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Case Report

Cutaneous Metastases From Esophageal Adenocarcinoma

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The aim of this study is to present 2 rare cases of cutaneous metastases originated from adenocarcinoma of the gastro-esophageal junction, thus, underline the need for early diagnosis and possible treatment of suspicious skin lesions among patients with esophageal malignancy. Metastatic cancer to the skin originated from internal malignancies, mostly lung cancer, breast cancer, and colorectal cancer, constitute 0.5 to 9% of all metastatic cancers.[5,8,15] Skin metastases, mainly from squamous cell carcinomas of the esophagus, are rarely reported. Cutaneous metastasis is a finding indicating progressiveness of the disease.[17] More precisely, median survival is estimated approximately 4.7 months.[2,14] This study is a retrospective review of 2 cases of patients with adenocarcinoma of the esophagus and a review of the literature. Two patients aged 60 and 32 years old, respectively, underwent esophagectomy. Both pathologic reports disclosed adenocarcinoma of the gastro-esophageal junction staged T3 N2 M0 (stage IIIB). During follow-up time, the 2 patients were diagnosed with cutaneous metastases originated from the primary esophageal tumor 11 and 4 months after surgery, respectively. The first patient is alive 37 months after diagnosis, while the second one died 16 months after surgery. Cutaneous metastasis caused by esophageal adenocarcinoma is possible. Therefore, follow-up of patients who were diagnosed with esophageal malignancy and underwent esophagectomy is mandatory in order to reveal early surgical stages.

Key words: Esophagus – Adenocarcinoma – Cutaneous – Metastasis – Classification description: general surgery – Oncologic surgery – Upper gastrointestinal surgery

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Cutaneous metastases are rare. They consist of 0.5 to 9% of metastatic tumors in total.[1,2] Primary tumors that metastasize to the skin are in descending order of frequency, lung, breast, and rectal cancer. Metastases from esophageal malignancy to the skin are considered to be even rarer. However, cases of cutaneous metastases in their majority from squamous cell carcinoma of the esophagus have been reported.[3–5] They mostly affect patients aged over 60 years old appearing with asymptomatic nodules.[5] The skin lesions may be observed in different locations of the human body.[2,6–13]

We describe 2 cases of cutaneous metastases in patients diagnosed with esophageal adenocarcinoma.

Materials and Methods

This study is a retrospective review of 2 cases of patients who were referred to our department and were diagnosed with adenocarcinoma of the esophagus. Furthermore, the study consists of a review and presentation of similar cases reported in the literature.

Results/Case Presentation

Case 1

A 60-year-old male presented with a 4-month history of dysphagia and regurgitations. We performed an upper gastrointestinal tract endoscopy where a tumor was identified in the lower third of the esophagus. Biopsies were obtained from the tumor. According to the pathologic report, the patient was diagnosed with esophageal adenocarcinoma of the gastroesophageal junction, enteral type by Lauren classification. The report was negative for Barrett's esophagus. Preoperative staging revealed no distant metastasis or lymph node involvement. The patient underwent an Ivor-Lewis esophagectomy. Histology revealed an esophageal adenocarcinoma, which infiltrated through the wall of the esophagus (T3). Three (1 periesophageal and 2 lesser omentum) of the 22 excised lymph nodes were infiltrated by the adenocarcinoma (N2). The tumor was staged as T3 N2 M0 (Stage IIIB). The postoperative course was uneventful. The patient was discharged on the 12th postoperative day and underwent postoperative chemotherapy (6 cycles of 5-FU-cisplatin).

Eleven months after surgery, after receiving the fourth cycle of chemotherapy, a painless cutaneous mass presented on the medial surface of the right arm. Computed tomography (CT) was performed in the first 3 and 6 months postoperatively and was negative for recurrence or metastases. Therefore, positron emission tomography (PET) was not recommended. Due to the rapid growth of the mass, an excisional biopsy was performed (Fig. 1). Pathologic findings revealed an adenocarcinoma considered to be a metastasis of the primary esophageal adenocarcinoma (Fig. 2). Six months after the last cycle of chemotherapy, 2 other masses were detected. The first one presented beside the first skin lesion on the right arm. It was removed and biopsied as well. A pathologic report disclosed an adenocarcinoma, which was attributed to the primary esophageal malignancy. The second one presented as a 1-cm nodule on the right side of the dorsum at the lumbar spine level. According to the ultrasound, the mass arose from the psoas major muscle. Histopathologic findings corroborated that the mass was originated from the primary esophageal adenocarcinoma. The patient again underwent a 6-cycle 5-FU chemotherapy, and is alive, 37 months after diagnosis.

