NEMESIS
Negative Effects in Medical Sciences Oral and Maxillofacial Surgery
UCL PRESSES UNIVERSITAIRES DE LOUVAIN

Cutaneous cervical metastasis from an esophageal adenocarcinoma mimicking a dental cervical cellulitis: A case report

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Abstract

Cutaneous metastases occur in 0.5 to 9% of all cancers. Esophageal cancer is one of the most aggressive cancers worldwide. Most cutaneous metastases from esophageal cancer were related to squamous cell carcinomas. Few cases have been described about cutaneous metastases related to esophageal adenocarcinomas. These metastases mostly affect patients over 60 years-old, and present as cutaneous asymptomatic nodules.

A 69-year-old male presented with a painless and extensive left neck cutaneous induration and erythema. The lesion that was initially diagnosed as a dental cervical cellulitis by his dental practitioner. The patient was known since 2019 to suffer from a esophageal adenocarcinoma whose first treatment was surgery. The patient was currently under immunotherapy for a local recurrence.

We firstly assessed the uncommon cervical cellulitis by carrying out an injected head and neck computed tomography (CT) scan which showed an unspecific skin, dermal and muscular infiltration of the left cervical region. The 18-FDG PET/CT demonstrated a suspicious fixation of the neck that was followed by a skin biopsy. The histological and immunohistochemical examination showed the metastatic adenocarcinomatous origin of the cervical skin lesion. The patient was upstaged to a stage IV of his esophageal cancer and started palliative chemotherapy.

Special attention must be paid in case of diffuse cervical skin infiltrations, even in the presence of a dental infection, in patients with cancer, in order to perform the correct diagnosis.

Keywords: esophageal adenocarcinoma, neck cutaneous metastasis, skin metastasis

Introduction

Cutaneous metastases occur in 0.5 to 9% of all cancers [1-3] . The most common primary tumors responsible for skin metastases are in descending order of frequency: 1) lung, 2) breast, and 3) rectal carcinomas [1-3]. Metastasis to the skin from other primary tumour location is uncommon [4].

Esophageal cancer is one of the most aggressive cancers worldwide. The overall 5-year relative survival rate ranges between 40% for localized tumor (N0-M0) and 4% for advanced metastatic tumors (M1) [5].

Regarding cutaneous metastases from esophageal cancer, the majority of cases were reported related with squamous cell carcinomas [3]. Few cases have been described in relation with esophageal adenocarcinomas [3]. These metastases mostly affect patients over 60 years-old, and present as cutaneous asymptomatic nodules [3].

Case report

A 69- year-old male patient was referred to the maxillofacial surgery department by his attending dentist for a cervical cellulitis originating from the tooth n°36 (Figure 1).

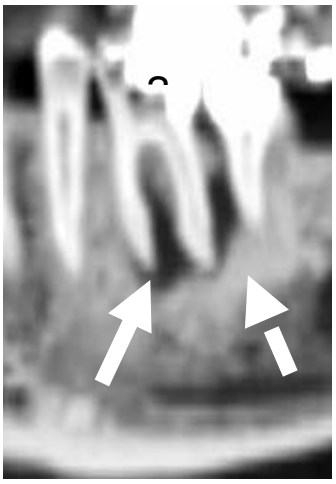

Fig. 1. Mandibular computed tomography (CT) scan showing osteolysis around the apices of the tooth n°36 (plain arrow), and osteocondensation around the teeth n°36 and 37 (dashed arrow).

The patient received amoxicillin 500mg three times per day and mouthwashes (Corsodyl, Glaxosmithkline, Belgium) without any improvement, followed by the association of amoxicillin 875mg and clavulanic acid 125mg three times per day. The aspect of the cellulitis was not modified after more than one month of antibiotics. Clinical examination showed a redness induration and retraction of the skin, that extended from lower edge of the mandible to the 2/3 of the neck on the left side with no anatomical boundaries, and crossing cervical midline (Figures 2A, 2B).

