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CASE REPORT

Cutaneous metastasis in the face as the first manifestation of esophageal Adenocarcinoma: case report and literature review

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Abstract Metastasis to the skin from carcinoma arising in other organs is uncommon, yet it may be the first presentation of neoplastic disease. The incidence of esophageal adenocarcinoma has been rapidly rising and now accounts for at least half of esophageal carcinomas. Cutaneous metastases of esophageal adenocarcinoma are extremely rare; less than 1 % of patients with metastatic disease have cutaneous involvement. We reported a rare cutaneous cheek metastasis from an adenocarcinoma in an 81-year-old white man, who was excised, and the defect repaired with a reverse cervicofacial flap. Subsequent investigations, based on the result of the pathological anatomy, detected the primary tumor in the esophagus, despite no symptoms. Although cancer of internal organs rarely presents with skin metastases, any suspicious lesions with rapid growth should be ruled out as their metastatic origin. We reported a case and reviewed the clinical characteristics of the few patients reported on the literature.
Level of Evidence: Level V, diagnostic study

Keywords Facial metastasis · Keratoacanthoma-like lesions

Introduction

Esophageal carcinoma has one of the highest cancer mortality rates. Less than half of the patients survive 1 year after diagnosis. The incidence of esophageal adenocarcinoma is rapidly rising and now accounts for at least half of esophageal carcinomas [1].

Approximately 5 % of oncology patients develop cutaneous metastasis, with only a small number of these patients, less than 1 %, having metastatic skin lesions as the first sign of their visceral cancer. Cutaneous metastases of esophageal adenocarcinoma are extremely rare; less than 1 % of patients with metastatic disease have cutaneous involvement. Herein, we review the characteristics of patients whose skin metastases are from an esophageal adenocarcinoma with clinical illustrations from our patient, an 81-year-old Caucasian man whose metastatic esophageal carcinoma is the first sign of his advanced disease stage. We also discuss the histopathological differential diagnoses of our patient´s tumor.

Case report

An 81-year-old man, with a history of hypothyroidism, presented with a skin nodule of 2.3 cm diameter over his right cheek, non-ulcerated, round, well-demarcated, dome-shaped, soft, mobile, painless, and clinically localized. The patient referred that the lesion had a 3-month evolution, with a progressive growth (Fig. 1). In the directed history and after a complete physical examination, no other findings were detected.

The skin lesion was initially considered as keratoacanthoma-type tumor. In the preoperative evaluation, including chest X-ray, there were no other relevant findings.

The lesion was excised with 1 cm of cutaneous margin including subcutaneous cellular tissue. After resection of the lesion, a defect, from approximately half of the aesthetic unit of the buccal cheek, remained. We

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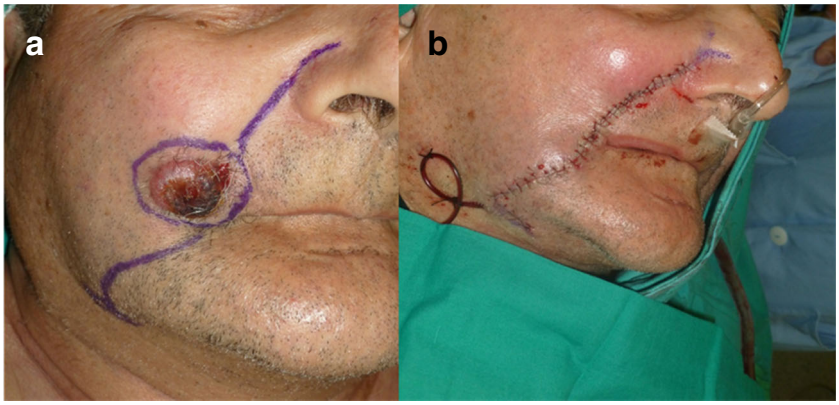

Fig. 1 **a** Skin nodule of 2.3 cm diameter over his right cheek, non-ulcerated. Wide local excision with 1 cm of margin. **b** Final intraoperative result. Reconstruction with reverse cervicofacial flap

designed the incisions of the reverse cervicofacial flap, planning the incisions at the level of melolabial and labiomental crease. To facilitate its advancement, we performed a back cut at the level of the mandibular ridge. The patient evolved without problems and was discharged the next day (Fig. 2).

