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Subcutaneous metastases from early stage esophageal adenocarcinoma case report

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ABSTRACT

The identification of subcutaneous metastatic lesions from primary visceral malignancies has increased over time, probably due to an increase in the awareness of their presentation and an increase in cancer survival times. Although the rate of subcutaneous metastases from breast,lung and colon cancer is more significant, the incidence of subcutaneous metastases from esophageal carcinomas is very low. These metastatic lesions usually present metachronously and may signify advanced disease and poor prognosis. We report three cases with early stage esophageal adenocarcinoma treated with surgery with curative intent presenting with subcutaneous metastases two months, two years and three years after their esophagectomy.

1. Introduction

Cutaneous metastases from visceral malignancies have been reported in 5–10% of cases [1–3]. Breast, lung and colon cancers are the tumors most likely to spread to the dermis and commonly present after the 6th decade of life [2]. In a large cohort of 838 patients with esophageal cancer, a rate of distant metastasis of approximately 20% was reported [4]. However, these metastatic lesions were most commonly seen in abdominal lymph nodes (45%), liver (35%) and lung (20%), with a significantly lower rate of 1% for metastatic lesions involving the skin [4].

Subcutaneous metastatic lesions have been reported to arise from both esophageal adenocarcinomas and squamous cell cancers. However, their presentation is very rare and their incidence may depend on the prevalence of the primary carcinoma, with esophageal adenocarcinoma being more common in white males, and squamous cell cancer more common in white women, blacks, and Asians [5].

The location of subcutaneous metastasis from esophageal carcinoma is variable. The scalp, neck and face have been reported as common locations [2,6,7], although metastatic lesions to the chest wall, back and axillary regions have been reported as well [6,8–10]. These lesions are indeed rare.

Associated factors predicting the risk for subcutaneous metastasis are not yet well known. However, poorly differentiated adenocarcinomas and the evidence of signet ring cell features may increase the risk of cutaneous spreading [11]. The identification of these pathological patterns after surgical resection may help in establishing the metastatic risk and may aid in the follow-up planning for this group of patients.

The overall prognosis and survival rates for esophageal adenocarcinoma is poor at 15% [5,12], although early stage tumors (T2N0M0 stage or less) have adequate cure rates of around 50% after surgical resection [13,14]. Patients with subcutaneous metastatic disease have a significantly poorer prognosis with reported survival rates of less than one year after the identification of metastatic lesions, and treatment is usually aimed to palliation through possible resection with chemotherapy and radiotherapy [7,15–17].

We describe three cases with early stage esophageal adenocarcinoma presenting with subcutaneous metastases between two months and three years after esophagectomy with curative intent.

2. Presentation of cases

2.1. Patient 1

A 61 year old man with a history of reflux esophagitis was evaluated for progressive dysphagia and 10% weight loss in three months. Endoscopy revealed long segment Barrett's esophagus and a fungating mass at the GE junction (Siewert II) nearly obstructing the lumen. Biopsies showed poorly differentiated adenocarcinoma with signet ring cell features (Fig. 1A). PET-CT showed a 4.6 cm hypermetabolic mass with standard uptake value (SUV) of 11.8 without evidence of lymph node or distant metastasis. He

