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Case Report

EMBOLIC STROKE AS THE INITIAL PRESENTATION OF AN INTRACARDIAC METASTATIC ADENOCARCINOMA OF THE LUNG

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ABSTRACT

Introduction: Metastatic cardiac tumors are relatively uncommon; we present a case of a patient with an embolic stroke secondary to a metastatic left ventricular mass from an undiagnosed adenocarcinoma of the lung.

Case report: 69 year old female presented with acute onset right hemiparesis and slurring of speech. Head computed tomography angiogram reported multiple areas of infarction with no evidence of intracranial hemorrhage. On day 2 of admission she developed new neurologic deficits with brain magnetic resonance imaging showing multiple new small ischemic infarcts of the left basal ganglia and left anterior temporal lobe. An embolic source was suspected. Echocardiogram revealed a ~1x1x2cm pedunculated mass originating from the left ventricle. Furthermore, chest CT revealed occlusion of the left mainstem bronchus with complete opacification of the left hemithorax by a left-sided pleural effusion. Bronchoscopy was performed recording no visible endobronchial lesions. Cytology from pleural effusion showed malignant cells positive for Cytokeratin 7, TTF-1 and Moc-31 consistent with primary adenocarcinoma of the lung with left ventricle metastasis.

Conclusion: Metastatic disease to the heart is a rare finding. Remarkably, these metastases are clinically silent, especially when obscured by the symptoms of the disseminated tumor disease.

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INTRODUCTION

Lung cancer remains the most common cause of cancer death in both men and women (Siegel *et al.*, 2013). Most patients present for diagnostic evaluation because of symptoms suspicious for lung or an incidental finding on chest imaging. Common sites of metastasis includes; contralateral lung, adrenal glands, bone, brain and liver. Rarely, lung cancer can metastasize to more distant organs like: heart, gastrointestinal tract and kidneys. Generally these are distinctive features of end-stage disease. Based on autopsy studies, the heart is an extremely rare site for metastasis with only less than 2% of all cases (Siegel *et al.*, 2013 and Al-Mamgani *et al.*, 2008). Embolic stroke secondary to metastasis from the left ventricle as the initial presentation of adenocarcinoma of the lung represents an extremely rare initial manifestation of this disease and demonstrates the importance of immunohistochemistry in distinguishing carcinomas of different origins when we encounter patient as complex as ours.

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Case Report

A 69-year-old Hispanic female with no significant past medical history presented with dyspnea on exertion for 3 weeks and acute onset right hemiparesis, left facial droop and slurring of speech. Patient was taken to the emergency department and initial head computed tomography (CT) revealed possible pontine and temporal ischemic infarcts with no intracranial hemorrhage. Due to the involvement of multiple brain lobes, tissue plasminogen activator (tPA) was withheld. Patient rapidly deteriorated developing respiratory failure and shock requiring endotracheal intubation and vasopressors. Follow up head CT scan reported multiple areas of lucency involving the posterior aspect of the right corona radiata and the external capsule, reflecting sites of acute infarction (Figure 1). At the time of presentation, family reported the patient had been experiencing shortness of breath for 3 weeks, which was initially present only while exercising but progressively worsened to dyspnea with minimal exertion but denied any hemoptysis, chest pain, fevers or any neurological symptoms. On social history, family denied any tobacco, alcohol or illicit drug use. Physical examination was notable for marked conjunctival pallor, tachycardia with no

murmurs or gallops, decreased breath sounds and dullness to percussion up to the level of the upper lobe in the left hemithorax and coarse breath sounds in right hemithorax.



Figure 1. Head CT scan, small to moderate sized focal lucency along the left ganglion capsular region and left corona radiata, compatible with an acute infarct

Neurologic examination revealed: left facial weakness and right hemiparesis with muscle strength 2/5. Blood gas on admission showed hypoxia (PH: 7.47, PO₂: 65mmHg, PCO₂: 25.2mmHG). Chest x-ray showed completed opacification of the left lung by a large pleural effusion and no acute infiltrates in the right lung. On day two of admission, the patient developed new neurologic deficits including left sided hemiparesis and worsening mental status despite minimal sedation.