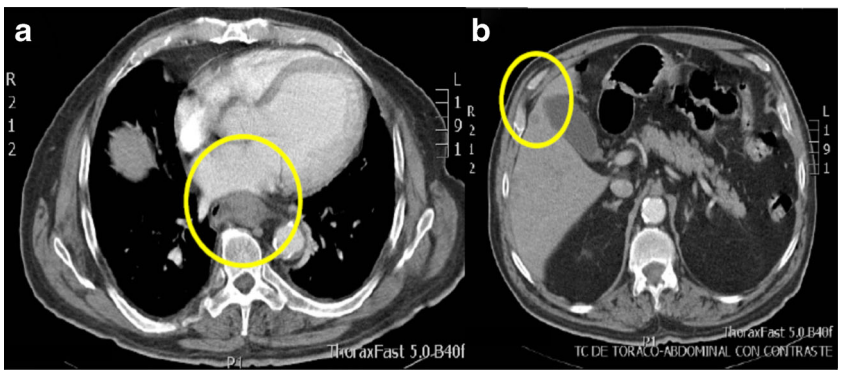

Fig. 2 **a** CT with contrast. Primary adenocarcinoma in the lower third of the esophagus associated with paratracheal lymphadenopathy. The esophageal lumen is barely visible. **b** Image compatible with liver metastasis of esophageal adenocarcinoma

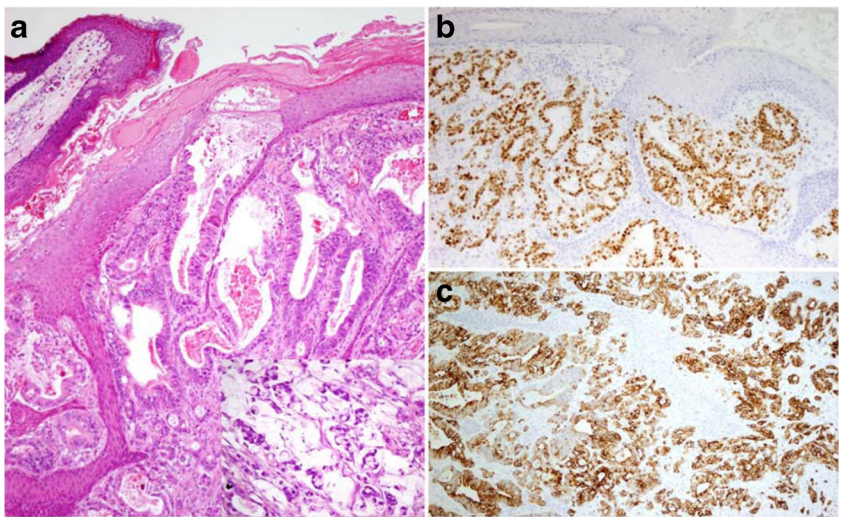

Fig. 3 **a** Proliferation of glandular structures in intimate contact with the epidermis (H/E; original magnification ×100); in the detail box, the tumor is composed of mucin lakes containing signet ring cells (H/E ×200). **b** CDX-2 staining positive (×200). **c** Staining with cytokeratin-7 positive (×200)

Table 1 Characteristics of cutaneous metastasis from esophageal adenocarcinoma found in the literature

Case (ref)[a]	Age/sex/ race	Metastasis location	Gross morphology	Onset of skin metastasis	Follow-up
[1]	77/M/W	Scalp	2 firm nodules 0.4×0.3 and 0.5×0.5 cm	5 years after the initial cancer diagnosis	Palliative chemotherapy and radiation
[2]	53/M/W	Lip scalp	7×5 mm crateriform nodule macule	3 months after discovery of cancer	XRT stopped and treatment with tesetaxel initiated
[3]	58/F/A	Scalp	10-mm nodule	7 months after discovery of cancer	NR
[4]	72/M/W	Lip	16-mm ulcerated nodule	1 month after discovery of cancer	NR
[5]	47/M/W	Scalp	3 painful nodules	At the same time of cancer diagnosis	Palliative radiotherapy
[6]	62/F/W	Left cheek	Round, well-demarcated, dome-shaped, soft skin nodule of 0.5 cm	Skin lesion prompted discovery of the underlying cancer	After 6 months of chemotherapy, the cancer remains stable
[7]	72/M/W	Scalp	2 small (<1 cm) painful nodules on the occiput and left postauricular region	After the treatment of primary esophageal cancer	Chemotherapy and he died 1 year later
[8]	81/F/W	Left temple	Large swelling (6 cm)	4 years after the initial diagnosis	NR
[9]	50/F/W	Right breast	Breast was red, swollen, and warm to the touch	22 months after the initial diagnosis	NR
[10]	67/M/W	Left occiput, abdominal	Nodule 2×3 cm, nodule 0.5 cm, mass 4.5×4 cm	24 months after the initial diagnosis	NR
[11]	54/M/B	Back	Multiple large painless nodules	At the same time of cancer diagnosis	Chemotherapy
[12]	59/M/W	Left scapula	Palpable subcutaneous nodule	2 years after the initial cancer diagnosis	Palliative care
[13]	76/M/W	Right scapula	Nodule	Skin lesion prompted discovery of the underlying cancer	Palliative surgery
[14]	61/M/W	Trunk	Nodule	13 months after the initial diagnosis	Rofecoxib. Died 4 months later.
[15]	60/M/W	Submental	3-cm ulcerated nodule	20 months after the initial cancer diagnosis	Non-treated. Eight months later, the patient is free of disease
[16] (Our)	81/M/W	Right cheek	2.3-cm non-ulcerated nodule	Skin lesion prompted discovery of the underlying cancer	Palliative care and died 3 months later

