Cutaneous erysipeloid metastasis of cholangiocarcinoma and evaluation by in vivo reflectance confocal microscopy

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INTRODUCTION

Cutaneous metastases are relatively uncommon, occurring in only 0.7% to 9% of all internal malignancies.[1] Cholangiocarcinoma is a rare bile duct neoplasm that accounts for less than 2% of maligancies.[2] Although it is well known that cholangiocarcinoma metastasizes to the lungs, liver, peritoneum, and retroperitoneal lymph nodes,[2] a retrospective review of the literature from 1978 to 2014 indicates only 30 cases of cutaneous cholangiocarcinoma, with 17 cases presenting without concurrent metastasis in other sites.[1] Among these patients, the cutaneous metastatic disease occurred evenly at adjacent and distant sites, presenting as 0.3-cm to 4-cm erythematous papules or nodules with or without ulceration.[1] The median overall survival after diagnosis of cutaneous cholangiocarcinoma metastasis is 4 months. Paradoxically, single-site metastases carry a significantly worse prognosis than multiple-site metastases[1] and may be attributed to difficulty in identifying a singular lesion.

In vivo reflectance confocal microscopy (RCM) is a novel, noninvasive diagnostic alternative to skin biopsy with comparable insurance reimbursement[3] that captures real-time, high-resolution, cellular-level images from the skin surface down to the reticular dermis (up to 300 μm depth).[4] This modality forgoes traumatic biopsy and has been used for diagnosis and monitoring of skin cancers and inflammatory dermatoses.[5,6]

Abbreviations used:

PET: positron emission tomography
RCM: reflectance confocal microscopy

REPORT OF CASE

A 78-year-old man presented with a 1-year history of extrahepatic cholangiocarcinoma with perineural and lymphovascular invasion and lymph node metastasis. His disease was treated with Whipple procedure and 3 months of gemcitabine/capecitabine. One year later, positron emission tomography (PET) scan detected 2 positive abdominal lymph nodes, which prompted chemoradiation with capecitabine. Three months later, he presented to a dermatology appointment with 1-month duration of a large, pruritic indurated, erysipeloid plaque over the right side of the abdomen (Fig 1, *A, left*) that he had attributed to irritation from an abdominal hernia binder. A 2-week empiric trial of triamcinolone 0.1% ointment yielded no improvement. Despite a recent negative PET scan, apprehension arose because of elevated CA19-9 levels (695 U/mL; normal, 0-37 U/mL) and low hemoglobin (12.2) with normal mean corpuscular volume (91.6), indicative of mild normocytic anemia. Subsequent immunohistochemistry of punch biopsy found well-differentiated tumor deposits composed of glandular structures lined by cuboidal to columnar cells with mild cellular atypia, irregular nuclear contours, and increased nuclear to cytoplasmic ratio with a desmoplastic stromal response (Fig 1, *B*). RCM images showed clusters of large, oval and polygonal refractile structures with a hyporefractile center indicative of dermal tumor