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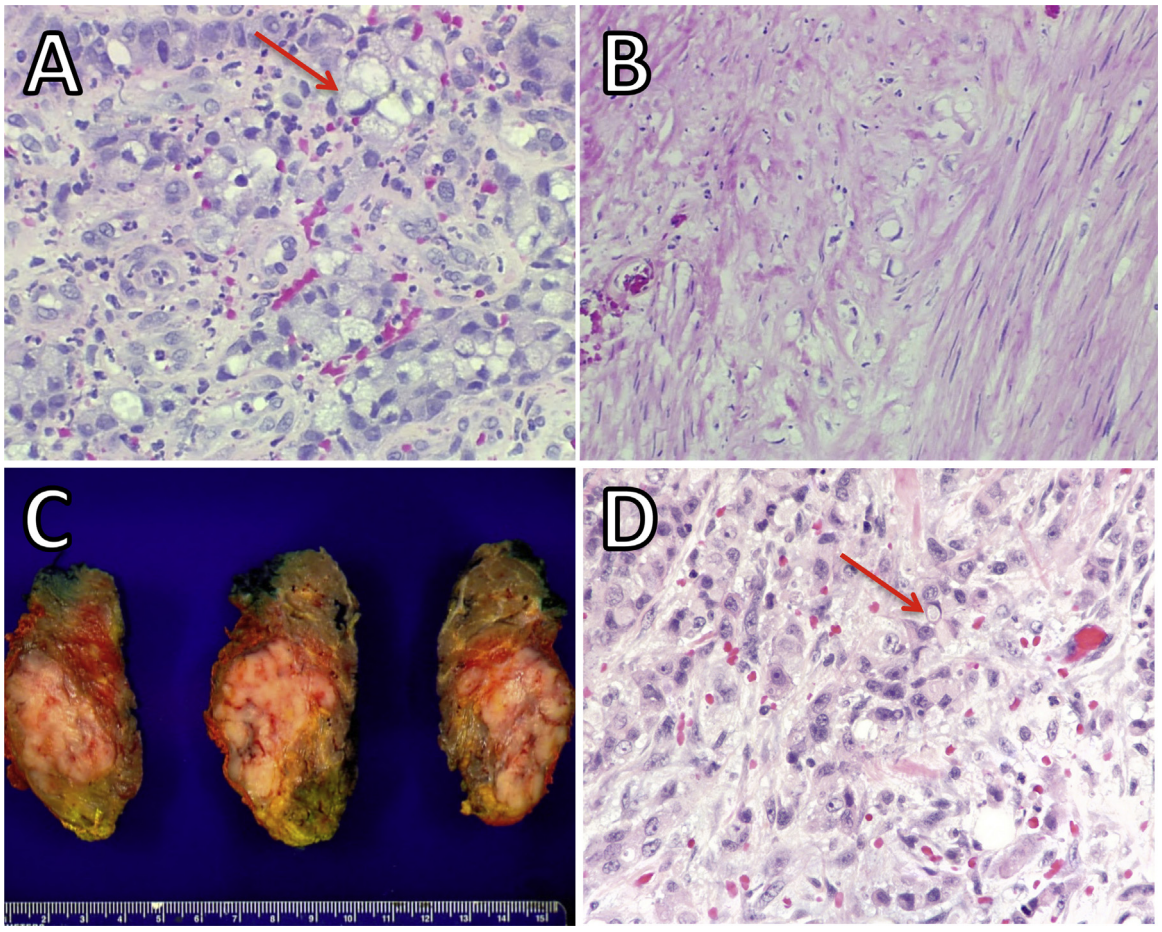

Fig 1. Biopsy showed an infiltrating poorly differentiated adenocarcinoma with signet ring cell features (arrow) (A). After chemoradiation therapy, the surgical resection specimen showed an 8.5 cm tumor bed involved by residual infiltrating poorly differentiated adenocarcinoma invading into the muscularis propria (B) with no regional lymph nodes involvement. Chest wall metastasis (C) and excisional biopsy demonstrated a metastatic poorly differentiated adenocarcinoma with signet ring cell features (arrow) (D) morphologically consistent with the esophageal tumor.

received neoadjuvant chemoradiation therapy with carboplatinum and taxotere and 50 Gy of external beam radiation in 25 fractions. Post-treatment PET-CT showed a 58% decrease in the SUV value and no evidence of distant disease. An open McKeown esophagectomy was performed. The final pathologic stage was T2N0M0 with no involvement of the 19 lymph nodes examined and no evidence of lymphovascular invasion (Fig. 1B). Two months later he presented with shortness of breath and a palpable 7 cm mass cephalad to a left chest tube scar (Fig. 1C). CT scan revealed the chest wall mass, a moderate sized left pleural effusion with no tumor cells on cytology, and pulmonary and hepatic metastases. The chest wall lesion was metastatic poorly differentiated adenocarcinoma morphologically similar to the patient's known esophageal cancer, also with signet cell features (Fig. 1D). The patient died one month later.

