Case Report

Esophageal Adenocarcinoma with Extensive Metastasis to Unexpected Sites: A Case Report

Vincent Louie Mendiola^a Maurice Willis^b

^aDepartment of Internal Medicine, University of Texas Medical Branch, Galveston, TX, USA;

^bHematology/Oncology, University of Texas Medical Branch, Galveston, TX, USA

Keywords

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Abstract

Background: Esophageal cancer (EC) with unexpected metastasis (UM) to unusual sites have been increasingly reported. EC with metastasis in general has a very high mortality and morbidity rate, and those with UM to unusual sites present another specific field that needs to be further studied in order to understand and manage the presentation. An extensive systematic review was recently completed regarding this field which identified characteristics and findings concerning patients with EC with UM sites. **Case Presentation:** We report a 61 year old Hispanic male who had an EC, adenocarcinoma subtype, with UM to an extensive number of sites such as the soft tissue of the cheek, subcutaneous forehead and scalp with penetration of the calvarium, occipital bone, base of tongue, neck muscles, paraspinal and iliopsoas musculature and, more typically, to an adrenal gland followed by a questionable new-onset finding of subcutaneous shoulder and flank nodules not initially identified by imaging. **Discussion/Conclusion:** The case reports a patient who not only had EC with UM to unusual sites, but also to a considerable number. The patient correlated well in terms of clinical features identified by the systematic review of this particular field, but his case also showed a new finding, another unexpected metastasis site. This case also shows an example of why the type of imaging is important when dealing with UM sites. With this, we hope to further add to the data in this particular field and provide some opinion on this matter.

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Background

Esophageal cancer, EC, is one of the most common malignancy worldwide and mainly divided into two subtypes: squamous cell carcinoma (sqCCa) versus adenocarcinoma [3]. Even though EC currently has a stable incidence in first world countries, it still boasts one of the most common cancer related deaths world-wide, with only a 4% survival rate for those with metastasis [5, 6]. In the United States, in particular, EC-adenocarcinoma have overtaken sqCCa in terms of incidence and prevalence, and deserves to be further studied [4].

It is also commonly understood that EC with metastasis presents a higher morbidity and mortality in general than localized neoplasm, and, in light of this, comes the importance of further understanding its metastatic pathways, especially, metastasis to unexpected areas. In response to this, a recent extensive systematic review was completed in 2017 which evaluated EC metastasis to different sites that were not part of the typical expected sites such as the liver, lung, bone and adrenal glands. The paper was written in order to further contribute to the understanding of this field due to the increasing frequency of reported cases [2]. The systematic review, analyzed in-depth a total of 147 articles (after narrowing from an initial number of 10,049 articles) that passed its inclusion and exclusion criteria, and reviewed 164 patients from 1982 to 2017 with these rare EC presentation that had unexpected metastasis, UM, to unusual sites [1]. In general, about 40% of the patients have EC adenocarcinoma with UM sites, and, per anatomic area distribution, about 42% of the patients have UM to the head and neck, 17% to the thoracic area, 25% to the abdomen and pelvis, 9% to the extremities, and 7% to the skin and other muscles [1].

With this, we report a 61 year old Hispanic male who had an EC, adenocarcinoma subtype, with UM to an extensive number of sites such as the soft tissue of the cheek, subcutaneous forehead and scalp with penetration of the calvarium, occipital bone, base of tongue, neck muscles, paraspinal and iliopsoas musculature and, more typically, to an adrenal gland followed by a questionable new-onset finding of subcutaneous shoulder and flank nodules that was not initially identified by imaging. This case also shows an example of why the type of imaging concerning UM sites is important.