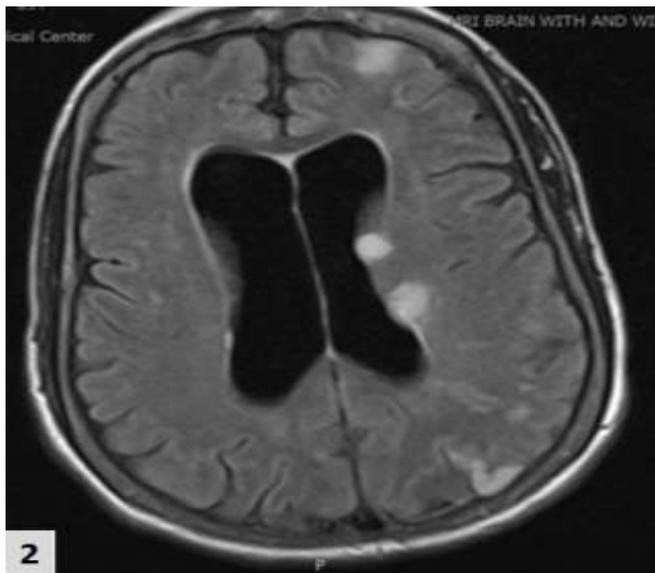


Figure 2. Brain MRI, multiple bilateral variable-sized increased signal intensity including the left anterior-inferior temporal lobe, anterior left frontal lobe, basal ganglia. Associated signal intensity consistent with multiple bilateral acute infarctions

Follow up brain MRI showed, multiple bilateral variable-sized increased signal intensity including the left anterior-inferior temporal lobe, anterior left frontal lobe, basal ganglia. There was also variable involvement at the left posterior frontal lobe, left inferior parietal lobe and the occipital lobe. Associated signal intensity was consistent with multiple bilateral acute brain infarctions (Figure 2). An embolic source was suspected. Transthoracic echocardiogram showed a ~1x1x2cm pedunculated mass originating from the left ventricle anteroapex (Figure 3). Furthermore, chest CT revealed occlusion of left mainstem bronchus, complete opacification of the left hemithorax by a low density pleural effusion (Figure 4). A chest tube was placed, draining 2 liters of exudative serous fluid. Intravenous heparin was started to prevent further embolic events. Bronchoscopy was performed revealing no visible endobronchial lesions, initial cytology from bronchoalveolar lavage was negative for malignancy; however, cytology from the pleural effusion showed malignant cells positive for Cytokeratin 7, TTF-1, Moc-31 and no EGFR overexpression consistent with primary adenocarcinoma of the lung.

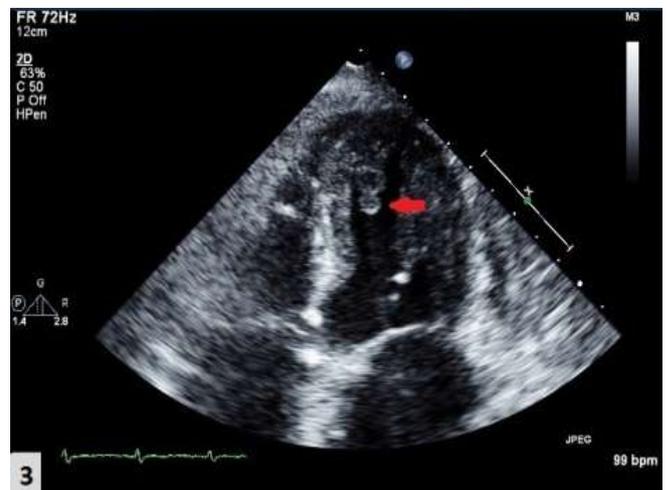


Figure 3. Transthoracic echocardiogram reveals a ~1x1x2cm pedunculated mass originating from the left ventricle anteroapex