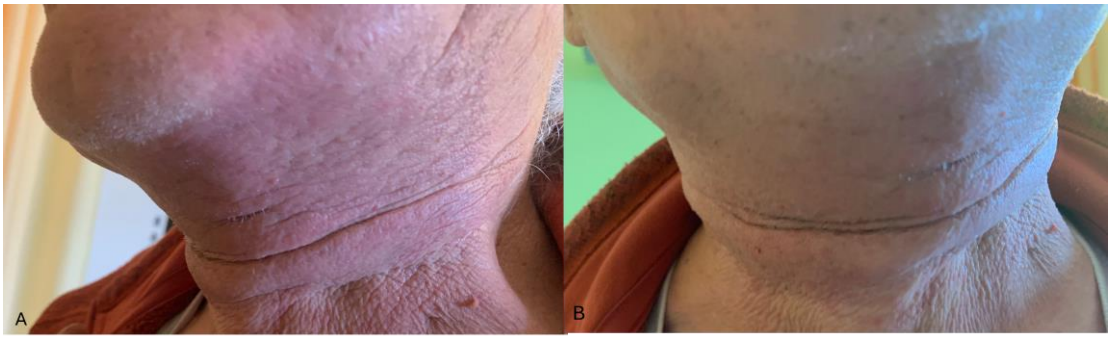

Fig. 2. Appearance of the neck skin. A. Redness induration of the skin with no anatomical boundaries. B. Retraction of the skin with "Erysipelas-like" pattern that extends from the lower edge of the mandible to the 2/3 of the neck, and crossing the cervical midline.

Patient's past medical history revealed hyperthyroidism, mitral valve prolapse, Barett's esophagus, chronic renal failure, and antiphospholipid syndrome. An esophageal adenocarcinoma (low third at the gastroesophageal junction) was diagnosed in 2019 and treated by surgery. The tumor was staged pT2pN1cM0, and the patient did not receive any adjuvant treatment. Two years later patient presented with a local recurrence and received systemic nivolumab. The disease was supposedly stable when the patient was referred to our department in 2023, with a good follow-up of the patient and no side effects related to immunotherapy.
Patient's usual treatment was perindopril and amlodipine, and omeprazole. No alcohol, tobacco or toxic consumption was reported by the patient.
Assessment of the cervical swelling included an injected head and neck CT scan showing a skin, dermal, fascial and muscular tissue infiltration of the cervical region (Figure 3). Differential diagnosis included carcinomatous lymphangitis, dermatomyositis, cellulitis, and cutaneous metastasis.

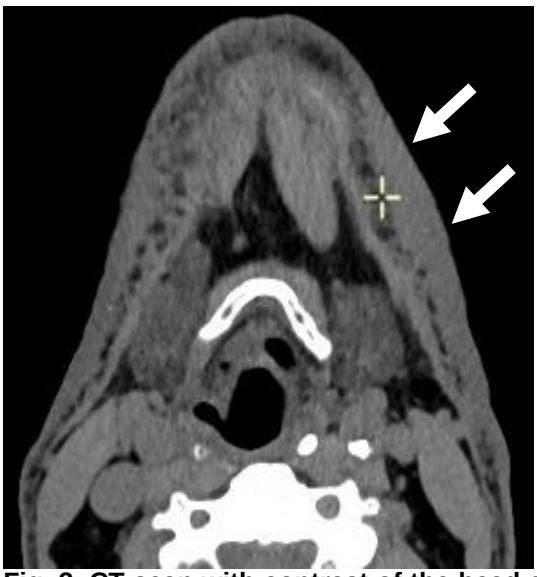

Fig. 3. CT scan with contrast of the head and neck region. Thickening of the tissues (skin, subcutaneous tissue, fascia and platysma muscle) of the left cervical region (arrows).

The 18-FDG PET/CT (Figure 4) exhibited a slight uptake (SUVmax < 5) of the subtutaneous tissues of the neck, and the persistence of hypermetabolism in the lower oesophageal prosthesis, which was relatively stable (SUVmax 7.5). No other lesion was visualized.

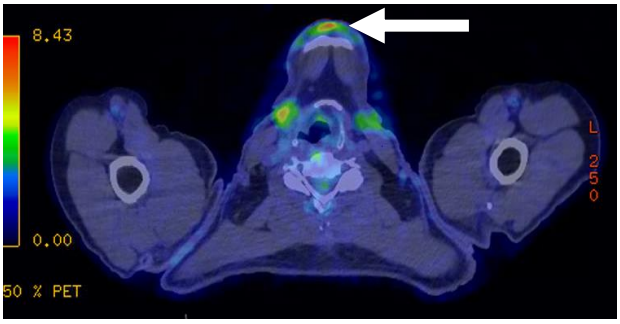

Fig. 4. 18-FDG PET/CT. Slight uptake of 18-FDG in the cervical subcutaneous tissues: SUV max<5 (arrow, red and yellow spots).