Case Presentation

A 61 year old Hispanic male with a past medical history of gastroesophageal reflux disease, hepatitis C treated with ribavirin and interferon, and ethanol and tobacco abuse presented to our clinic with a complaint of 2 months of progressing dysphagia starting from solids then liquids, unintentional 15 lb weight loss and occasional nausea and vomiting with noted streaks of blood on vomitus after prolonged retching. Dysphagia was first noted when he started eating mainly cold drinks followed by cold trays. He felt that food was getting stuck in his mid-esophageal region and has constantly pounded his chest with his fist to make the food go down. On physical examination, the patient was noted to have the following: cachectic features of the face and body, a painless and firm 2 cm nodule along the left zygomatic crest and a firm and fixed ~1 cm nodule of the right base of tongue. On further questioning about the nodules, the patient took notice of only the left cheek nodule which had been present for about 5 months, but did not notice if it progressed in size. The patient was then initially scheduled for an esophagogastroduodenoscopy (EGD) but was lost to follow-up until presentation at the emergency room about 1 month after due to weakness, fatigue and decreased oral intake secondary to progressive dysphagia. The patient was afebrile and his vitals were stable. The

complete blood count, metabolic count, liver function tests, coagulation studies were within normal limits.

The patient initially underwent fluoroscopy which showed a 3 cm distal esophageal mass followed by computed tomography (CT) soft tissue neck, thorax, abdomen and pelvis with contrast. The CT soft tissue neck revealed a 1.8 cm mass in the left anterior face at the level of the left nare without cystic components or inflammatory fat stranding, a $1.2 \times 1.7 \times 1.3$ cm soft tissue density nodule of the right floor tongue root adjacent to the geniohyoid muscle, a 9 mm hyper dense nodule of the left rectus capitis muscle, a 7 mm hypodense nodule of the left trapezius muscle, a 5 mm enhancing nodule of the right rectus capitis and a more superior 7 mm nodule of the right rectus capitis that is better visualized on delayed images (Fig. 1). CT thorax showed an eccentric circumferential thickening of the right distal esophageal wall that is ~1.8 cm in thickness with a length of 4.6 cm and an 8 mm lymph node adjacent to the distal esophagus (Fig. 2). CT abdomen/pelvis showed a liver with a 6.9 cm enhancing dome more likely from a perfusional defect but, over-all, with normal contour, a left adrenal gland that was diffusely enlarged and enhancing, several scattered areas of hyper-enhancement of the right iliopsoas with the largest measuring ~1.8 cm, multiple left para-spinal musculature nodules about ~1 cm in size, and several subcutaneous nodules measuring up to 0.6 cm of the left flank (Fig. 3). Per initial radiologists' discussions, the chest findings showed an esophageal mass that was highly concerning for malignancy. The face and neck findings raised the possibility of soft tissue metastasis from the esophagus which was unusual; thus, a possible second primary such as melanoma was in the differential. The abdomen/pelvis findings of the left adrenal gland was concerning for metastasis, the multiple nodules were nonspecific but still suspicious for metastasis and once again, a secondary primary such as metastatic melanoma was in the differential along with metastasis from an esophageal primary.

An EGD was then done which showed the following: Barrett's-like features in the mid and distal esophagus, a large fungating and ulcerating mass which bleeds on contact in the lower third esophagus that was partially obstructing and circumferential involving two-thirds of the lumen circumference, and a large hiatal hernia (Fig. 4). Biopsies of the esophageal mass were then sent for evaluation, and revealed a poorly differentiated adenocarcinoma with squamocolumnar mucosa showing Barrett's and dysplasia. The tissue biopsy was microsatellite stable, p40– and *HER2/NEU*+ (verified with *ERBB2/HER2* FISH). The esophageal brushing also revealed findings consistent with poorly differentiated adenocarcinoma. Oncology was then consulted for further recommendations and requested to for a sample of the left cheek nodule. A fine needle aspiration of the left cheek nodule was then performed which also revealed a poorly differentiated adenocarcinoma favoring metastasis from the esophageal primary per pathologists' consensus after reviewing the esophageal biopsy and reviewing its cytomorphology. Immunostains of the left cheek nodule were noted to be CK7+ and p40–.