Case 2

A 32-year-old male with a 3-month history of gastroesophageal reflux presented with dysphagia. Upper gastrointestinal tract endoscopy was performed, which showed a mass of the gastroesophageal junction and Barrett's esophagus. Biopsies from the mass were obtained and pathologic findings revealed adenocarcinoma. Preoperative staging, which included CT of the chest and upper and lower abdomen, and PET revealed no distant metastases or adjacent organ infiltration. The patient underwent total esophagectomy with right thoracotomy and 2-field lymphadenectomy. A pathologic report of the tumor revealed a poorly differentiated gastro-esophageal adenocarcinoma infiltrating through the wall of the esophagus (T3) and 6 of the 30 periesophageal lymph nodes (N2). The disease stage was T3 N2 M0 (Stage IIIB). Postoperatively the patient developed (sixth postoperative day) chylothorax, which was managed conservatively (nil per os, bullau). The patient received 6 cycles of chemotherapy postoperatively.

Four months after surgery, while on chemotherapy, 2 painless nodules were observed on the frontal area of the skull. An excisional biopsy was performed, because of the rapid growth of the nodules, and pathologic report showed metastatic skin cancer

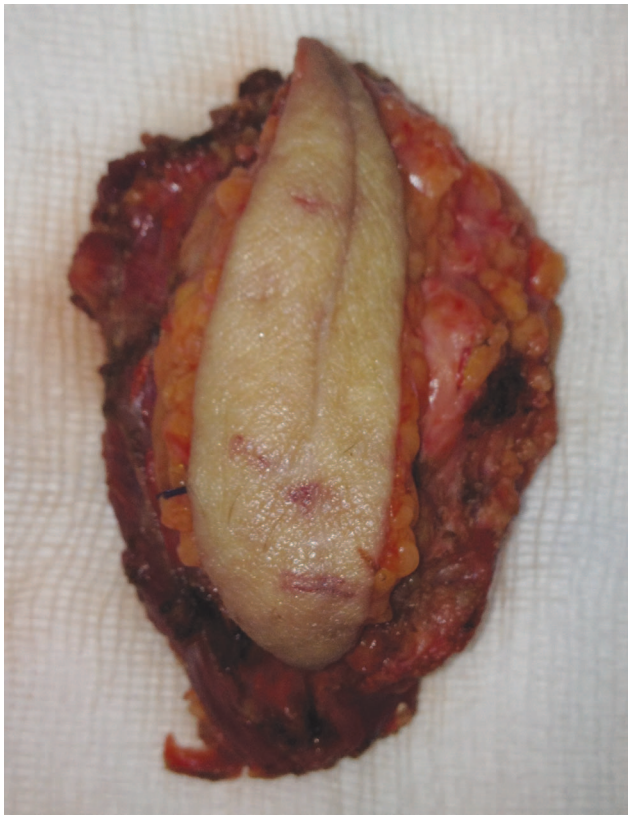

Fig. 1 A painless cutaneous mass on the medial surface of the right arm.

from the primary adenocarcinoma of the esophagus. The patient died 16 months after surgery with metastases to the liver and the cerebellum.

