

## BRIEF ARTICLES

## A Case of Widespread Cutaneous Metastases from Esophageal Adenocarcinoma

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### ABSTRACT

Cutaneous metastases from internal malignancies are very rare, and only a few cases from esophageal cancer have been reported. We describe the case of a 61-year-old patient with recently diagnosed esophageal adenocarcinoma who presented with multiple skin nodules. Immunohistochemical analysis of the nodules matched the immunohistochemical profile of the patient's previous esophageal biopsy specimen, confirming the diagnosis of cutaneous metastases. This case highlights the importance of including cutaneous metastases in the differential diagnosis of any suspicious lesion in patients with a history of internal malignancy.

### INTRODUCTION

Cutaneous metastases from internal malignancies are very rare and occur in only 0.5 to 9% of cases.<sup>1,2</sup> It often indicates a poor prognosis, with an average survival time of about 7.5 months.<sup>3</sup> Metastasis to the skin most commonly originates from lung, breast, and colorectal cancers, and only a few cases of cutaneous metastases from esophageal cancer have been reported.<sup>2,4,5</sup> Here, we present the case of a 61-year-old patient with recently diagnosed esophageal adenocarcinoma and widespread cutaneous metastases.

### CASE REPORT

A 61-year-old male with past medical history of gastroesophageal reflux disease, hepatitis

C, and hypothyroidism was originally admitted for progressive dysphagia and significant weight loss. After an endoscopic biopsy, he was diagnosed with poorly differentiated esophageal adenocarcinoma. Dermatology was consulted for the evaluation of multiple skin nodules which were concerning for cutaneous metastases. Oncology wanted to determine whether the metastases were from the patient's esophageal cancer or from a different primary source, in order to better formulate their treatment plan. The patient reported recent enlargement of some of the lesions, with associated pain. He denied any pruritus or bleeding associated with the nodules.

On physical examination, there were firm, indurated, slightly mobile subcutaneous nodules present on the scalp, left cheek, back, abdomen, hands, and right thigh

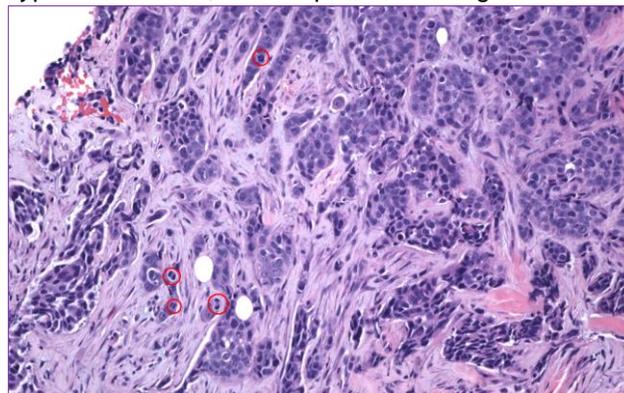
# SKIN

(Figure 1). A punch biopsy was taken from a nodule on the left anterior shoulder and from a nodule on the left flank. Histopathologic analysis revealed a tumor in the deep dermis composed of atypical epithelial cells with focal gland formation (Figure 2). Immunohistochemical analysis revealed the tumor to be CK7+ (Figure 3), CK20-, and p40- and to express HER2 with 2+ positivity; this matched the immunohistochemical profile of the patient's previous esophageal biopsy specimen. These findings were consistent with cutaneous metastases from the patient's esophageal adenocarcinoma.

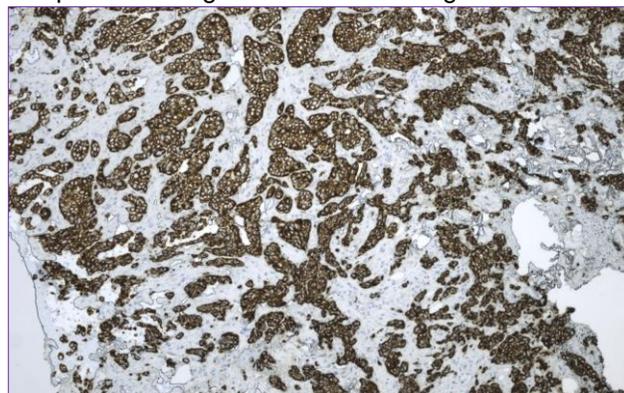
**Figure 1.** Indurated subcutaneous nodules present on the patient's left flank.



