

Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Journal of Cancer Research and Practice

journal homepage: <http://www.journals.elsevier.com/journal-of-cancer-research-and-practice>

Case report

Ampullary carcinoma with cutaneous metastasis



I-Ting Liu, Chia-Jui Yen*

Division of Hematology and Oncology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

ARTICLE INFO

Article history:

Received 27 July 2015

Accepted 11 September 2015

Available online 19 March 2016

Keywords:

Ampullary carcinoma
Cutaneous metastasis
Chemotherapy

ABSTRACT

Carcinoma of the ampulla of Vater is a rare gastrointestinal tumor. Additionally, cutaneous metastasis from such an internal malignancy is also uncommon. We reported the case of a 55-year-old man afflicted with ampullary carcinoma with cutaneous metastasis. The patient did not undergo the standard Whipple procedure but received chemotherapy due to apparent left neck lymph node metastasis noted by initial PET/CT imaging. The skin metastasis presented as a left neck infiltrating purpuric lesion, which was confirmed by skin biopsy approximately one year after the patient's disease was first diagnosed. Thereafter, the patient received further chemotherapy pursuant to his course of medical management. Skin metastasis usually represents a poor patient prognosis. In these cases, treatment of cutaneous metastasis typically includes systemic chemotherapy and local management such as radiation therapy or tumor excision. And when choosing a chemotherapy regimen for the ampullary cancer, the histological subtypes (intestinal or pancreatobiliary) should be comprehensively considered. In our review of the literature, the intestinal type seems to have less distant lymph node metastasis, advanced local invasion, as well as recurrence than pancreatobiliary type of ampullary cancer.

Copyright © 2016, The Chinese Oncology Society. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

When carcinoma of the ampulla of Vater is diagnosed, it is generally recognized to be a rarely occurring tumor. The overall incidence rate of the ampulla of Vater cancer was around 0.49 per 100,000 individuals in the United States, and represents only 0.2–0.5% of all gastrointestinal malignancies.¹ Cutaneous metastasis from internal malignancy is also uncommon, and estimated to represent around 0.7%–9% of all patients with internal cancers.² Lookingbill et al found that only 367 (5%) of 7316 oncology patients developed cutaneous metastasis in the tumor registry as noted in the Milton S. Hershey Medical Center (Hershey, PA, USA). Of that final 367 patients, 59 (0.8%) had skin involvement as their first sign of undiagnosed cancer. Breast cancer was the most commonly reported primary cancer involving skin (64.6%). Rosen and Schwartz describe neoplasm of the breast, colon, kidney, lung and ovary relatively likely to have cutaneous metastasis.³ Abdomen and chest were the most reported sites of skin metastasis.

In a Taiwanese report, Hu et al found 124 cases (1.02%) with cutaneous metastases from 12,146 patients with internal malignancies at Kaohsiung Medical University Hospital (Kaohsiung, Taiwan). The rate of skin metastasis was highest in patient with breast cancer (2.42%), followed by cancer of the lung (1.78%), oral mucosa (1.75%), colorectum (0.81%), stomach (0.80%) and esophagus (0.74%).² Compared to Caucasians, the overall rate of cutaneous metastasis appears to be lower in Taiwanese patient.

Here, we have presented a case of progressive ampullary cancer with cutaneous metastasis. Generally, pancreaticoduodenectomy (Whipple procedure) is the standard treatment for ampullary and periampullary adenocarcinoma.⁴ If metastatic disease is noted, chemotherapy schemes generally recommended for pancreatic cancer or intestinal malignancy may be considered according to the histological type.⁵

2. Case report

In February 2012, a 55-year-old man without previous systemic disease suffered from abdominal pain radiating to the back, and yellowish skin color. Ampulla of Vater cancer, cT2N1M1, cstage IV, with local and left neck lymph node metastasis were formally diagnosed by esophagogastroduodenoscopic biopsy, magnetic

* Corresponding author. Division of Hematology and Oncology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, No.138, Sheng Li Road, Tainan 704, Taiwan.

E-mail address: yencj@mail.ncku.edu.tw (C.-J. Yen).

