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METASTATIC LIP CANCER OF UNKNOWN PRIMARY

Jonathan Dunn, MD, Jerry Hsieh, MD

Background

As housestaff, we seldom have the chance to admit a patient with cancer of unknown primary. Even if a patient presents with metastatic cancer, it is frequently evident what the primary cancer is based on epidemiology and imaging. However, in this case we have the unique opportunity of describing a metastatic cancer that presented as a lip carcinoma with several possible primary sources. Our goal is to guide the reader through the thought process involved with determining the primary malignancy in patients presenting with metastatic disease.

Case Presentation

A 54-year-old female with a 30-pack-year smoking history presented to the emergency department with pain and swelling of the right lower lip. The symptoms started one month ago with mild to moderate pain, and progressed within one week to significant swelling. She had developed a lip abscess two weeks prior that was incised and drained, but now presented with worsening drainage, swelling, and pain. She also had fevers and a non-productive cough for one month.

Investigation

On admission to the hospital, the patient was afebrile and had normal vital signs. Her right lower lip was noted to be indurated, with no fluctuance. There was no area of warmth or erythema surrounding the area of induration. Admission labs were within normal limits. Initial chest x-ray revealed consolidation within the right middle lobe and right lower lobe, as well as a moderate right pleural effusion. Maxillofacial CT with contrast revealed an organized rim-enhancing fluid collection within the soft tissues overlying the right mandible with overlying skin ulceration and surrounding inflammatory changes in the adjacent subcutaneous tissues.

Hospital Course

The initial differential diagnosis of the patient's lip lesion included abscess, cellulitis, and malignancy. On admission, she was empirically treated for cellulitis and community acquired pneumonia. On hospital day 2 she was taken for a lip biopsy, which revealed ulcerated lesions with clusters of markedly atypical cells, most consistent with an ulcerated squamous cell carcinoma (SQCC). Immunohistochemistry stains showed that the tumor cells were positive for cytokeratin CK7 and negative for CK20, TTF1/Napsin, CK5/6 and mucicarmine. These were not consistent with a cutaneous SQCC as will be discussed



Figure 1. CXR: Apparent widening of the superior mediastinum. Mild atelectasis in the left midlung is noted.

later on. These results necessitated a metastatic workup to determine the primary source. A CT of the chest was obtained which showed a large right hilar mass, a new spiculated 7mm nodule in the inferior left lower lobe, and new mediastinal and hilar adenopathy. It also showed a large hypodense lesion with irregular margins within the right hepatic lobe. Based on these findings, a fine needle aspiration of the lung was obtained. The immunohistochemistry of the lesion matched that of the lip. These findings favored a diagnosis of primary lung cancer with metastasis to the lip, but could also represent either unknown primary or synchronous malignancies. Primary squamous cell carcinoma of the lip was deemed unlikely since these cancers are most often CK7 negative. Based on these findings, the decision was made by the primary oncologist to go forward with treatment of primary lung cancer, and platinum based chemotherapy was initiated.

Discussion

In the initial approach to a cancer of unknown primary, an evaluation of immunohistochemical markers can help narrow the list of possible cancers. The first step is often to stain for cytokeratins, specifically CK7 and CK20. The patient tested positive for CK7, and negative for CK20, which could indicate any of the following cancers: non-small cell lung, small cell lung, breast, endometrial, nonmucinous ovarian, mesothelioma, and squamous cervical carcinoma.¹ In general, CK7+/CK20-strongly favors lung carcinoma.² After a metastatic workup with imaging that yielded a lung and liver nodule, it was thought that the lip lesion was most metastatic from the lung.

Further analysis of the lesion involved lung cancer specific markers. Napsin and TTF1 are markers for lung adenocarcinoma (ADC) and both used in conjunction have 74% sensitivity and 87% specificity for ADC.³ These were both negative indicating a low likelihood of lung ADC. Additionally, p63 and CK5/6 markers were analyzed, which are used for distinguishing SQCC from ADC of the lung. ADC does not express either marker, whereas SQCC has approximately 75% chance of positive expressivity. Virtually all ADC and SQCC will not express CK20.⁴

Metastatic carcinomas tend to be poorly differentiated, as is the case with this patient. Unfortunately, the immunohistochemistry of this particular carcinoma does not strongly favor ADC or SQCC; however, the histology more closely resembles poorly differentiated SQCC. At this time, the diagnosis favors a lung SQCC metastatic to the skin of the face.

Key Points

A thorough pathological examination is important in the diagnosis and treatment of tumors of unknown primary. Important components of this examination include cytokeratin markers CK7 and CK20, as well as other markers such as TTF1, Napsin, CD5/6 and mucicarmine. Further analysis depends largely on the clinical picture. For our patient, a closer look at her long smoking history along with the information gathered from cytopathology favored a diagnosis of lung cancer, and appropriate treatment was given.

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