During the course of his work-up, within a few weeks' span, the patient started mentioning new sub-centimeter nodules on the left and right forehead and scalp, left shoulder and flank and right thigh which were painful to palpation. A magnetic resonance imaging (MRI) of the head with and without contrast was then done which revealed a well circumscribed homogeneously enhancing 2×2 cm lesion of the left pre-maxillary soft tissue, a 1×1.7 cm lesion of the left lateral pterygoid muscle, a 7×1.4 cm lesion of the right genioglossus muscle adjacent to the root of the tongue which all correlated with past CT findings (Fig. 5). Additional findings showed an enhancing 10.9 mm left parietal scalp and 11.8 mm right frontal scalp lesions with possible extension into the right calvarium, an enhancing 0.8×1.6 cm lesion of the right spinalis capitis, and an enhancing focus in the left occipital bone which correlated with the fluid attenuated inversion recovery (FLAIR) hyperintensity suspicious for calvarial

metastasis (Fig. 5). Per radiologists' consensus, findings were concerning for metastasis that were more likely from an esophageal primary due to prior pathology findings.

Dermatology was also consulted to get a biopsy of the left shoulder and left flank nodules. Per histopathology, a tumor was identified in the deep dermis with no relation to the overlying epidermis. The tumor was composed of atypical epithelial cells, with focal gland formation. Immunohistochemistry showed tissue to be CK7+, diffusely, on all cells, CK20– and p40–. The profile was consistent with metastasis from the esophageal primary, a poorly differentiated adenocarcinoma. *HER2* immunostaining was also done and was positive. Due to this, per discussions, the patient's findings such as nodules in the subcutaneous areas of the face, within the base of the tongue, neck muscles, paraspinal and iliopsoas musculature were deemed to be more likely metastasis from the EC primary.

A tumor board discussion was held, and due to the patient's over-all performance status and social circumstances, it was decided that hospice with palliative radiation therapy was the best course of action. The patient agreed to the plan and was made DNR/DNI. The patient then underwent esophageal stenting and started receiving daily fractions of radiation treatment for his esophageal mass. The patient started experiencing continuous nausea without vomiting and had a mechanical fall without head trauma. During this time, the patient also started refusing his oxygen and requested to be switched to comfort measures. He expired one night from cardiopulmonary arrest.

Discussion

Our patient presented with an EC, adenocarcinoma subtype that had UM to an extensive number of unusual sites which was very interesting due to the multiple atypical locations that the EC spread to. Some points will be discussed with reference to the findings in the recent and extensive systematic review of EC with UM sites by Dr. Shaheen et al. [1].

First, in terms of demographics and clinical features: our patient's age was within the median age of 60.7 years for those identified in the review. In addition, most of the patients found to have EC with UM were dominantly male, and had lower/distal EC as the primary site similar to our patient [1].

Second, in terms of anatomic site distribution of the UM, our patient who had an adenocarcinoma subtype, had most of his UM to the head and neck which correlated with the finding that most of the head and neck UM was from an adenocarcinoma subtype (60%) rather than sqCCa. In the review article, the number of cases of EC with UM to specific organs was also recorded, and our patient had UM to multiple specific sites that were generally uncommon and rarely identified even in the systematic review. These include UM to the following: Soft tissue of the cheek, which per review article, was not identified within the 164 patients reviewed, the base of the tongue, wherein only 1 other patient was recorded to have, subcutaneous areas of the forehead, scalp, shoulder and flank, the calvarium and occiput of the skull, the neck muscles, and the iliopsoas and paraspinal musculature. In terms of how the EC spread to this atypical sites, at least in areas nearby such as the neck, tongue or cheek, it has been suggested that the absence of a serosal coating of the peri-esophageal adventitia coupled with the extensive lymphatic network and possible obstruction by the EC mass on these vessels could have led to retrograde flow to nearby structures [1, 7, 8]. Our patient did have an esophageal mass that was 1.8 cm in thickness and 4.6 cm in length involving the two-thirds of the entire luminal circumference as well. In terms of the more distal UM such as the paraspinal and iliopsoas musculature or the subcutaneous areas of the face, shoulder and flank, an

arterial route could have been the more likely route of spread, especially, due to how the esophagus has multiple arterial branches leading to the inferior thyroid artery, the thoracic part of aorta or the left gastric artery.

