Case Report

Diabetes Insipidus: An Unusual Presentation of Adenocarcinoma of the Lung in a Patient with no Identifiable Lung Mass

Shuchi Gulati, Christoper Kiefer[1], Nagla Abdel Karim

Division of Hematology/Oncology, [1]Division of Pathology and Lab Medicine, University of Cincinnati, Cincinnati, Ohio, United States

Abstract

Context: Lung cancers are known to metastasize to unusual sites. Despite this knowledge often times the diagnosis of a primary lung cancer gets delayed especially when the patient presents without respiratory symptoms. **Case Report:** The patient discussed in our review is a 47-year-old female, smoker who had presented to several hospitals with months of headache, nausea and intermittent episodes of vomiting. She was noted to have hypernatremia due to diabetes insipidus and a pituitary lesion on her magnetic resonance images. The pituitary mass on biopsy was found to represent a metastatic focus from a primary lung adenocarcinoma. **Conclusion:** Clinicians should be aware of malignancies that are well known to metastasize to the posterior pituitary. Conversely, since not every patient presents with symptoms of metastasis, there is a need to recognize the clinical syndromes (e. g., diabetes insipidus-like symptoms or more subtle symptoms like cranial nerve palsies) associated with potential metastasis to the pituitary.

Keywords: Adenocarcinoma, adults, diabetes insipidus, humans, pituitary neoplasms

Address for correspondence: Dr. Shuchi Gulati, Department of Internal Medicine, University of Cincinnati, 231 Albert Sabin Way, ML 0535, Cincinnati, Ohio-45220, United States. E-mail: Shuchi.Gulati@uc.edu

Introduction

Throughout the world, especially in developing countries, the incidence of lung cancer is on the rise. In the United States, lung cancer is the most common cause of cancer-related deaths.[1] The last decade has seen an increased availability of techniques to aid screening, early diagnosis and targeted treatment of all forms of lung cancer,[2] despite which the incidence continues to rise. Early diagnosis is important to enable improvement in the overall survival of these patients. Patients usually present with advanced stage disease, generally with respiratory symptoms. However other systemic manifestations as well as signs and symptoms related to metastatic spread and paraneoplastic syndromes should be kept in mind. Through this case presentation and review of the literature, we aim to discuss one such scenario, where a patient presented with central diabetes insipidus (DI) related to pituitary metastasis, even though there was no identifiable primary lung lesion at the time of presentation. Metastatic lesions account for about 1% of all sellar and parasellar pituitary tumors[3,4] and have to be borne in mind when evaluating patients.

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Case Presentation

A 47-year-old female with a 20-pack year smoking history presented to an outside hospital after she overdosed on acetaminophen for relief of her headache. She had been presenting to various hospitals with complaints of headache, nausea and intermittent episodes of vomiting for 18 months. She had previously been evaluated at our institution a year before for headache and had a computed tomography scan done, which was reported negative for any intracranial lesions. Her review of systems was positive for polyuria and polydipsia, which had started about 2 weeks prior to presentation. Her initial laboratory studies at the outside hospital revealed serum sodium of 157 Meq/L (Nl: 135-146 Meq/L) in addition to abnormal liver function studies; the latter attributed to acetaminophen overdose. She was treated with high dose desmopressin (DDAVP) for presumed DI and transferred to our facility, which is a tertiary level referral hospital. A magnetic resonance imaging (MRI) study of her brain done at the outside hospital had revealed a lesion, 2.5 × 1.5 cm in size, in-homogeneously enhancing in the sellar with some extension into the suprasellar cistern and erosion of the posterior wall of the sphenoid sinus. The optic chiasm was not noted to be compressed. No other brain lesions were noted on this scan.

On admission to our institute, she continued to have headache, polyuria and polydipsia. Her serum sodium on presentation was 166 Meq/L. Her CBC revealed anemia, with hemoglobin of 9.5 g (Nl: 11.7-15.5 g), normocytic and normochromic in nature. Based on her hormonal assay, namely low TSH of 0.3 mIU/L (Nl 0.45-4.5 mIU/L), low FSH of 0.5 mIU/L, LH <0.1 mIU/L, normal prolactin and cortisol levels, she was thought to have a non-functioning pituitary mass. She was presumed to have a diagnosis of central DI and was given a dose of DDAVP again. An MRI of her brain was repeated in our institution with contrast this time, which revealed a large, invasive suprasellar mass with heterogeneous enhancement and extension into the adjacent sphenoid sinus. The mass was associated with mild suprasellar extension and compression of the optic chiasm [Figure 1a]. Another ring-enhancing centrally cystic lesion was identified in the right superficial frontal lobe with mild surrounding edema [Figure 1b]. Although the sellar mass could represent an invasive pituitary macroadenoma with preferential inferior growth, given the relatively rapid growth of the sellar lesion and the concomitant presence of additional frontal lobe lesion, the possibility of a metastatic disease needed to be considered at this time.

