

## Cutaneous metastases from gastric adenocarcinoma 15 years after curative gastrectomy\*

Fang Liu<sup>1</sup>  
Min Zhang<sup>1</sup>

Wen Liang Yan<sup>1</sup>  
Hong Sang<sup>1</sup>

Haibo Liu<sup>1</sup>

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**Abstract:** We report the case of a 38-year-old man, who developed cutaneous metastases in the left inguinal groove 15 years after curative gastrectomy for advanced gastric adenocarcinoma. Histopathologic examination revealed poorly differentiated adenocarcinoma cells. They were stained positive for villin, CDX-2, CKpan (AE1/AE3), CEA, CK8/18, CK19, CK7, EMA, Ki-67 (50%), and negative for S-100, CK20, CD34, GCDFP-15 and TTF-1. The patient underwent local excision, after the presence of other metastases was excluded. Nevertheless, local recurrence developed at the surgical bed one year later and PET/CT revealed metastases to lymph nodes, bone and skin. He died 2 years after the appearance of cutaneous metastases. We have reviewed the literature and described the immunohistochemical characteristics of cutaneous metastases from gastric adenocarcinoma.

**Keywords:** Neoplasm metastasis; Skin neoplasms; Stomach neoplasms

### INTRODUCTION

Gastric adenocarcinoma (ADC) is one of the most common causes of cancer deaths around the world. Cutaneous metastases from gastric ADC are rare, and generally occur at a very end-stage in the course of disease. We report an extraordinary case of a young man with gastric ADC, who developed cutaneous metastases in the left inguinal groove 15 years after gastrectomy. To our knowledge, this case represents the longest interval from gastric ADC to cutaneous metastases after curative gastrectomy.

### CASE REPORT

A 38-year-old man complained of a rash and subcutaneous nodules over the inguinal groove in March 2011. He had been previously diagnosed with

poorly differentiated gastric ADC and underwent total gastrectomy in May 1997, followed by subsequent adjuvant chemotherapy using cisplatin and etoposide for 2 years. Periodical gastroscopy examination did not reveal abnormalities after surgery in the following years. Physical examination showed multiple, reddish-colored, fixed nodules, measuring between 0.5 and 3cm in diameter in the left inguinal groove area (Figure 1). Moreover, there were palpable enlarged lymph nodes in the left groin. Histopathological examination revealed tumor cells with hyperchromatic nuclei, numerous mitoses and prominent ductal formation, consistent with adenocarcinoma, and tumor nests extending from the epidermis into the dermis (Figure 2). Immunohistochemical examination

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<sup>1</sup> Department of Dermatology, Jinling Hospital affiliated to Nanjing University School of Medicine - Nanjing, China.

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showed that these cells were positive for cytokeratin pan (CKpan), carcinoembryonic antigen (CEA), villin, CK8/18, caudal type homeobox transcription factor 2 (CDX-2), Ki-67 (50%), epithelial membrane antigen (EMA), CK7, CK19, but negative for S-100 protein, CK20, GCDFP-15, TTF-1, CD34 (Figure 3). Examination with 18F-fluoro-2-deoxy-D-glucose (FDG)-positron emission tomography/computed tomography (PET/CT) revealed lymph node metastases and skin metastases in the left inguinal groove. The nodules were surgically removed and inguinal lymph nodes were cleared. He was prescribed chemotherapy with 5-fluorouracil in combination with paclitaxel for four cycles, and paclitaxel plus capecitabine for two cycles. However, there were red papules again on the former



FIGURE 1: Multiple, reddish-colored, fixed nodules, measuring between 0.5 and 3cm in diameter in the left inguinal groove area

surgical bed in October 2012. Also, the patient reported bone pain bilaterally over the knees and hip joints. PET/CT revealed multiple areas of focal activity on the femur, vertebral column and ribs. The Radiotherapy Department used stereotactic radiosurgery with total irradiated dose (TD) of 33Gy/3 fractions (fx) with 75% isodose line. The patient's pain caused by bone metastases subsided. Nonetheless, chemotherapy did not improve his general condition, skin nodules persisted, and he died in December 2013.