The blood sample demonstrated a normal white blood cell count and a slightly elevated CRP (11,5 mg/l [normal value: <5]). Carcinoembryonic antigen CEA (1µg/l) and carbohydrate antigen CA 19-9 (9 kU/l) were below the maximum normal values (<3,8 µg/l and <34 kU/l respectively). The value of alkaline phosphatase was normal (64 U/l [normal value: 40-130]). Because of the specific clinical and radiological aspect of the skin and underlying tissues, a skin biopsy was conducted because of the lack of conclusive radiological findings. The sample showed a subcutaneous infiltration by neoplastic cells (hematoxylin-eosin, original magnification by 5) (Figure 5). At higher magnification (hematoxylin-eosin, original magnification by 10), neoplastic cells showed up a typical signet ring appearance (Figure 6).

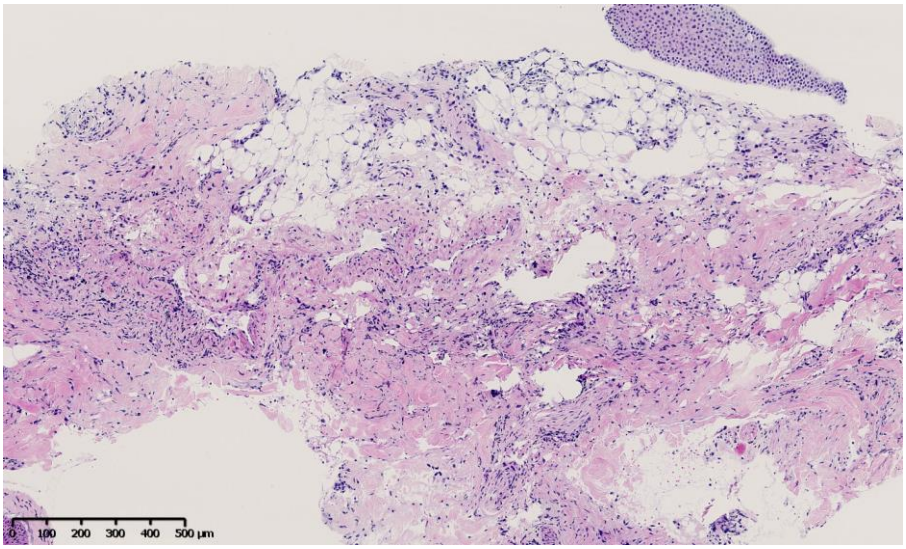

Fig. 5. Histological examination (Hematoxylin-eosin) with magnification by 5. Subcutaneous infiltration by neoplastic, non-cohesive cells.

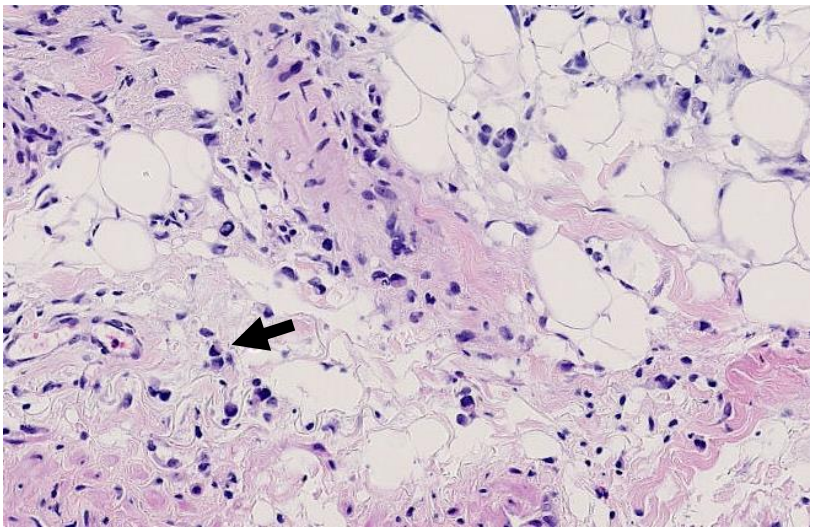

Fig. 6. Histological examination (Hematoxylin-eosin) with magnification x10. Neoplastic cells with typical "signet ring" appearance with intracellular mucin that displaces nucleus to side. Black arrow: **"**signet ring" cell.

The immunostainings (CK-Ae1/Ae3) highlighted the epithelial nature of the tumor (Figure 7).