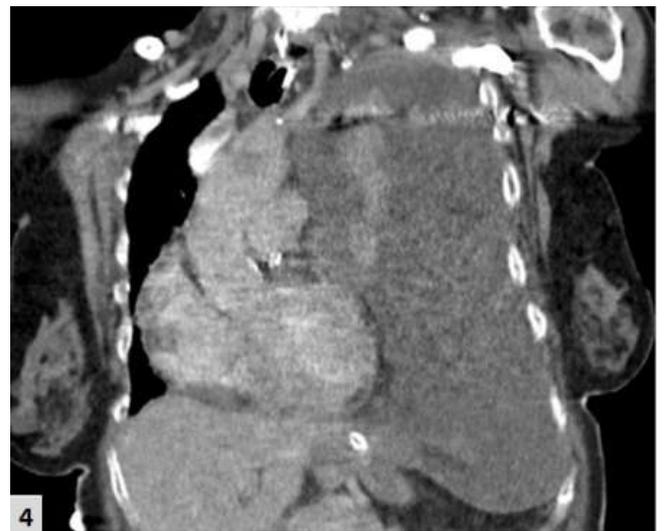


Figure 4. Chest CT scan shows occlusion of left mainstem bronchus, complete opacification of the left hemithorax by a low density pleural effusion

Whole body positron emission tomography (PET) scan confirmed metastatic disease with hypermetabolism in the left lung lower lobe, perihilar and subcarinal lymph nodes and left adrenal gland (Figure 5). Given the high risk for other embolic events, the patient was placed on chronic anticoagulation with warfarin. After discharge the patient followed up with oncology. Fluorescence in situ hybridization (FISH) results revealed adenocarcinoma of the lung being ALK and EGFR negative. Due to her advanced disease, patient was offered several palliative chemotherapy regimens. She refused chemotherapy and continued symptomatic treatment. Six months after initial diagnosis, the patient started experiencing new onset tonic-clonic seizures and multiple falls. Brain MRI this time revealed new 10 supratentorial and 2 infratentorial metastatic lesions with associated vasogenic edema (Figure K). The patient was started on steroids to reduce intracranial edema and levetiracetam for seizure prophylaxis. Whole brain radiation was recommended but her family opted for a more conservative approach. The patient was discharged to home hospice and expired 14 days after the second admission.

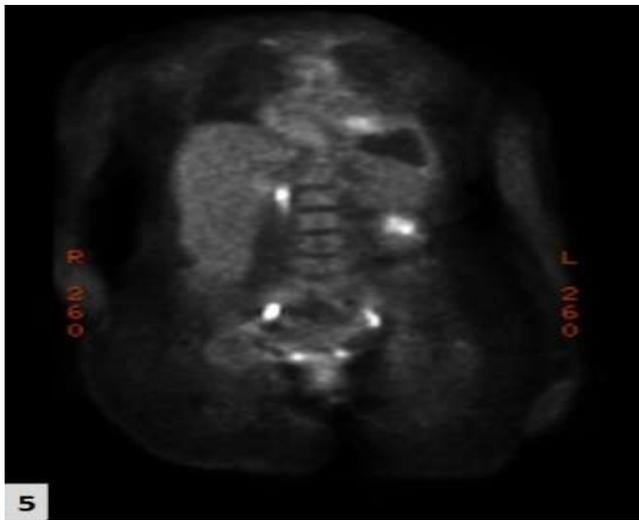


Figure 5. PET scan demonstrates hypermetabolism in the left lung lower lobe and left adrenal gland

DISCUSSION

Adenocarcinoma is the most common type of lung cancer in contemporary series, accounting for approximately one-half of lung cancer cases (Mukai *et al.*, 1988). The majority of patients who present with clinical signs or symptoms due to lung cancer have advanced disease. The most common presenting manifestations include dyspnea, cough, hemoptysis and chest pain (Mukai *et al.*, 1988). Less common manifestations are signs and symptoms or laboratory abnormalities of distant metastases or paraneoplastic syndromes. In our case, the initial presentation was right sided hemiparesis secondary to an embolic phenomenon from intracardiac metastasis. Only a handful of cases with similar presentation have been reported in the English literature and most of them involve carcinoid tumors. The most common neurologic manifestations seen in adenocarcinoma of the lung are secondary to brain metastasis including seizures, visual loss and confusion such as in our patient 6 months after initial diagnosis.