In terms of the patient's new complaints of subcutaneous nodules in the left shoulder and left flank that were not noted on admission and even on initial CT thorax and abdomen/pelvis, it is unlikely that the nodules newly appeared within such a small time frame. More likely, CT was not a good enough imaging tool by itself. In relation to this, a past study using a combination of fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) was able to identify more soft tissue masses at unusual sites as UM from EC to the point that a higher prevalence of EC with UM sites was actually identified compared to lymphoma [9]. This has led to the hypothesis that limited scanning may underestimate the true prevalence of EC with UM [9]. Just like our patient who had initial CT images, that more likely missed the subcutaneous nodules in the shoulder and flank, it may be justifiable to consider going straight for a FDG PET when there considerable concern for possible UM.

Conclusion

There is a growing frequency of people with EC with UM to unusual sites. It is concerning due to how EC with metastasis in general already has a very high mortality rate, and now, further data is needed to study EC with an atypical metastasis presentation. This case showed a patient with EC with an UM to an extensive number of unusual sites, including the cheek which has not been reported yet to the best of our knowledge, as well as, how our patient correlated with findings of a systematic review about EC with UM sites. We also provided an example of why the type of imaging is important when dealing with UM sites. With this, we hope to further add to the data in this particular field and provide some opinion on this matter.

Statement of Ethics

Ethics approval: Not applicable (case report). Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure Statement

The authors declare that they have no competing interests

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Author's Contributions

V.M., primary author; M.W., reviewer.

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Fig. 1. CT soft tissue neck w/ contrast; transverse views; A hyperattenuating round mass measuring 1.8 cm in the left anterior face at the level of the left nare (but discrete from the nasolabial fold) (box 1); A soft tissue density nodule along the right floor tongue root adjacent to the geniohyoid muscle measuring $1.2 \times 1.7 \times 1.3$ cm (box 2); A hyperdense nodule in the left rectus capitis muscle measuring 9 mm (big arrow) and a hypodense nodule in the left trapezius muscle measuring 7 mm (small arrow) (box 3); A 7 mm enhancing nodule in the right rectus capitis (box 4).

Fig. 2. CT thorax w/contrast; coronal view; There is an eccentric circumferential thickening of the distal esophageal wall, eccentric to the right measuring up to 1.8 cm in thickness for a length of approximately 4.6 cm.

Fig. 3. CT abdomen and pelvis w/contrast; transverse views; The left adrenal gland is diffusely enlarged and enhances heterogenous lesion with attenuation higher than expected for a benign adenoma (box 1). Several scattered areas of hyperenhancement in the muscles with examples as follow: Right iliopsoas measures 1.8 cm (box 2) and left paraspinal musculature measures 0.8 mm–1 cm (box 3).

Fig. 4. EGD; Lower third of esophagus showing large, fungating, friable and ulcerating mass that bled easily. The mass was partially obstructing and circumferential (involving 100% of the lumen circumference). The distal margin of the mass was at the gastroesophageal junction at 34 cm without extension to the gastroesophageal junction.

Fig. 5. MRI head w/contrast; T1; A sagittal view shows an enhancing right spinalis capitis muscle lesion measuring 0.8×1.6 cm (box 1); The transverse view shows a well-circumscribed enhancing lesion in the left premaxillary soft tissues measuring approximately 2×2 cm (big arrow) and a well-circumscribed enhancing mass within the left lateral pterygoid muscle measuring approximately 1×1.7 cm (small arrow) (box 2). A sagittal view shows an enhancing lesion within the right genioglossus muscle adjacent to the root of the tongue on the right side measuring 1.7×1.4 cm (box 3). Transverse views showing an enhancing right frontal scalp lesion with possible extension into the right calvarium measuring 1.2 cm (small arrow) (box 4) and an enhancing left parietal scalp lesion measuring 1.9 cm (big arrow) (box 5).