Peer review under responsibility of The Chinese Oncology Society.

resonance cholangiopancreatography (MRCP) and positron emission tomography and computerized tomography (PET/CT) (Fig. 1A–C). Plastic and metallic biliary stents were placed for

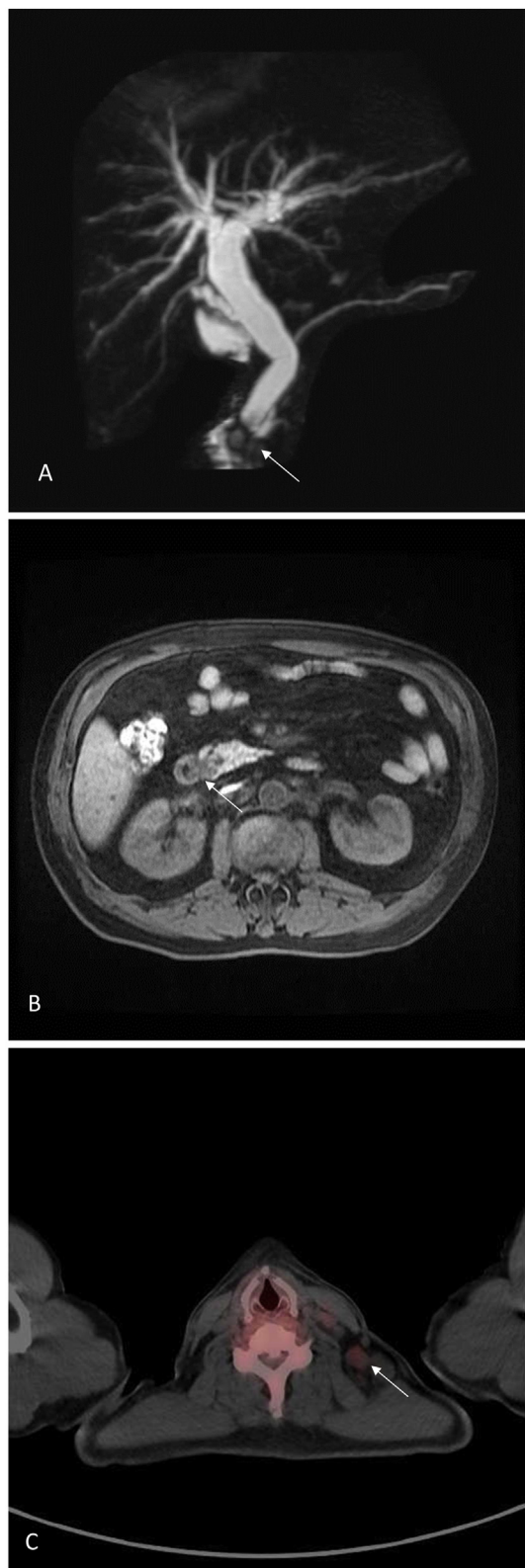


Fig. 1. (A–B) A low signal intensity soft tissue mass (arrow) in the ampulla of Vater with dilatation of common bile duct as seen on MRCP. (C) P PET/CT showed FDG uptake metastatic lymph nodes over left neck (arrow).

obstructive jaundice. Due to the patient's metastatic disease, chemotherapy with high-dose fluorouracil was started. However, severe vomiting was noted after the first chemotherapy treatment. Therefore, the chemotherapy regimen was shifted to gemcitabine plus oxaliplatin. The patient's disease was deemed stabilized after 6 cycles of therapy, and he received uracil/tegafur (UFUR) as maintenance therapy.

In February 2013, a left neck infiltrating purpuric lesion around a previous surgical scar (lymph node biopsy) with mild pain was noted. A subsequent skin biopsy revealed metastatic adenocarcinoma, compatible with ampulla of Vater primary, thereby confirming disease progression with skin metastasis. Consequently, chemotherapy with gemcitabine, oxaliplatin plus UFUR and local radiation therapy were administered. However, the lesion progressed with local itching, and chemotherapy with gemcitabine, oxaliplatin plus cetuximab was prescribed from Nov. 2013 to Feb. 2014. Unfortunately, the disease continued to progress and extended to his left chest wall, flank and back (Fig. 2A–B), so he received palliative chemotherapy with docetaxel, followed by cisplatin plus high-dose fluorouracil and FOLFIRI (last cycle on June 17 2015). Palliative radiation therapy for skin and lymph node metastasis was also performed. Gram negative bacteremia and neutropenic fever were noted after recent chemotherapy. After further discussion with the patient about reasonable options, the patient opted to receive palliative care due to poor response to chemotherapy as well as multiple comorbidities. Presently, he remains under outpatient follow-up for palliative care.