2.2. Patient 2

A 69-year-old man with a long history of Barrett's esophagus was diagnosed with a distal esophageal (Siewert I) moderately to poorly differentiated adenocarcinoma. Endoscopic ultrasound showed a non-circumferential, non-obstructing mass with two malignant-appearing lymph nodes, which was staged as T2N1MX by endosonographic criteria. PET-CT showed a mild hypermetabolic area in the distal esophagus with SUV of 3.8 and no evidence of hypermetabolic lymph nodes or distant metastasis. This patient did not undergo neoadjuvant therapy prior to surgical resection with a minimally invasive Ivor Lewis esophagectomy. The final pathologic stage was T1bN0M0 with 23 lymph nodes negative for metastasis and an absence of lympho-vascular involvement (Fig. 2A). Two years later he presented with a tender subcutaneous mass measuring 2 × 2 x 1 cm on his right temple. Biopsy evidenced metastatic moderate to poorly differentiated adenocarcinoma with similar morphology to the original tumor and positive stains for carcinoembryonic antigen (CEA) and mucin, as well as cytokeratin 7 (CK7), confirming an upper gastrointestinal source (Fig. 2B–D). PET-CT showed diffuse metastatic disease in the bones and lungs. He received palliative chemotherapy and died two months later.

2.3. Patient 3

A 61-year-old man presented with progressive dysphagia and weight loss of 25 pounds in three months. Endoscopy revealed a non-circumferential mass 35 cm from the incisors. Biopsy demonstrated poorly differentiated adenocarcinoma with focal signet ring cell features (Fig. 3A). Endoscopic ultrasound was done showing a partially obstructing mass with clinical stage T3N0MX. PET-CT showed hypermetabolic activity at the gastroesophageal junction (Siewert II) with SUV of 9.6 and no evidence of metastatic disease. Induction chemoradiotherapy was done followed by an open McKeown esophagectomy. He had a complete pathologic response with 14 negative lymph nodes and no lymphovascular invasion in the pathology report. Approximately three years later the patient presented with a small nodule on his scalp, which was excised and identified as a poorly differentiated metastatic adenocarci-