She underwent a trans-sphenoidal pituitary biopsy subsequently and had to be transferred to the intensive care unit after the biopsy due to acute hypoxic respiratory failure.

The pathological examination of the mass in pituitary revealed the typical features of an adenocarcinoma: Solid nests and glands formed by tumor cells that have abundant cytoplasm containing intracellular mucin and pleomorphic nuclei [Figure 2a]. Immunophenotyping of the cells provided additional information regarding the origin of the adenocarcinoma. The cells were positive for thyroid transcription factor-1 (TTF-1) [Figure 2b], which is a sensitive and specific marker of lung adenocarcinoma. The tumor cells demonstrated a cytokeratin profile typical of lung adenocarcinoma (CK-7 and CAM 5.2-positive, CK-20-negative) and

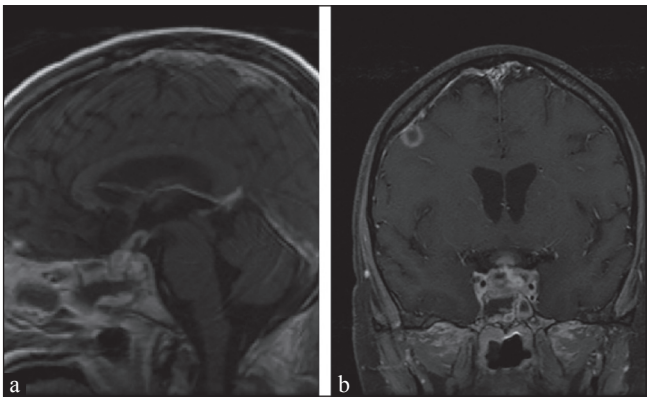

Figure 1: (a) Sagittal view of the brain demonstrating an invasive suprasellar mass with heterogeneous enhancement and extension into the adjacent sphenoid sinus, (b) Ring-enhancing centrally cystic/necrotic lesion in the right superficia l fronta l lobe with mild surrounding edema

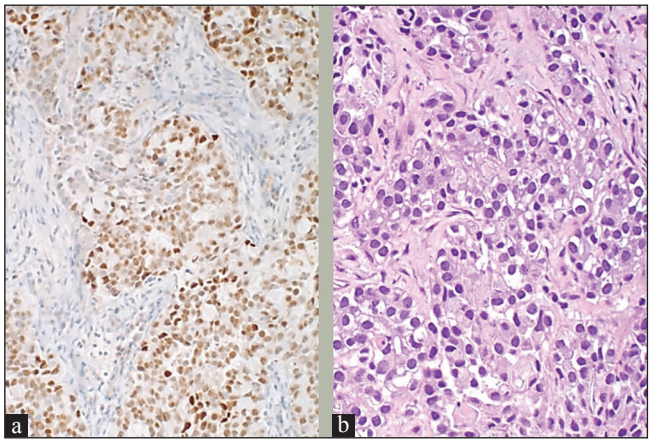

Figure 2: (a) Trans-sphenoidal resection of pituitary mass. Solid nests of cells with abundant clear cytoplasm and focal formation of gland-like structures with eosinophilic cytoplasm (H and E, magnification × 60), (b) Trans-sphenoidal resection of pituitary mass. Immunohistochemistry stain highlights the expression and nuclear localization of TTF-1 in the neoplastic cells, which supports the diagnosis of metastatic lung adenocarcinoma (TTF-1 IHC, magnification × 20)

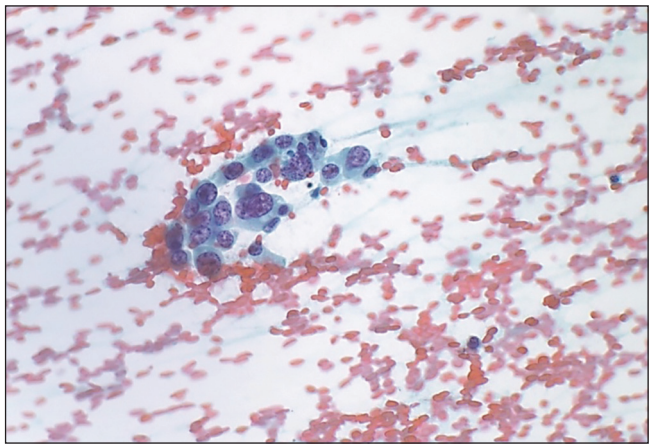

Figure 3: Aspirate of hilar lymph node. Cytological examination of the hilar lymph nodes reveals malignant cells with eccentric nuclei and prominent nucleoli on Papanicolaou stain

were negative for the neuroendocrine markers (CD-56, chromogranin, and synaptophysin). An identical immunophenotype can be found in thyroid carcinomas, which have a distinctly different histologic appearance, and some primary adenocarcinomas of the head and neck, including sinonasal carcinoma, which can express TTF-1 in rare cases.