Discussion

Cutaneous metastases are rare. In fact, less than 1% of all tumors metastasize to the skin.[5,8,15] More precisely, Quint *et al* estimated that the incidence of all cutaneous metastases originated from esophageal carcinomas, including adenocarcinomas and squamous cell carcinomas of the esophagus, was 1%.[17] In most cases, metastases to the skin are considered to be a poor prognostic factor due to the aggressiveness of the disease. As a result, median survival has been reported to be 4.7 months.[2,14] According to literature, the average time of occurrence of the metastatic disease was estimated to be approximately 2.9 years after the onset of the primary tumor.[1]

Esophageal adenocarcinoma may metastasize to various tissues of the human body. Most frequently esophageal adenocarcinoma metastasizes to the

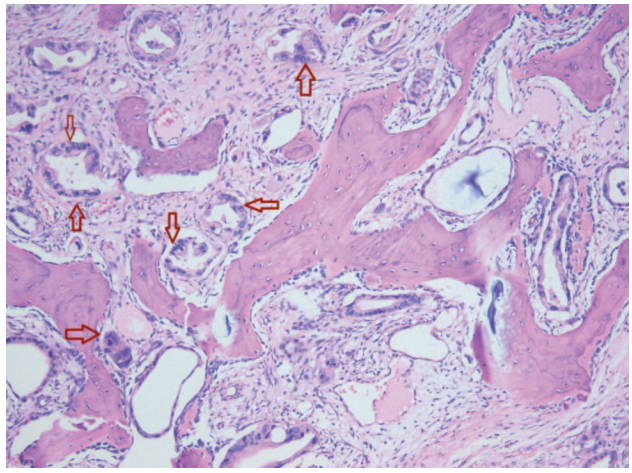

Fig. 2 Pathologic figure of the skin lesion excised. The arrows indicate infiltration of the dermis by poorly differentiated cells of the adenocarcinoma, the features of which are the same as in the pathologic report of the primary adenocarcinoma (H&E, ×200).

liver, lungs, and brain. On the other hand, metastases to the skin from esophageal primary tumors are less common. Cases of patients with metastases to the skull, the upper lip, the scalp, neck, chest, and abdominal wall have been reported.[2,6–13] Metastatic skin lesions are often asymptomatic. However, their physical examination may reveal inflammatory rashes, papules or patches, alopecia neoplastica, erythematous, indurated plaques or skin nodules, as in the 2 cases presented.[18]

Furthermore, the majority of the cases concern cutaneous metastases from primary tumors located in the lower third of the esophagus. More precisely, most of the primary tumors that develop at or near the gastroesophageal junction arise from Barrett's esophagus, as a complication of chronic gastroesophageal reflux disease.[1,14]

Although in Western countries, the squamous cell carcinoma used to be the most common type of cancer, nowadays it is the adenocarcinoma that appears to be the most frequent one.[16] Histopathologic report of the biopsies obtained from the esophagus should be taken under consideration as it has been observed that the tumor subtype is a strongly connected to the survival rate factor. In comparison to the squamous cell carcinoma, it has been proven that the adenocarcinoma subtype is a longer survival rate factor.[1]

Given the fact that the patient in case 2 underwent a CT and a PET during the preoperative staging and that both diagnostic methods were negative as they showed no distant metastases, the

sensitivity of these methods seems to be limited. Recent achievements in revealing primary tumors include immunohistochemical stains capable of detecting antigens of malignancies via the utilization of labeled antibodies. Therefore, this ability was used in order to indicate the origination of the metastases. The antibodies used were CEA and EMA, found as antigens in tumors as well, while CK7/CK20 was stained in the esophagus and stomach recognizing the metastasis with high sensitivity and specificity.[1,6] However, the contribution of immunohistochemistry in the identification of metastases from esophageal malignancies has been poorly studied yet. Hence, further studies and results to come may lead to the widespread use of immunohistologic issues. The antibody-antigen match may have the potential to be included as a routine examination performed preoperatively during the staging of an esophageal carcinoma or postoperatively as an advantage of the follow-up of patients in order to identify early the origination of a metastasis and prevent the extension of the metastatic disease in the future.

Conclusion

Therefore, considering the rarity of metastatic disease to the skin from adenocarcinoma of the gastroesophageal junction, we emphasize the importance of the follow-up of patients who have been treated for primary esophageal malignancy. Constant awareness and concern of the physician is required. Every high-risk skin lesion has to be revealed and removed. Such specimens should be biopsied and histopathologically evaluated. However, as in the 2 cases we described, the removal of the skin lesion has no impact on the survival of the patients, but it can be performed for cosmetic reasons. Further knowledge is required in the field of the diagnosis and the options of treatment of the skin metastatic disease from esophageal carcinomas.

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