Skeletal muscle metastasis from signet ring cell esophageal adenocarcinoma

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Abstract: Symptomatic skeletal muscle metastasis from esophageal adenocarcinoma is rare. Here we report the case of a 49-year-old man who presented with right thigh pain, and was found to have symptomatic psoas muscle metastasis as the presentation of esophageal adenocarcinoma. The primary tumor was notable for signet ring cells (SRC), a poor prognostic indicator as well as a predictor of biologic aggressiveness. The patient passed away within 1 month of diagnosis due to disease progression, supporting the aggressiveness of such SRC esophageal lesions. Lastly, a literature review reveals a differential pattern of metastatic spread between esophageal adenocarcinomas and squamous cell carcinomas as regards muscle metastases. Skeletal muscle metastases are more likely to be due to esophageal adenocarcinoma, whereas myocardial metastases are almost exclusively due to esophageal squamous cell carcinoma (ESCC). These differences may represent an example of the ‘seed and soil’ hypothesis of metastasis.

Keywords: Esophageal adenocarcinoma; skeletal muscle; neoplasm metastasis; signet ring cell (SRC)

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Introduction

Distant metastasis of esophageal adenocarcinoma to skeletal muscle is exceedingly rare. Most of these metastases are asymptomatic, detected with imaging modalities such as computed tomography (CT) or positron emission tomography (PET) during staging of the primary tumor (1-3). Here we report an unusual case of symptomatic skeletal muscle metastasis as the presentation of signet ring cell (SRC) esophageal adenocarcinoma. This case illustrates the poor prognosis associated with both skeletal muscle metastasis and SRC esophageal adenocarcinoma. Finally, the ‘seed and soil’ hypothesis of cancer metastasis is highlighted by this case, differentiating the preferred sites of muscle metastasis for esophageal adenocarcinoma versus esophageal squamous cell carcinoma (ESCC).

Case presentation

A 49-year-old man with no significant past medical history presented with progressive right anterior thigh pain, worse with hip flexion. Initial plain radiographs of the abdomen and pelvis were unrevealing. Non-contrasted CT of the abdomen and pelvis, however, revealed a 6x5x8 cm partially-calcified mass within the right psoas muscle, as well as diffuse retroperitoneal lymphadenopathy concerning for malignancy (Figure 1). Magnetic resonance (MR) imaging of the abdomen confirmed the presence of a large solid neoplasm expanding the right psoas muscle. Laboratory investigations were remarkable for elevated carcinoembryonic antigen (CEA) at 96 ng/mL and elevated carbohydrate antigen 19-9 (CA 19-9) at 179 U/mL. CT-guided biopsy of the
right psoas revealed poorly-differentiated carcinoma with SRC features (Figure 2). The lesion was thought to be of upper gastrointestinal (GI) origin due to its immunohistochemical staining pattern, with tumor cells positive for cytokeratin-7 (CK-7) and CDX-2, but negative for CK-20 (Figure 2). Further imaging with contrasted CT of the chest revealed a soft tissue prominence within the distal esophagus as well as diffuse axillary and subpectoral lymphadenopathy. Upper endoscopy was performed, demonstrating an ulcerated esophageal mass extending into the gastroesophageal junction and gastric cardia (Figure 3). Biopsy of this lesion was consistent with that of the right psoas mass: poorly-differentiated adenocarcinoma with SRC features (Figure 4). The tumor cells, notably, were positive for HER2/neu amplification by immunohistochemistry (Figure 4). Palliative chemoradiation were considered for this patient with symptomatic metastatic esophageal adenocarcinoma. However, the patient’s clinical status deteriorated rapidly, with intractable nausea and vomiting as well as failure to thrive. The patient was transitioned to hospice care, and expired within 4 weeks of his initial presentation.

Discussion

Skeletal muscle metastases from esophageal cancer are uncommon. These metastases are often diagnosed during staging, using combined PET/CT imaging (1-3).
Symptomatic skeletal metastases as the presentation of stage IV esophageal lesions have only been reported in one case prior to this report (4). This case demonstrates the grim prognosis associated with metastatic disease to skeletal muscle. One series of patients with skeletal muscle metastases from diverse primaries reported mean survival of 9 months from diagnosis of muscle metastasis (5). Despite the relatively young age of the patient in this report, progression of symptoms was sufficiently rapid that expiration occurred within 1 month of diagnosis.

In addition to the overall poor prognosis associated with skeletal muscle metastasis, this case highlights the prognostic value of SRCs in esophageal cancer. Several recent studies have shown that SRCs in esophageal adenocarcinoma predict more aggressive biologic behavior, and are associated with more advanced disease at presentation (6-8). While only approximately 5% of esophageal adenocarcinomas have SRC features, this report is the second to describe SRC esophageal adenocarcinoma with skeletal muscle metastasis (7,9). It is also noteworthy that the primary esophageal lesion in this case was HER2/neu amplified, which has similarly been shown to be associated with poor survival and higher odds of nodal metastasis (10). This case therefore underscores the importance of pathologic features such as SRCs and HER2/neu amplification in esophageal adenocarcinoma as both prognostic indicators and predictors of tumor aggressiveness.

Metastatic disease to both skeletal and cardiac muscle is believed to occur through hematogenous spread of tumor, as these tissues are well-vascularized (2,11). However, a literature review of esophageal carcinomas with muscle metastases reveals a pattern of spread based on tumor histology. Twenty-one cases, including the present report, have described esophageal cancers with skeletal muscle metastases and specified the histology of the primary tumor. Sixteen of these cases (76%) are adenocarcinomas (2-4,9,12-20), whereas only five (24%) are ESCCs (1,3,21,22). By contrast, 13 cases of ESCC metastatic to myocardium have been reported (11,23-25), but no reports of esophageal adenocarcinoma metastatic to myocardium were found. One possible explanation for this is the ‘seed and soil’ hypothesis of cancer metastasis, which advocates that specific tumors and tumor histologies have preferential sites for distant spread (26). These patterns of spread are based on a complex interplay of properties of both the ‘seed’ (the primary tumor) and the ‘soil’ (specific sites of spread). Despite the common hematogenous route of spread to both skeletal and cardiac muscle, the data above suggest that esophageal adenocarcinoma may have a preference for skeletal muscle, whereas ESCC may prefer myocardium. Given the rarity of any muscle metastasis from esophageal cancers, this hypothesis requires larger series to validate.
Nevertheless, the ‘seed and soil’ hypothesis provides a fascinating possible explanation for these differential patterns of spread. Together, this case provides a rare example of symptomatic skeletal muscle metastasis from esophageal adenocarcinoma. The presence of SRCs and HER2/neu amplification in this lesion illustrate the poor prognosis and biologic aggressiveness associated with both of these features. Lastly, a literature review for similar cases suggests differential patterns of spread to skeletal and cardiac muscle based on esophageal tumor histology, a possible example of the ‘seed and soil’ hypothesis applied in a clinical setting.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: 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.

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