To evaluate further for a primary lesion, a CT scan of the chest was obtained which revealed multiple pulmonary emboli, mediastinal lymphadenopathy, and patchy ground-glass opacity within the lateral aspect of the right lower lobe with no distinctly visible mass.

Endobronchoscopy with ultrasound-guided fine needle aspiration of the right hilar lymph nodes yielded malignant cells that had the cytological appearance of lung adenocarcinoma [Figure 3]. A biopsy performed concomitantly revealed tumor cells that resembled those in the pituitary mass. With this evidence of a primary lung adenocarcinoma, the pathologist concluded that the pituitary mass most likely represented metastasis from a lung malignancy and not local spread of a sinonasal adenocarcinoma.

Thereafter the patient had a rapid decline in her performance status. She refused further treatment and was transferred to hospice care.

Discussion

Pulmonary adenocarcinoma, a subtype of the non-small cell type is the most common type of lung cancer in the United States and also accounts for the most frequent type in non-smokers.[5]

While lung cancers rarely metastasize to unusual locations, they do so most commonly to the liver, adrenal glands, bones, and the brain parenchyma.[6] According to a recent Swedish study, small cell lung cancer most commonly metastasizes to liver and central nervous system while adenocarcinoma metastasizes to bone and respiratory system.[6] Rare cases of adenocarcinoma of the lung like ours do metastasize to the pituitary gland.

In addition to metastatic lesions, the differential diagnosis for tumors in the sellar and suprasellar region of the pituitary gland include pituitary adenomas, craniopharyngiomas, optic or hypothalamic gliomas, germ cell tumors, lipomas, and choristomas.[7] Metastatic lesions account for about 1% of all sellar and parasellar pituitary tumors.[3,4] Lung cancer is the second most common type of malignancy to metastasize to the pituitary gland (breast cancer being the leader).[8] According to a recent meta-analysis, breast and lung cancer account for 37.2% and 24.2% of the pituitary metastatic lesions, respectively.[8] Despite this knowledge, when patients with primary lung cancers present without respiratory symptoms their diagnosis is often delayed due to a delay in making the connection between pituitary symptoms and lung cancer, similar to our patient.

When a patient presents with a pituitary mass, benign lesions like adenomas are difficult to distinguish from metastatic pituitary lesions based on imaging studies.[4,9] There are certain clinical characteristics that help discern whether a pituitary lesion is benign vs. whether the lesion needs a more thorough work up to rule out metastasis from a distant primary. Studies, including a recent meta-analysis indicate that DI is the most common clinical manifestation in patients who have pituitary metastasis.[8] Reports have indicated that DI may be used to distinguish between an adenoma and a metastatic lesion,[10] in that it is more commonly associated with the latter. This is because metastases target the posterior lobe of the pituitary gland and the infundibulum in preference to the anterior lobe,[4] likely due to a preference of the metastases to follow the pattern of pituitary blood flow in the neurohypophoseal blood vessels.[9] Therefore, if a patient with DI is found to have a pituitary mass, the suspicion for a primary lesion elsewhere should increase and aggressive search to look for a primary malignancy should ensue. Sometimes DI associated with pituitary metastasis may be transient or intermittent.[4] Several case series have demonstrated how patients have presented with symptoms related to pituitary dysfunction, and have ultimately been diagnosed with other primary malignancies.[11] However, a study also indicates that only about 50% patients who present with a sellar mass have a *known* primary malignancy.[9] Thus in a female patient search for primary breast cancer and in a male patient search for primary lung cancer should ensue since these are the most common cancers metastasizing to the pituitary gland.

Other clinical characteristics that raise the suspicion for a pituitary lesion to represent a metastatic lesion rather than a benign adenoma include headaches, visual field deficits due to cranial nerve palsies (especially abducens nerve palsy), presence of skull-bone destruction, demonstration of rapid growth on serial scans, and presence of coexisting focal lesions (metastasis).[9,12,13] Hormonal assay to be most commonly affected is high prolactin levels, which is however the case in both metastatic lesions and macroadenomas; hence does not help distinguish the two.[13]

Conclusion

Involvement of sellar structures is an unusual presentation of metastatic lesions. Our patient had an unusual situation where there was no discernible primary lesion in the lungs, and yet the biopsy histopathology was suggestive of lung-based adenocarcinoma. Clinicians should be aware of malignancies that are well known to metastasize to the posterior pituitary and consider breast and lung as potential sources. Conversely, since not every patient presents with symptoms of metastasis there is a need to recognize the clinical syndromes (e. g., DI like symptoms or more subtle symptoms like cranial nerve palsies) associated with potential metastasis to the pituitary. Work up should then include dedicated imaging of the involved region and potential primary malignancies. Early recognition will result in timely institution of therapy for such patients and improved quality of life.

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Conflicts of interest

There are no conflicts of interest.

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