigation, Data curation. **Ghazi Manai:** Data curation, Conceptualization. **Saber Rebii:** Visualization, Data curation, Validation. **Kamel Karma:** Conceptualization, Data curation, Visualization. **Ayoub Zoghlami:** Supervision, Data curation, Validation.

Ethics statement

Ethical review and approval were not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Data availability statement

No new data was generated for the research described in the article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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N/A.

References

[1] S. Rizvi, S.A. Khan, C.L. Hallemeier, R.K. Kelley, G.J. Gores, Cholangiocarcinoma — evolving concepts and therapeutic strategies, Nat. Rev. Clin. Oncol. 15 (2017) 95–111.
[2] R. Gabriele, M. Conte, F. Egidi, M. Borghese, Umbilical metastases: current viewpoint, World J. Surg. Oncol. 3 (2005) 13.
[3] I.H. Dar, M.A. Kamili, S.H. Dar, F.A. Kuchaai, Sister Mary Joseph nodule-A case report with review of literature, J. Res. Med. Sci. 14 (2009) 385–387.
[4] B.W. Ullery, H. Wachtel, S.E. Raper, Sister Mary Joseph's nodule presenting as large bowel obstruction: a case report and brief review of the literature, J. Gastrointest. Surg. 17 (2013) 1832–1835.
[5] M.L.M. Tan, A.K. Padhy, Umbilical metastatic deposit from recurrent cholangiocarcinoma: F18-FDG-PET-CT findings, Singap. Med. J. 52 (2011) 236–238.
[6] M. Palaniappan, W.M. Jose, A. Mehta, K. Kumar, K. Pavithran, Umbilical metastasis: a case series of our Sister Joseph nodules from four different visceral malignancies, Curr. Oncol. 17 (2010) 78–81.
[7] F. Al-Mashat, A.M. Sibiany, Sister Mary Joseph's nodule of the umbilicus: is it always of gastric origin? A review of eight cases at different sites of origin, Indian J. Cancer 47 (2010) 65–69.
[8] V. Agrawal, P.K. Garg, D. Mohanty, V. Jaswal, Umbilical nodule in cholangiocarcinoma, Saudi J. Gastroenterol. 18 (2012) 345–346.
[9] M.C. Reichert, G. Farmakis, R.M. Bohle, F. Lammert, V. Zimmer, Cholangiocarcinoma presenting as Sister Mary Joseph's nodule: case report and short review of the literature, J. Gastrointest. Cancer 45 (2) (2014 Jun) 231–233.

[10] M. Higuchi, S. Shibata-Kikuchi, T. Ito, C. Gondo, M. Takahara, Y. Moroi, et al., Marked melanocyte colonization of pigmented Sister Mary Joseph's nodule from intrahepatic cholangiocarcinoma, Eur. J. Dermatol. 24 (1) (2014 Jan-Feb) 125–126.
[11] M. Premkumar, D. Rangegowda, T. Vyas, S. Grover, Y.K. Joshi, C. Sharma, et al., Cholangicarcinoma presenting as a Sister mary Joseph nodule, ACG Case Rep J 3 (3) (2016) 209–211.
[12] D. Harrington, C. George, H. Ibrahim, S. Bhagani, Cholangiocarcinoma with a metastatic umbilical lesion, BMJ 363 (2018) k4041.
[13] V. Muppidi, S. Meegada, J.D. Eason, et al., Recurrent cholangiocarcinoma presenting as Sister Mary Joseph nodule after liver transplantation, Cureus 12 (11) (2020) e11673.
[14] M. Barbu, M. Mardare, R. Iosifescu, I. Bondoc, A. Văcărașu, A. Păunescu, L. Ali, C. Iacobescu, C. Călin, O. Ginghină, Sister mary JOSEPH'S nodule: first sign of cholangiocarcinoma recurrence, Romanian Journal of Clinical Research 5 (2) (2023).