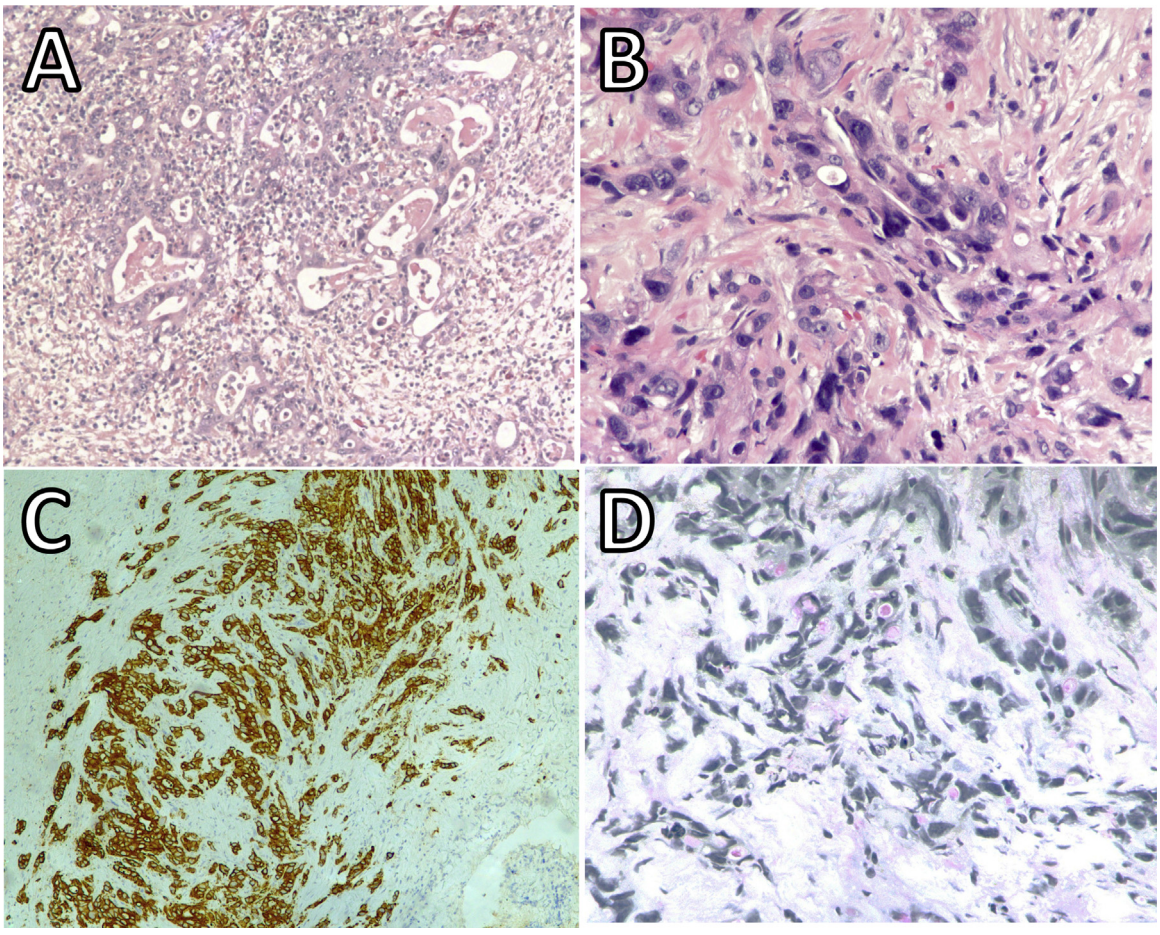

Fig. 2. Esophagectomy specimen showed a moderately differentiated adenocarcinoma (A). Punch biopsy of a subcutaneous metastasis found in the right temple revealed a moderate to poorly differentiated adenocarcinoma (B). Immunohistochemical profile showed tumor cells positive for cytokeratin 7 (C), carcinoembryonic antigen and mucicarmine (D), but negative for cytokeratin 20, thyroid transcription factor 1 and cluster of differentiation 31, consistent with a metastasis from the patient's known esophageal adenocarcinoma.

noma with mucin containing cells. It stained positive for Villin and CK7, indicating an upper GI source (Fig. 3B–D). The patient started chemotherapy at another institution and was lost to follow-up.

3. Discussion

The incidence of subcutaneous metastases from underlying tumors has increased over time [2]. However, the development of cutaneous metastases from esophageal cancer is still very rare. We present three patients who had early stage disease pathologically confirmed after surgery, who nonetheless showed cutaneous metastases at variable time points after esophagectomy.

Although these patients had no lymphovascular invasion within the primary tumor, no pathological evidence of disease in any of the lymph nodes resected, and received treatment with curative intent with good pathologic response, cutaneous metastases were evident between as short as two months and as long as three years after treatment. All three patients had adenocarcinoma, two of them had primary tumors with signet ring cell features, indicating more aggressive behavior [11], and all three cases demonstrated moderate to poorly differentiated primary tumors, which also indicates a more aggressive disease.

Two of our cases showed metastases to the scalp and face, in keeping with the trend mentioned previously [2,6]. One case however, presented with metastases to the chest wall separate from an incision. This demonstrates that subcutaneous metastases may develop within a variable interval of time, to variable locations, and can occur in patients with early stage disease and no evidence of lymphovascular spread at the time of resection. These unusual recurrences complicate the search for ideal biomarkers that would help stratify outcomes for esophageal adenocarcinoma.

It has been found that any form of treatment can significantly improve survival time in patients with oligometastases in the form of fewer than three metastases, although this may be biased by patient selection [18].

4. Conclusion

Although cutaneous metastases from esophageal adenocarcinoma are rare and unusual, they cannot be dismissed, even in patients with low-grade tumors that have been resected with curative intent and shown complete pathological response. Prompt identification and diagnosis is especially crucial given the poor prognosis of patients who are found to have subcutaneous metastases. Once these metastases are identified, treatment to improve survival time can be offered and palliative measures can be started. Patients should be followed to monitor for any metastases, including cutaneous metastases with special consideration for the scalp and face. Additionally, any cutaneous lesions found either by the patient or on follow-up should be investigated immediately for possible metastatic features, regardless of length of interval since primary tumor resection. It is also important to study any biomarkers involved in such lesions so that we may one day be better able to