3. Discussion

Cutaneous metastases can occur due to direct invasion of the tumor to the surrounding tissue, by hematogenous spread, or through lymphatic drainage. Particular sites of metastasis are seen in specific primary malignancies, but the pathogenesis is still unclear. It has been observed that skin metastasis is a poor prognostic feature. Some reports showed that skin metastasis from breast cancer had a median survival of 31–42 months, yet patient survival was less than 6 months among those from other primary cancers.³

According to our search of the literature, there have been only two cases of cutaneous metastasis from ampullary cancer previously reported.^{6,7} The ampulla of Vater is a vital structure traversed by important ducts and surrounded by the pancreas and duodenum. Preoperative staging may include such imaging and diagnostic tools as necessary, including extracorporeal ultrasonography (US), CT, MRCP, esophagogastroduodenoscopic biopsy, endoscopic US (EUS), and endoscopic retrograde cholangiopancreatography (ERCP). For non-metastatic disease, pancreaticoduodenectomy (Whipple procedure) is the gold standard treatment. Local resection or endoscopic papillectomy are also recognized as treatments of choice for selected early stage cases.⁵ Recent studies revealed that adequate regional lymph node dissection provided a survival benefit for T1 stage ampullary cancer (hazard ratio 0.19), compared with local resection/ampullectomy without regional lymphadenectomy.^{8,9} Our patient was diagnosed with ampullary cancer with distant lymph node metastasis by PET/CT, so he did not undergo surgical intervention but instead received biliary stenting by ERCP followed by chemotherapy.

Ampullary cancer may arise either from the intestinal epithelium or the epithelium covering the pancreatobiliary ducts. Ninety percent of all ampullary malignancies are adenocarcinoma, which consist of two main histological subtypes: intestinal and pancreatobiliary.¹ The two histological subtypes tend to have different clinical characteristics. The incidence of histological lymph node metastasis is much higher in cases of the pancreatobiliary type than in those of the intestinal type (50.0% versus 23.8%). Pancreatobiliary