**Figure 2.** Punch biopsy, H&E, 200x: rudimentary gland formation, pleomorphism, nuclear hyperchromatism, and frequent mitotic figures.



**Figure 3.** Punch biopsy, CK7, 100x: diffuse positivity with CK7. Immunohistochemical staining for CK20 and p40 were negative. HER2 staining was 2+.



## DISCUSSION

The incidence of cutaneous metastases from esophageal adenocarcinoma is about 1% and typically involves the overlying skin of the primary tumor or the scalp.<sup>6</sup> The clinical manifestations of cutaneous metastasis vary widely, but it usually presents as an asymptomatic, firm nodule.<sup>3</sup> Cutaneous metastases represent advanced progression of the primary malignancy, and removal of these lesions does not have any impact on the survival rate of the patient.<sup>5</sup> We present an unusual case as our patient was relatively functional at the time of

presentation with multiple areas of metastasis to the skin.

Worldwide, squamous cell carcinoma is the most common type of esophageal cancer.<sup>7</sup> However, the incidence of esophageal adenocarcinoma in developed countries has increased dramatically since the 1970s, and this subtype now predominates in the United States.<sup>7</sup> The pathogenesis of esophageal adenocarcinoma is not fully understood, but Barrett's esophagus is a well-known risk factor.<sup>8</sup> Barrett's esophagus results from acid biliary reflux from the stomach into the esophagus, leading to the replacement of native squamous epithelium with columnar epithelium. The combination of esophageal inflammation and somatic genomic instability promote carcinogenesis, and over time, can lead to the development of esophageal adenocarcinoma.<sup>9</sup>

One possible genomic alteration can involve the amplification and overexpression of the human epidermal growth factor 2 (HER2) oncogene. HER2 is an established target in esophageal and gastric cancers as it regulates cell growth, survival, differentiation, and migration.<sup>10</sup> The status of HER2 is important to assess in patients with esophageal adenocarcinoma as it can help guide chemotherapy with the use of targeted agents like trastuzumab.

Immunohistochemical staining provides diagnostic guidance and helps distinguish between adenocarcinoma and squamous cell carcinoma.<sup>11</sup> More specifically, the staining pattern for cytokeratin 7 (CK7) and cytokeratin 20 (CK20) can aid in the identification of esophageal adenocarcinoma. CK20 is typically expressed in tumors of the lower gastrointestinal tract, while CK7 is expressed in Barrett's esophagus and esophageal adenocarcinoma.<sup>12</sup> Ormsby et

al. found that Barrett's-related adenocarcinomas consistently revealed a CK7+/CK20- pattern, whereas gastric adenocarcinomas demonstrated much more variation in the CK7/20 immunophenotype.<sup>13</sup> The CK7+/CK20- pattern was present in both the cutaneous and esophageal specimens from our patient, supporting the diagnosis of cutaneous metastasis from esophageal adenocarcinoma. Also, p40 is a marker of squamous cell carcinoma and helps distinguish from adenocarcinoma.<sup>11</sup> It was negative in both the cutaneous and esophageal specimens, which further supported the diagnosis of cutaneous metastasis from esophageal adenocarcinoma. In cases of either adenocarcinoma or squamous cell carcinoma that have become advanced, typical immunohistochemical markers may be lost, and sometimes only a diagnosis of poorly-differentiated carcinoma can be made.<sup>11</sup>

This case highlights the importance of including cutaneous metastases in the differential diagnosis of any suspicious lesion in patients with a history of internal malignancy. These lesions should be biopsied and evaluated histopathologically. It is imperative to determine the primary source as it can alter the direction of treatment as exemplified in the case of our patient. Despite the rare incidence of cutaneous metastases, patients with esophageal malignancies and growing or changing skin lesions should follow up with dermatology.

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