M male, *F* female, *W* White, *A* Asiatic, *B* Black, *XRT* radiotherapy, *NR* not reported

[a] References in order

Histopathological examination revealed a neoplasm with diffuse infiltration of the dermis with structures that looked like ducts and glands within a desmoplastic stroma. The tumor grew forming glandular structures, neoplastic cords, and single cells. In some areas, the tumor was composed by mucin lakes that contained signet ring cells (Fig. 3). In other areas, prominent intraluminal necrotic cellular debris ("dirty necrosis") was observed. This is not a common feature of adnexal tumor; however, "dirty necrosis" is a classic histopathological finding for adenocarcinoma of gastrointestinal origin.

The tumor cells showed diffuse immunostaining with AE1/AE3 and diffuse membrane stained with epithelial membrane antigen. Immunostaining was also positive for CK20, CK7, CEA, EMA, and CDX-2 and negative for CK5/6 and P63. A diagnosis of metastatic adenocarcinoma of probably primary digestive origin was made. A body scanner was performed, and a 5-cm mass was detected in the lower third of the esophagus associated with paratracheal lymphadenopathy and hepatic metastasis (Fig. 2). The patient underwent palliative symptomatic treatment and died 3 months after initial diagnosis as a result of natural evolution of his illness.

In Table 1, we showed the characteristics of cutaneous metastasis from esophageal adenocarcinoma found in the literature.

Discussion

Cutaneous metastases from internal malignancies are infrequent. They may be the first sign of disease and the first signal of progression. The propensity of different tumors to metastasize to the skin may vary, and the frequencies of skin metastases match the incidence of the primary tumors in the population, association not found by all authors. Cutaneous metastasis from esophageal adenocarcinoma is extremely rare. In two studies of 11,336 cancer patients, only three patients show metastases from primary esophageal cancer and the primary tumors are a squamous carcinoma, undifferentiated carcinoma, and one adenocarcinoma [16, 17].

The clinical appearance of cutaneous metastasis from esophageal adenocarcinoma is variable, ranging from red patches to dermal and subcutaneous nodules. They can also mimic other dermatologic conditions such as benign cysts, dermatitis, erysipelas, herpes zoster, inflammatory papules, and pyogenic granuloma (Table 1). Like in our patient, solitary lesions may be misdiagnosed as primary skin tumors.

In our review, a predominance of esophageal adenocarcinoma metastases was observed in the head (scalp and face) similar to other malignancies that metastasize to the skin. In women, 75 % of cases were found on the anterior chest and abdomen; in men, around 75 % cutaneous metastases were observed on the head and neck. To explain the high percentage of scalp metastases, literature says that vertebral venous system is avalvular, including the epidural and head and neck veins, which are interconnected with the portal, pulmonary, and caval venous system.

In the case, we presented herein that the immunohistochemical features in the tumor specimens were suggestive of metastatic origin. Immunohistochemical features with p63 and podoplanin were negative. It is generally shown that metastatic malignancies to the skin do not express p63 or podoplanin and that the majority of primary skin neoplasm will have focal or variable positivity for these markers. Our

lesion showed positivity for CDX-2, which seemed specific for metastatic urothelial and intestinal carcinomas.

Cutaneous metastases may occur in the setting of widely disseminated disease, or they may be the only sign of metastatic involvement. In a large series of cutaneous metastasis, the skin involvement is the first sign of cancer in 0.8 % of patients with cancer and only 0.23 % also has distant metastases, as in our case. In only three patients, the topographic diagnosis of adenocarcinoma was made at the same time of skin lesions; they had digestive symptoms and they have been studied for the digestive disturbance. Only our patient and the Fereidooni's patient [4] did not have any gastrointestinal symptoms and could be considered metastases of unknown primary origin. Then, skin involvement is the first manifestation of esophageal cancer in only two patients. In the studies, the unusual capacity for "herald metastasis," wherein skin involvement is the initial manifestation of an internal malignancy growth, shows that the most frequent sites of primary tumor origin is the lung, kidney, stomach, and internal female genitals.

Although cancer of internal organs rarely presents with skin metastases, any suspicious lesions with rapid growth should be ruled out as their metastatic origin; also, recent apparition of lesions in oncological patients, non-healing dermal ulcers, persistent indurated erythema, and skin nodules of undetermined cause need to be biopsied as soon as possible. In patients diagnosed with visceral cancer, it is necessary to explore the presence of skin lesions, especially on recent diagnosis, for the presence of cutaneous metastases that can modify tumor staging and change therapeutic approach.

Conflict of interest None

Patient consent Patients provided written consent for the use of their images.

Ethical Standards For this type of study formal consent from an ethics committee is not required

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