## DISCUSSION

Gastric ADC usually metastasizes to the liver, peritoneal cavity and regional lymph nodes. Cutaneous metastases are rare, developing in less than 5% of gastric ADC patients. Cutaneous metastases may be the first presentation of such malignancies, or occur during follow-up.<sup>1,2</sup> They usually manifest as solitary or multiple red or violaceous dermal or subcutaneous painless nodules, and may also appear as cellulitis-like or erysipelas-like erythematous plaques.<sup>2,4</sup>

This case is remarkable for several reasons. Firstly, it is noteworthy for the rarity and the unusual cutaneous metastases localization in the left inguinal groove. Most cutaneous metastases usually derive from breast cancer (18.6%-50%) in females or lung cancer (3%-7.5%) in males, with gastric ADC accounting for only 6% of all skin metastases.<sup>3</sup> Cutaneous metastases from gastric ADC usually develop on the abdominal skin, including the umbilicus (sister Mary Joseph nodule). Less common sites have also been reported such as face, scalp, breast, eyelids, dorsal area, neck, extremities and palms.<sup>3,5-8</sup> Inguinal groove metastases, however, are rare. Tumor cells metastasize to skin through several routes, including direct invasion

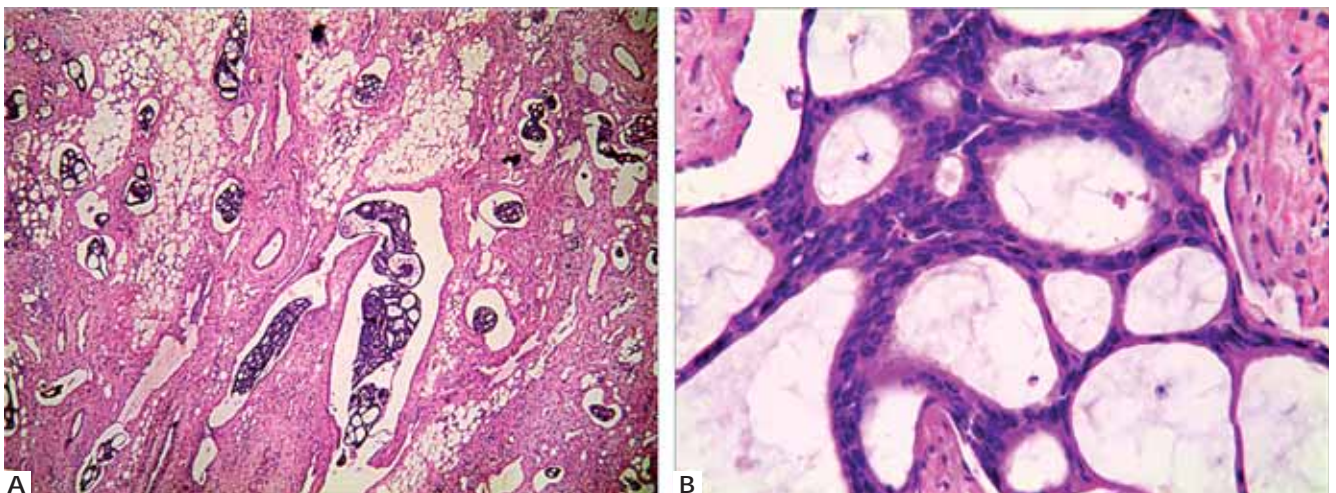
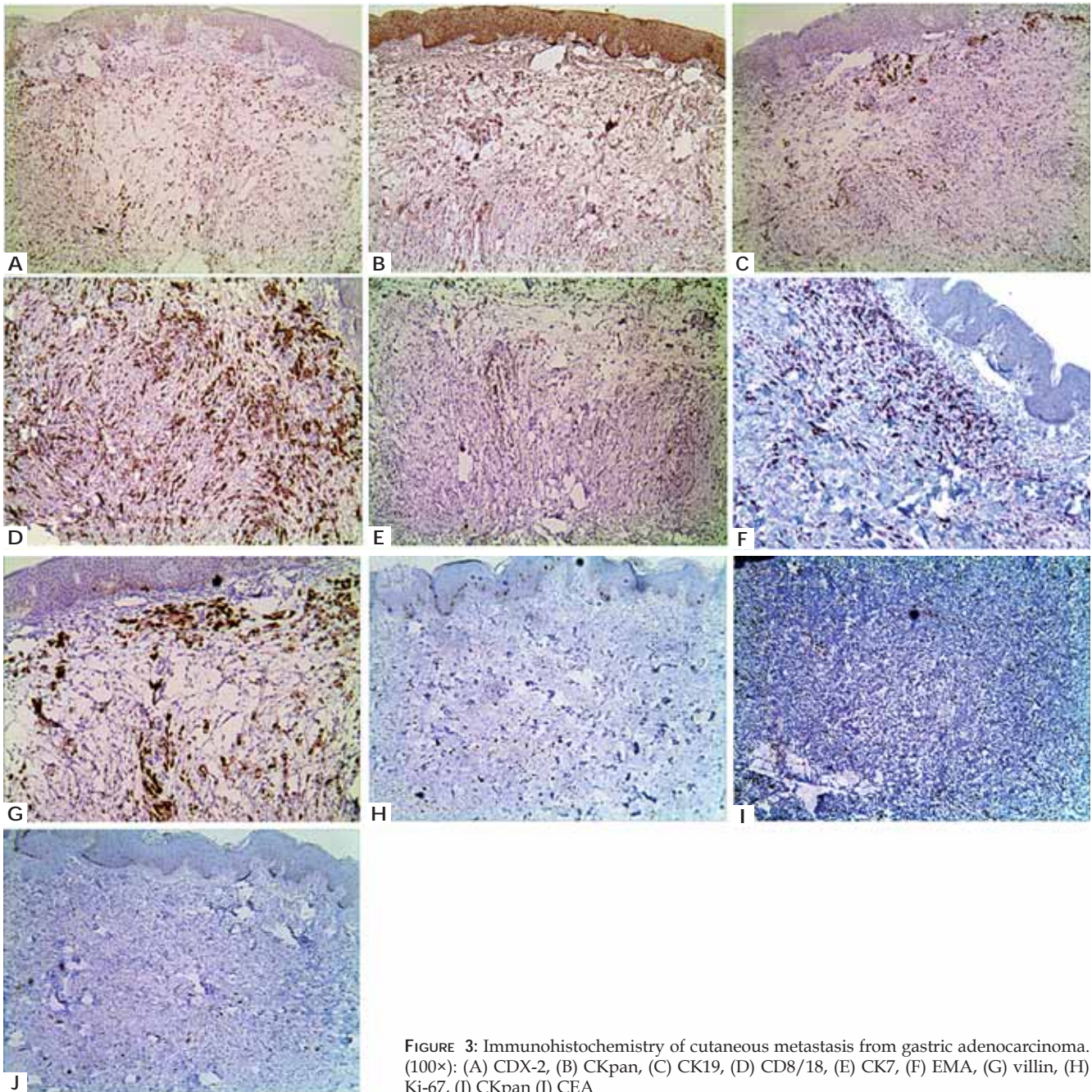


FIGURE 2: Histopathological examination revealed that tumor cells had hyperchromatic nuclei, numerous mitoses and prominent ductal formation, consistent with adenocarcinoma, and tumor nests extended from the epidermis into the dermis. (A HE×100, B HE×400)





**FIGURE 3:** Immunohistochemistry of cutaneous metastasis from gastric adenocarcinoma. (100×): (A) CDX-2, (B) CKpan, (C) CK19, (D) CD8/18, (E) CK7, (F) EMA, (G) villin, (H) Ki-67, (I) CKpan (J) CEA

from underlying structures, extension and embolization through lymphatic and blood vessels, and accidental implantation during surgery.

