Distant skin metastases as primary presentation of gastric cancer

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Distant gastric metastasis to the skin is uncommonly a presenting symptom, although nonspecific paraneoplastic syndromes with dermatologic manifestation including diffuse seborrheic keratoses (Leser-Trelat sign), tripe palms, and acanthosis nigricans have been described in the literature.We report here the case of a 49-year-old woman with gastric adenocarcinoma who presented with cutaneous metastasis as an initial symptom. In our case, metastatic skin lesions responded significantly to EOX chemotherapy (epirubicin + oxaliplatin + capecitabine) despite progression of systemic disease. In similar presentations, a high index of clinical suspicion and skin biopsy are important.

Gastric cancer is a common cancer worldwide and has geographical, ethnic, and socioeconomic differences in distribution. A total of 1,658,370 new cancer cases and 589,430 cancer deaths are projected to occur in the United States in 2015.[1] The usual presenting symptoms are weight loss, epigastric pain, dysphagia, or symptoms related to gastric outlet obstruction. Distant metastatic disease is rarely the presenting symptom in gastric cancer. Skin metastasis is a rare process in the natural history of this disease.

Case presentation

A 49-year-old Hispanic woman with history of smoking 1 pack per day and no other medical problems, presented to a community hospital with multiple painless lesions ranging from 2-8 cm in diameters around her scalp, face, forearms, right shoulder, back, and chest (Figure 1). She had not sought medical advice earlier because she was asymptomatic. The results of a physical exam were unremarkable except for the abovementioned skin lesions. No treatment or work-up performed. Six months after initial presentation, she started experiencing weight loss, anorexia, abdominal pain, dyspepsia, dysphagia, and ascites. Her symptoms warranted work-up with upper gastrointestinal endoscopy (EGD), which revealed a distal gastric tumor that was confirmed with a biopsy. The patient elected not to be treated.

Four months later, the patient deteriorated clinically with uncontrolled nausea and worsening ascites, so she sought medical advice at our facility. A computed-tomography scan of her abdomen and pelvis revealed bilateral adnexal masses, omental caking, gastric mucosal thickening, and large volume ascites (Figure 2). Her physical exam was remarkable for raised, firm cauliflower-like nodules in the aforementioned distribution, in addition to gross ascites and clubbing of fingers. Her laboratory blood tests were unremarkable except for iron deficiency anemia. The results of a skin lesion fine-needle aspiration from her right shoulder revealed metastatic adenocarcinoma. She underwent another EGD, which confirmed the finding of malignant-appearing distal tumor around the gastric cardia with reflux esophagitis, and a biopsy confirmed the diagnosis of poorly differentiated adenocarcinoma (Figure 3). Palliative chemotherapy with EOX (epirubicin + oxaliplatin + capecitabine) was started. After 3 cycles, the patient had partial response, and all her skin lesions became almost flat. After 6 cycles, her skin lesions became minimal but she developed gastric outlet obstruction, malignant ascites, and peritoneal carcinomatosis. The patient's performance status deteriorated, and she elected to proceed with hospice care 7 months after starting therapy.

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FIGURE 1 A, Right shoulder fungating mass (biopsy proven metastatic gastric adenocarcinoma). B, Scalp metastatic nodule. C, Right pre-auricular metastatic nodule.

Discussion

Nonspecific gastric cancer paraneoplastic syndromes with dermatologic manifestations have been described in the literature, including diffuse seborrheic keratoses (Leser-Trelat sign) , tripe palms and acanthosis nigricans.[2,3] Other reported paraneoplastic disorders include Trousseau's syndrome,[4] microangiopathic hemolytic anemia[5,6] and membranous nephropathy.[7] Gastric cancer dermatologic manifestation can be part of other cancer syndromes (Table 1).

Bazex syndrome or acrokeratosis paraneoplastica is another rare paraneoplastic syndrome that is characterized by acral psoriasiform lesions.[8] It is rarely described as paraneoplastic phenomenon with gastric cancer nevertheless it more described in association with esophageal squamous carcinoma.[9]

Curth et al proposed criteria to assess relationship between dermatoses and potential underlying malignancy.[10] These proposed criteria include: both neoplasia and paraneoplasia began simultaneously; development of a parallel course; skin lesion is not associated with a genetic syndrome; there is a specific type of neoplasia that occurs with paraneoplasia; the dermatosis is rare in the general population; and there is a high frequency of association between both conditions.[11]