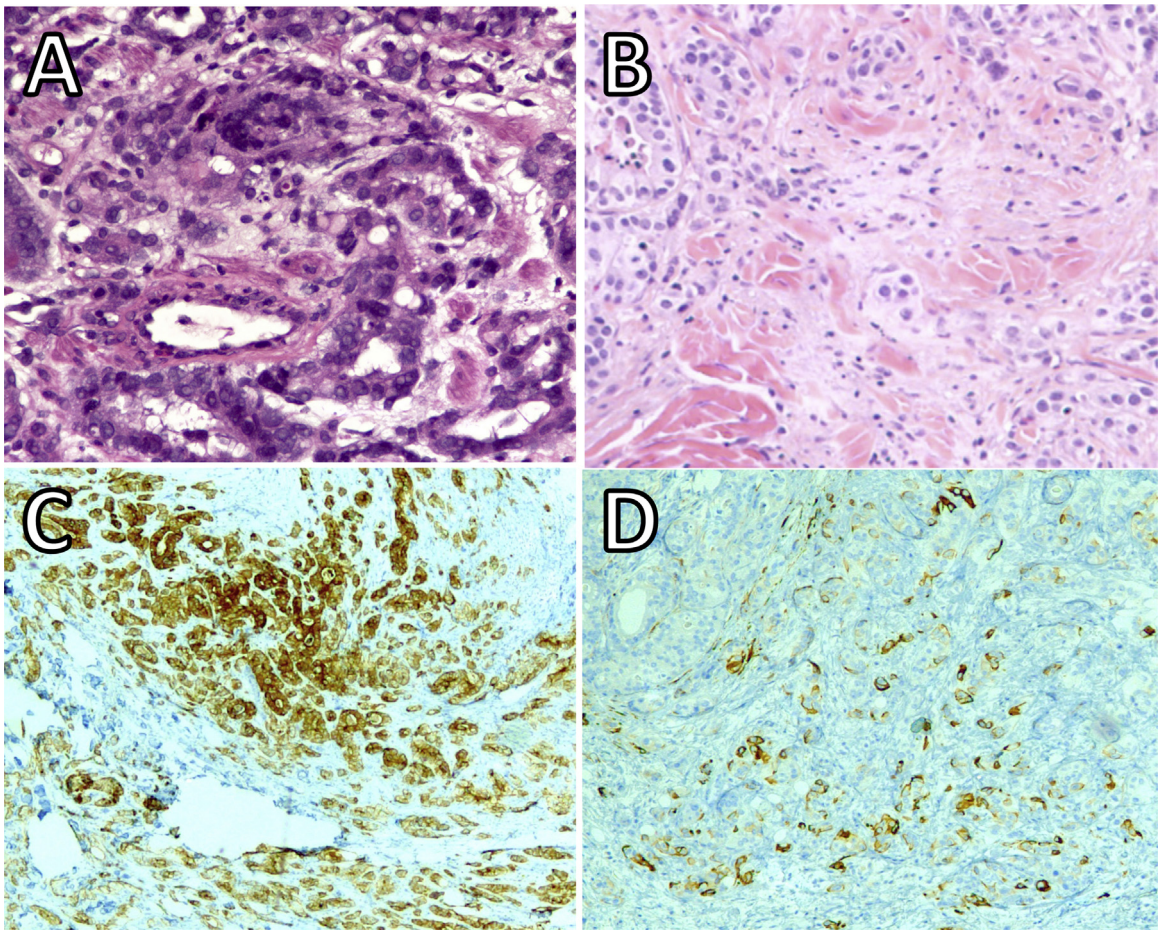

Fig. 3. Biopsy of a gastroesophageal junction mass was confirmed to be a poorly differentiated adenocarcinoma, signet-ring type (A). Biopsy of a scalp mass three years later revealed a moderately to poorly differentiated adenocarcinoma (B) with tumor cells positive for villin (C) and cytokeratin 7 (D), but negative for cytokeratin 20, thyroid transcription factor 1, prostate specific antigen and thyroglobulin, consistent with an esophageal adenocarcinoma metastasis.

stratify patients for risk of metastases after resection of the primary esophageal tumor.

This case report has been written in line with the SCARE criteria [19].

Conflicts of interest

No conflicts of interest.

Ethical approval

No ethical approval required.

Consent

Consent was obtained for every patient and identifying labels were omitted.

Author contribution

Sujata Datta – data collection, data interpretation, writing the paper.

Juan A. Munoz-Largacha – study design, data collection, data interpretation, writing the paper.

Lei Li – data interpretation.

Grace Zhao – data interpretation.

Virginia R. Litle – study concept and design, data collection, writing the paper.

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Dr. Virginia R. Litle.

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