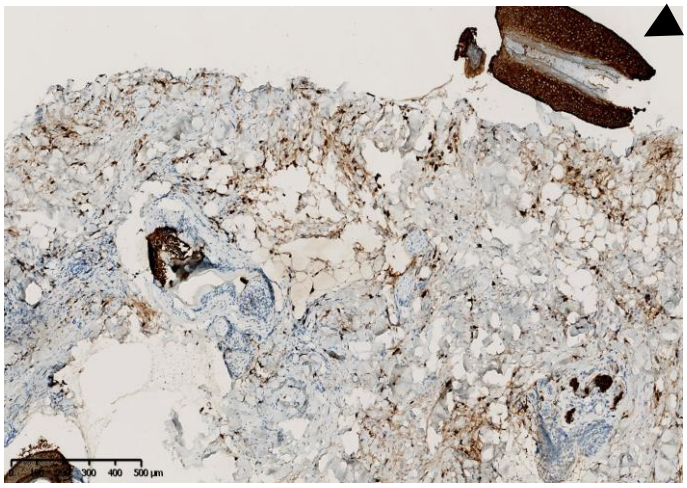

Fig. 7. Immunohistological examination (original magnification by 10). CK-Ae1/Ae3 immunostaining highlights the normal epithelium (arrow) and infiltrative cells, supporting the epithelial nature of the tumor.

Finally, immunohistochemistry examination of cytokeratin (CK7) (Figure 8) and cytokeratin 20 (CK20) (Figure 9) showed explicit expression of an adenocarcinoma, compatible with a metastasis of the known esophageal adenocarcinoma.

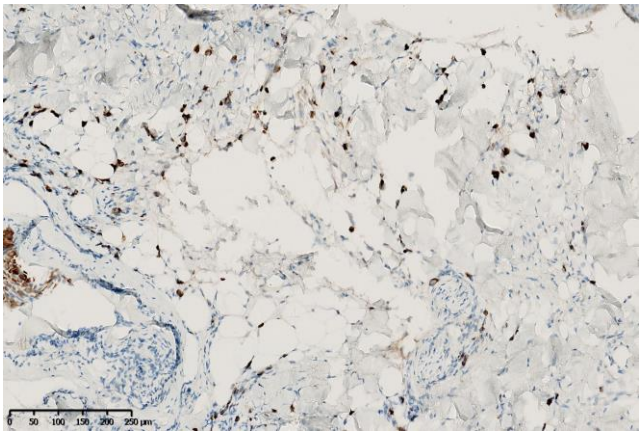

Fig. 8. Immunohistochemistry examination of cytokeratin (CK7). The tumor cells are positive for cytokeratin 7 (CK7).

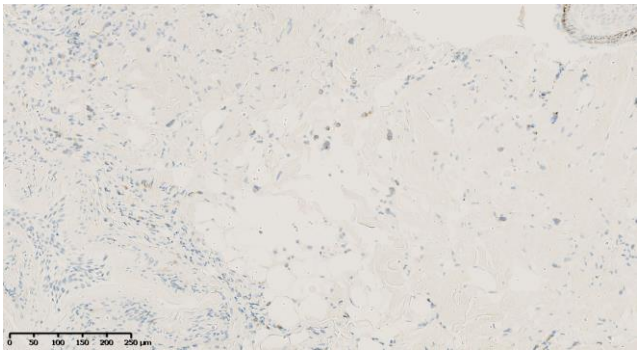

Fig. 9. Immunohistochemistry examination of cytokeratin 20 (CK20). The tumor cells are focally positive for cytokeratin 20 (CK20) supporting the small intestine origin of the infiltration.

The patient was addressed to our multidisciplinary oncological consultation, and was upstaged to cM1 (stage IV) of the esophagus cancer. Systemic nivolumab was proposed to be carry on, and the patient was advised that from now on, the cancer was controllable but not curable.

Overall, the timing in between the first dentist attending and the final diagnosis of the metastatic expression of patient's cancer was three months.

Discussion

Esophageal cancer is one of the most aggressive cancers and has an increasing incidence with 400,000 cases diagnosed per year, with a predominance of adenocarcinoma in the Western countries [3, 5, 6].
Fifty to 64% of patients present with unresectable disease, with the majority of patients with inoperable disease are dying within 21 months [1, 6]. Skin metastases account for less than 1% of all cancer metastases [3]. Cutaneous metastases originated from internal malignancies, mostly lung, breast and colorectal cancers, constitute 0.5% to 9% of all metastatic cancers [1-3]. The primary tumor is usually known before skin metastases are detected, with 95 % of patients presenting with stage III or IV disease, but sometimes skin metastases can be the first symptom of an unknown tumor [2, 4].

The incidence of cutaneous metastases from esophageal adenocarcinomas and squamous cell carcinomas is around 1% [3]. They rarely occur in the cervical region where they may be confused with a local infection, delaying diagnosis, particularly in this case, partly because of the time spent using antibiotics, and partly because of the delay in obtaining routine imaging (CT scan, MRI, PET/CT). Moreover, in the present case, there was a long history of local chronic infection on tooth n°36, which could add confusion on the etiology of this cervical induration.