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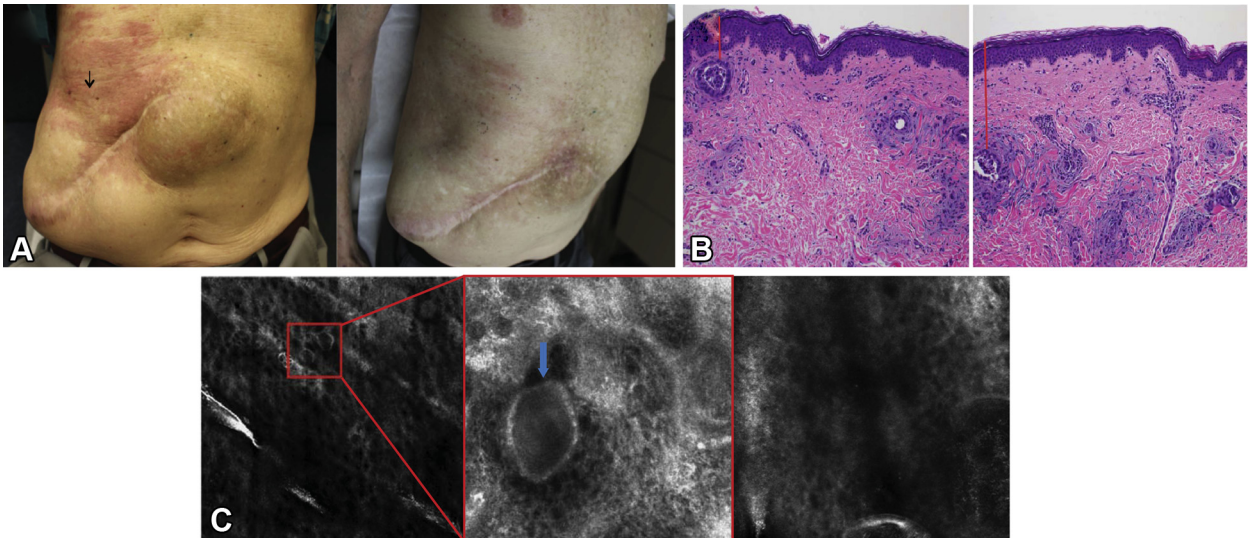

Fig 1. Clinical, histopathologic, and reflectance-confocal microscopic images of cutaneous cholangiocarcinoma. **A**, Initially, the patient presented with a brightly erysipeloid, partially blanchable indurated plaque extending over the right abdominal wall, including the Whipple procedure scar (*left*). The arrow represents the initial punch biopsy site. After chemotherapy, the plaque became significantly smaller, faintly erythematous, and no longer indurated (*right*). **B**, Images show well-differentiated tumor deposits at 105 μm (*red line*, left panel) and 355 μm (*red line*, right panel) from the skin surface, which are composed of glandular structures with a desmoplastic stromal response. The malignant glands are lined by cuboidal to columnar cells with mild cellular atypia, irregular nuclear contours, and increased nuclear to cytoplasmic ratio. The epidermis appears unremarkable. (Hematoxylin-eosin stain; original magnification: $\times$10.) **C**, At 305 μm (left and middle panel), RCM detects clusters of large, oval and polygonal refractile edges with a hyporefractile center (*blue arrow*) indicative of tumor nests filled with mucinous material. Scanning of the same site (right panel) after treatment at multiple depths up to 305 μm across a 2-cm area failed to reveal evidence of tumor nests.

nests filled with mucinous material at a depth of 305 μm (Fig 1, *C*). Three months after repeat chemotherapy (gemcitabine/Abraxane), his CA19-9 normalized, and the plaque became significantly smaller, nonindurated, and faint in color (Fig 1, *B, right*). Tumor nests were replaced by inflammatory cell infiltration upon RCM reimaging of the same location (Fig 1, *C*). The patient is currently in remission 10 months after the diagnosis of his cutaneous metastasis.

DISCUSSION

Our patient represents an unusual case of cutaneous cholangiocarcinoma metastasis presenting as an erysipeloid plaque and evaluated using RCM. This case represents an important diagnostic pearl for the multidisciplinary team. Despite an unexplained increase in CA19-9, the initial PET scan failed to detect cutaneous involvement as recurrent cholangiocarcinoma. PET scans detect positron emission from a radionuclide fluorodeoxyglucose infusion that deposits in metabolically hyperactive tissues. It detects metabolically hot foci that have a volume thickness of at least 6 to 9 mm.[7] Our patient's tumor nest (0.3 mm) fell below a PET scan's resolving power. In these instances, we recommend the use of RCM for diagnosis and monitoring of cutaneous metastasis. When tumor markers increase in the setting of a negative PET scan, a prompt dermatology referral is imperative for assessing cutaneous metastasis.

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