Secondly, the patient presented long-term survival and tumor-free survival after surgery. Gastric cancer is a disease with high mortality rate. This case represents, to our knowledge, the longest interval from primary cancer to cutaneous metastases after curative gastrectomy. Cutaneous metastases from gastric ADC are considered to be a predictor of poor prog-

nosis. Therefore, cutaneous metastases must be distinguished from primary cutaneous carcinoma, which is critical for clinical diagnosis and outcome assessment. Histologic phenotype is a crucial feature in the diagnosis of cutaneous metastases, as it is similar to that of the primary tumor. The primary gastric specimen of our patient was unavailable, because the resection had been done too long ago and the sample was not saved. According to literature review, we found that tumors from gastric origin are distinguished by the expres-

**TABLE 1:** Immunohistochemical characteristics of cutaneous metastases from gastric ADC in currently available reports

Year of report and REFERENCES	Age/ gender	Duration of cutaneous metastases	Location	Immunohistochemical analysis		Outcome
				Cutaneous	Gastric	
2005 <sup>7</sup>	60/M	2y	Face, scalp, right thigh	Positive for CK 1, 5, 10, 14, 7, 8, 18, 19, CEA, weakly positive for CK20, negative for CK13	Positive for CK 1, 5, 10, 14, 7, 8, 18, 19, CEA, weakly positive for CK20, negative for CK13	Death
2009 <sup>1</sup>	54/M	First clinical manifestation	Scalp	Positive for CK20, CK7, MIB-1, Pancyto, negative for CDX2, TTF1,S-100	Positive for CK20, CK7, MIB-1, Pancyto, negative for CDX2, TTF1, S-100	Death
2014 <sup>2</sup>	61/M	8y	Left groin and thigh	Positive for CK7, partially positive for CK20, negative for S100 and LCA	Not performed	Death
2010 <sup>8</sup>	69/M	First clinical manifestation	Chest	Positive for AE1/AE3, CK20, CK18, negativity for GCDFP-15, CK7, S-100, HMB-45, MELAN A, CD45	Not performed	Death
2010 <sup>5</sup>	68/F	3 year history of gastric ulcer	Neck	Positive for CK7, negative for CK20	Not performed	Not mentioned
2008 <sup>9</sup>	61/M	First clinical manifestation	Neck	Positive for CK7, CEA, negative for CK20	Positive for CK7, CEA, negative for CK20	Not mentioned
2005 <sup>6</sup>	73/M	3.5y	Scalp and upper forehead.	Positive for AE1/AE3	Not performed	Death
2008 <sup>10</sup>	48/M	First clinical manifestation	Lower abdomen, thorax, left side, arms, face	Positive for EMA, CEA, AE1 / AE3, TTF-1, negative for S-100, CK20, CK7, HHF-35, AML	Not performed	Deterioration
Present case	38/M	15y	Left inguinal groove	Positive for villin, CDX-2, CKpan, CEA, CK8/18, CK19, CK7, EMA, Ki67(50%), negative for S-100, CK20, CD34, GCDFP-15, TTF-1	Not performed	Death

sion of some adenoepithelial and/or gastrointestinal markers including Ckpan (AE1/AE3), CK7, CK8/18, CK19, CEA, CDX-2 or EMA, which were all positive

in our case (Table1).<sup>1,2,5-10</sup> The clinical history is usually helpful. Therefore, we diagnosed this patient with cutaneous metastases from gastric adenocarcinoma. □

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*MAILING ADDRESS:**Hong Sang**Department of Dermatology, Jinling Hospital affiliated to Nanjing University school of Medicine, Nanjing, 210002 China.**E-mail: sanghong@nju.edu.cn.*

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