The incidence of cardiac metastases from any malignancy is highly variable, ranging from 2.3% and 18.3% (more frequently in melanoma and mediastinal primary tumors) (Goldberg *et al.*, 2013). The cardiac metastases can be found in any structures of the heart (pericardium, epicardium, myocardium, endocardium or vessels). The spread of malignant cells into the heart can be through direct extension, the bloodstream or the lymphatic system and by intracavitary diffusion from the venous system (Goldberg *et al.*, 2013). In our case, the left ventricle was the site of metastasis and this can be explained as the result of hematogenous route or direct extension from the intrathoracic cancer. Pathologically, heart metastases are usually small, firm, and nodular, microscopically resembling the primary lesion (Goldberg *et al.*, 2013). Pedunculated tumor masses like the one observed in our patient can cause considerable interference with blood flow through the heart, changing the hemodynamics inside the chambers and increasing the risk for thrombus formation.

The presence of neoplastic emboli is a distinguishing feature of this case; tumor embolization via lymphatic or venous system is generally seen after chemotherapy, radiation or surgical treatment by promoting the fragmentation of the tumor mass (Goldberg *et al.*, 2013) but in our case was the direct result of embolization from an intracardiac mass. Once the echocardiogram revealed a pedunculated mass of unknown origin, further investigation to determine the site of the primary malignancy was pursued. Here immunohistochemistry played an important role in determining the final diagnosis. Cytology from the pleural effusion showed large atypical cells positive for Cytokeratin 7, TTF-1, Moc-31, with no EGFR overexpression and negative for Cytokeratin 20, calretinin, wt-1, CDX2, chormogranin, and GATA3. All these findings were consistent with primary adenocarcinoma of the lung. When studying cell of lung origin it is important to differentiate between the various subtypes. Adenocarcinoma cells are typically positive for CK-7 and TTF-1, and negative for p63 and CK5/6. On the other hand, squamous cells are characterized by keratinisation and/or formation of intercellular bridges with positive staining for P63 and CK5/6 and concurrent lack of staining for TTF-1 (Tan and Zander, 2008). Due to the metastatic presentation of the disease, small cell carcinoma (SCLC) of the lung was included in the differential as well.

Neoplastic cells from SCLC are small "blue" malignant cells about twice the size of lymphocytes, with positive staining for chromogranin and synaptophysin. Other several newer antibodies, including p63 and high molecular weight keratin, also help differentiate SCLC from non-small cell lung cancer (Tan and Zander, 2008). Another differential that was considered was a primary and secondary cardiac tumor. Primary cardiac tumors are very rare with 75% of them being benign, and the majority of which are myxomas, these are described as pedunculated and gelatinous in consistency. About 80% of myxomas arise in the left atrium and most of the remainder are found in the right atrium. Primary malignant tumors of the heart are even more rare tumors; most of these are sarcomas. Generally sarcomas are rapidly progressive tumors and they can cause death through infiltration of the myocardium, by obstructing circulation, or by distant metastases (Pinede *et al.*, 2001 and Molina *et al.*, 1990).

Secondary cardiac tumors, in contrast to primary malignant cardiac tumors, metastatic involvement of the heart is relatively common. For example, in one autopsy series of over 1900 cancer patients, 8% had metastatic disease involving the heart (Silvestri *et al.*, 1997). Cardiac or pericardial metastasis should be considered whenever a patient with known malignancy develops any cardiovascular symptoms or systemic embolic events. However, cardiac metastases are rarely the first manifestation of malignant disease as seen in our case. Besides lung cancer, other solid tumors are commonly associated with cardiac involvement including melanoma, breast cancer, soft tissue sarcomas, renal carcinoma, esophageal cancer, hepatocellular carcinoma, and thyroid cancer (Silvestri *et al.*, 1997). There is also a high prevalence of secondary cardiac involvement with leukemia and lymphoma. The various ways in which lung cancer can present keep changing the way we perceive this neoplasm. In our case, the initial presentation was mostly composed of neurologic deficits secondary to the stroke and the lack of risk factors placed the possibility of lung cancer in the lower end of our differential, but the unusual and extensive emboli disease to the brain triggered the search for a possible cause that could explain all of our patient's findings, including the pleural effusion and the intracardiac mass. The results of the pleural effusion cytology provided us with the answer that would tie together all the clinical manifestations of our patient, an undiagnosed adenocarcinoma of the lung with intracardiac metastasis. Our case serves as an important reminder that lung cancer can present in very diverse ways and that sometimes there is more history behind an ischemic stroke.

Conflict of interest: To the best of our knowledge, no conflict of interest, financial or other, exists for any of the authors involved in the creation of this manuscript.

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