The usual locations of esophageal metastasis are the abdominal lymph nodes, lung, liver, bones and adrenal glands [2]. Cutaneous metastasis from esophageal carcinoma are most often found on the scalp, neck and face [6]. Skin metastases may take the form of inflammatory papules or patches, erythematous or indurated plaques, or subcutaneous nodules, which appear to be the most common presentation in esophageal carcinoma.

In most cases, skin metastases are considered of a poor prognostic factor, given the aggressive nature of the disease. The rare cases of skin metastases described in the literature concern adenocarcinomas located in the lower third of the esophagus, and more particularly primary tumors located at or near the gastroesophageal junction in relation with Barrett's esophagus, as was the case with our patient [3]. Cutaneous metastases are usually of nodular type, unlike our patient, who presented with diffuse infiltration of the skin. "Erysipelas-like" pattern as in the present study, is very rare and only 6 cases were actually described in the literature in the cervical region, from a primitive esophageal adenocarcinoma [7, 8].

One of the explanations of this uncommon metastatic site could be related to the anatomy of blood vessels and of lymph nodes. A recent anatomical feature (2017) showed the presence of an aorto-esophageal ligament that encounter the periesophageal adventia and connects it with the mediastinum [9]. There is a shared vascularization starting from the inferior thyroid artery to the splenic artery across different arterial supplies that could explain the tumor metastasis into nearby and distal organs. Moreover, the esophagus extrinsic veins drain into the jugular veins or the azygos and hemizygous veins superiorly and to the left gastric and splenic veins inferiorly. These features could explain the existence of distal unexpected metastases in some patient with low-stage cancer (T1 or T2), including the fact that the lymphatic network in the esophagus can spread with a "nodal skip" feature (bidirectional and retrograde), probably due to intramural lymph vessels obstruction by the tumor [10]. However, some authors claim that distal metastatic dissemination such as the skin, penis, lips or retina, could barely be explained by the only lymphatic or venal routes [5, 11].

The factors that predict the risk of skin metastases are not well known. However, poorly differentiated adenocarcinomas and the presence of "signet ring" cell features may increase the risk of cutaneous spreading as was the case with our patient [6].

Effective treatment depends on treatment of the underlying tumor but usually, some palliative care is given if lesions are asymptomatic and the primary cancer is untreatable. Small cutaneous metastasis can be removed surgically (excision), but otherwise multiple grouped lesions or painful lesions can be treated by radiotherapy (usually 30 Gy). Locally some hydrocolloids can help to prevent secondary infection, but the primary care is to keep lesions clean and dry, debriding the lesions if they are crusted.
Chemotherapy and/or immunotherapy remains the main standard of treatment of the metastatic disease based on the histology of the primary tumor [12].

This case illustrates the important role of physicians and dentists in evaluating skin lesions taking into account the patient history and to be aware that cancers can show multiple faces. Esophageal carcinomas can express a painless induration and erythema on the skin, mimicking other soft tissue pathology, such as cellulitis with a dental origin. In case of doubt especially in patients with or who have had cancer, a biopsy is indicated after imaging, even if the primary tumor is locally controlled. Sometimes cutaneous metastasis might be the first sign of a primary cancer or a

recurrence and prompt initiation of a bloodwork and imaging (injected CT scan/MRI and PET/CT) should be done while waiting the final histological diagnosis. Patients with skin metastatic disease usually have significantly poorer prognosis with reported survival rates of <1 year after the identification of metastatic lesions. The treatment is usually aimed to palliation through possible with chemotherapy/immunotherapy and radiotherapy in case of pain [1].

- **Acknowledgements**: We would like to thank Cliniques universitaires Saint Luc (Public healthcare Institution, Brussels, Belgium) for their invaluable help in patient treatment and observation
- **Funding sources statement**: This study does not receive any funding.
- **Competing interests**: All authors declare no competing interests related to this study.
- **Ethical approval**: There was no need for the ethical approval for this case report.
- **Informed consent**: There was no need for the informed consent for this case report as all the images were anonymized and no private data were provided allowing the patient's identification.

Authors contribution:

Author	Contributor role
Arnal-Etienne Andréa	Conceptualization, Investigation,Writing original draft preparation,Writing review and editing
Fourneau Eleonore	Writing original draft preparation,Writing review and editing
Dewaele Nathan	Writing original draft preparation,Writing review and editing
Mengeot Nathalie	Investigation,Writing original draft preparation,Writing review and editing
Magremanne Michele	Conceptualization, resources, methodology, supervision, project administration, Writing original draft preparation,Writing review and editing

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