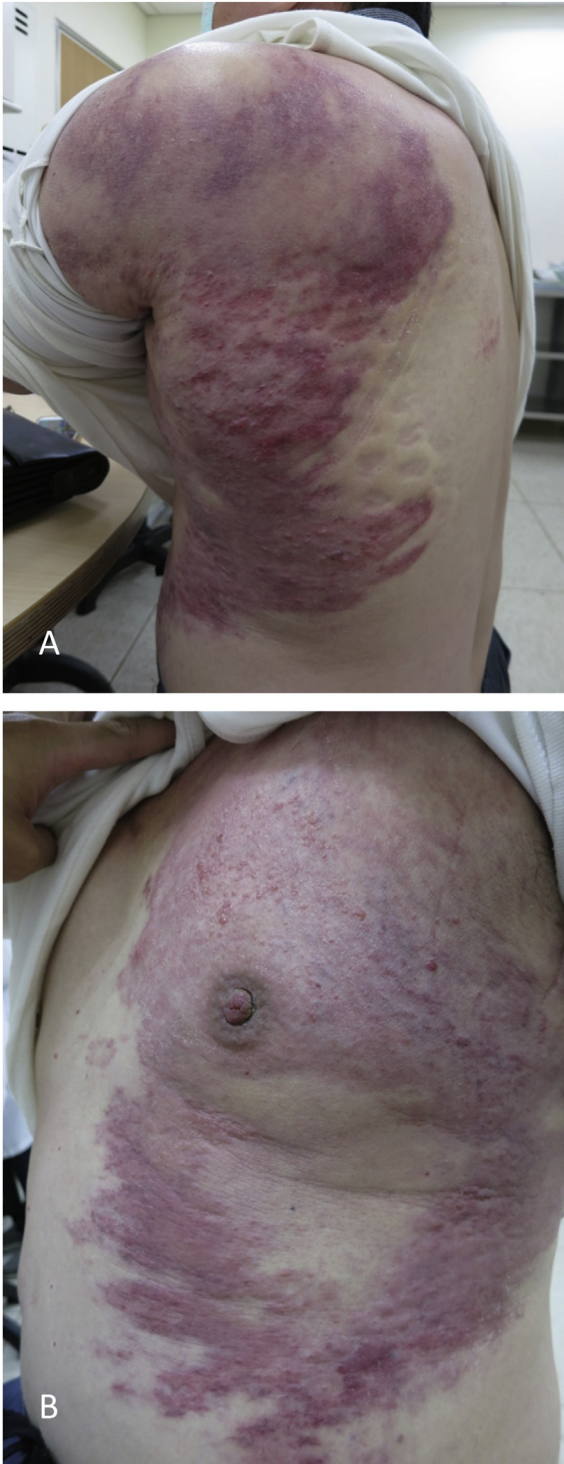


Fig. 2. (A–B) The skin metastasis manifested as erythematous to violaceous, bizarre shape, infiltrating lesions over left chest and back areas.

type also had an elevated likelihood of advanced local invasion and recurrence (5-year disease free survival rate 47.8% versus 73.1%).¹⁰ Our patient's pathology was pancreatobiliary type, and distant lymph node metastasis was noted at diagnosis. The immunohistochemical stain of skin biopsy from cutaneous metastasis was positive for cytokeratin 7 (CK7) and negative for cytokeratin 20 (CK20) (Fig. 3A–C), which was also compatible with pancreatobiliary origin instead of intestinal type (usually CK20(+) and CK7(-)).¹¹