On the other hand gastric cancer is an extremely rare source of skin metastases.[12] The frequency of gastric cancer as a primary lesion was 6% in cutaneous metastases of men, and cutaneous metastases occurs in only 0.8% of all gastric cancers.[13] Gastric cancer causes only 6% of all skin metastases while the frequency of skin infiltration by solid organ malignancies ranges from 0.7% to 9%.[14,15] Breast cancer is the most common origin of cutaneous metastasis in females while lung cancer is in men.[16]

Cutaneous gastric metastasis appears late in the course of the disease[17] and usually occur in the vicinity of the tumor around the anterior abdominal wall. Skin gastric metastasis has dismal prognosis. Growth pattern of skin metastases is unpredictable and may not reflect that of a primary tumor. The average survival is 11.4 weeks with a range of 2 – 34 weeks.[18]

TABLE 1 Dermatologic disorders associated with gastric cancer

Source	Dermatologic disorder	Cutaneous manifestations
Dantzig[2]	Leser-Trelat sign	Multiple seborrheic keratoses
Brown[3]	Acanthosis nigricans	Pigmented papillomatous plaques
Douwes[8]	Bazex syndrome or acrokeratosis paraneoplastica	Acral psoriasiform lesions
Abreu Velez[19]	Tripe palms or palmo-plantar keratoderma	Diffuse hyperkeratosis of the palms and soles with enhancement of the epidermal ridges
Sagara[20]	Cronkhite-Canada syndrome	Hyperpigmented macules; nail plate separation, discoloration, and atrophy; alopecia
Sereno[21]	Peutz-Jeghers syndrome	Hyperpigmented macules

FIGURE 2 Computed-tomography, sagittal image of abdomen, showing gastric mucosal lining thickening.

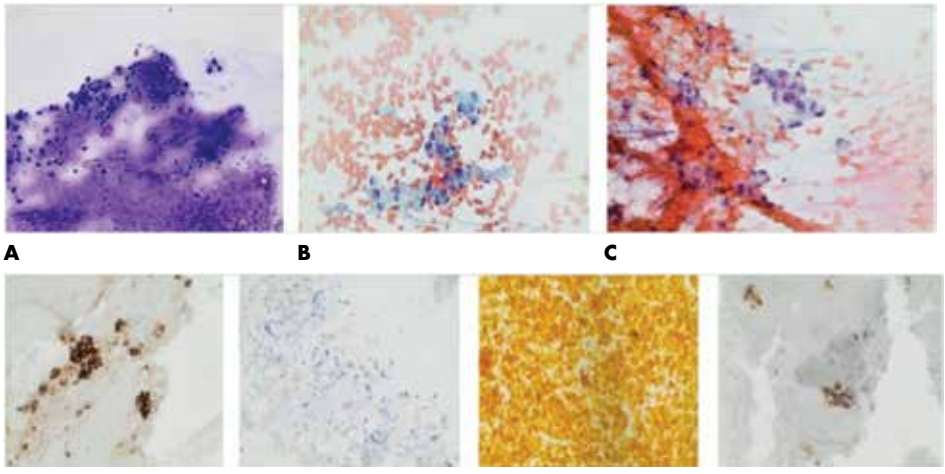

FIGURE 3 Pathology microscopy of shoulder skin lesion biopsy. A, Diff-Quik stain. B and C, PAP smear stain. D, CK7 stain. E, CK20 stain. F, Mucicarmine stain. G, Villin stain. Direct smears are moderately cellular and contain scattered and small clusters of tumor cells with prominent signet ring morphology. Immunophenotype staining is positive for cytokeratin 7 and villin, focally positive for cytokeratin 20 while mucicarmine stain was negative. CDX-2, TTF-1, PAX8 were negative (not shown). Final pathology diagnosis is consistent with metastatic adenocarcinoma.

In summary, cutaneous metastasis of gastric cancer is rare. We report a patient with gastric adenocarcinoma who presented with cutaneous metastasis as initial symptoms. In this case, metastatic skin lesions responded significantly to chemotherapy despite progression of systemic disease. High clinical suspicion index of skin metastasis and prompt recognition of skin disorders associated with gastrointestinal cancers may lead to earlier diagnosis and in certain cases may improve the prognosis.

Our case demonstrates that although cutaneous metastasis of gastric cancer is rare, it should be considered in the differential diagnosis of clinically atypical skin lesions. A high index of suspicion and the use of various diagnostic modalities may be necessary for making an accurate and prompt diagnosis.

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