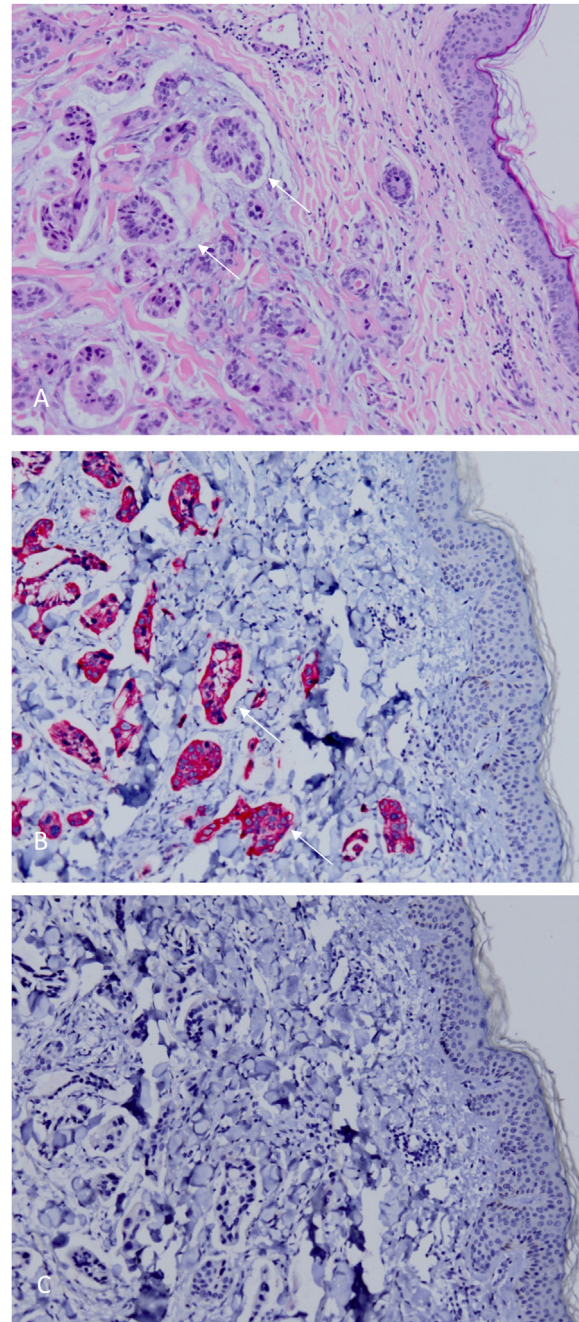


Fig. 3. (A) Skin biopsy (100x) of the purpuric infiltrating plaques reveals many mucin abundant atypical glandular structures with cuboidal endothelial cells (arrow), which is compatible with metastatic adenocarcinoma from ampulla of Vater. (B–C). Immunohistochemical stain of skin biopsy (100x) was positive for cytokeratin 7 (3B, arrow) and negative for cytokeratin 20 (3C), compatible with pancreatobiliary subtype.

Effective medical management of cutaneous metastasis arising from internal malignancy is usually difficult. Systemic chemotherapy and local excision or radiation therapy may be considered. As for metastatic ampulla of Vater cancer, the more recent histological differentiation in intestinal and pancreatobiliary subtype may influence the choice of regimen; whereas duodenal cancers would routinely be treated like colon cancer, pancreatic cancer is usually treated by systemic chemotherapy with a gemcitabine-based regimen.⁵ Our patient suffered from local pain as the initial symptom of skin metastasis, and itching sensation was noted with disease progression. No obvious sensory loss or paresthesia was

mentioned. Although several courses of systemic chemotherapy and local radiation therapy were given, his skin metastasis showed poor response to our management, and local pain and pruritus were still noted.

In conclusion, internal malignancy with cutaneous metastasis is not so common and represents poor prognosis. We reported a rare case of ampulla of Vater cancer with skin metastasis. Ampullary cancer with intestinal subtype seems to be less aggressive and have better treatment response than pancreatobiliary subtype. Therefore, immunohistochemical staining should be done at first to distinguish these two subtypes, which may help us to predict the patient's outcome as well as to choose the better chemotherapy regimen.

Conflict of interest

We declare no conflict of interest.

References

1. Perysinakis I, Margaris I, Kouraklis G. Ampullary cancer—a separate clinical entity? *Histopathology*. 2014;64:759–768.
2. Hu SC, Chen GS, Wu CS, et al. Rates of cutaneous metastases from different internal malignancies: experience from a Taiwanese medical center. *J Am Acad Dermatol*. 2009;60:379–387.
3. Riahi RR, Cohen PR. Clinical manifestations of cutaneous metastases: a review with special emphasis on cutaneous metastases mimicking keratoacanthoma. *Am J Clin Dermatol*. 2012;13:103–112.
4. Ramfidis VS, Syrigos KN, Saif MW. Ampullary and periampullary adenocarcinoma: new challenges in management of recurrence. *Jop*. 2013;14:158–160.
5. Heinrich S, Clavien PA. Ampullary cancer. *Curr Opin Gastroenterol*. 2010;26:280–285.
6. Cho EY, Kim TH, Park SD, et al. Acral metastasis in a patient with ampullary carcinoma. *Korean J Intern Med*. 2007;22:55–58.
7. Lamarca A, Martinez-Marin V, Feliu J. Cutaneous relapse of an ampullary carcinoma: an unusual presentation. *BMJ Case Rep*. 2012.
8. Amini A, Miura JT, Jayakrishnan TT, et al. Is local resection adequate for T1 stage ampullary cancer? *HPB (Oxford)*. 2015;17:66–71.
9. Lemke J, Schaefer D, Sander S, et al. Survival and prognostic factors in pancreatic and ampullary cancer. *Anticancer Res*. 2014;34:3011–3020.
10. Kim WS, Choi DW, Choi SH, et al. Clinical significance of pathologic subtype in curatively resected ampulla of Vater cancer. *J Surg Oncol*. 2012;105:266–272.
11. Zhou H, Schaefer N, Wolff M, et al. Carcinoma of the ampulla of Vater: comparative histologic/immunohistochemical classification and follow-up. *Am J Surg Pathol*. 2004;28:875–882.