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Case Report

Metastasis of lung adenocarcinoma to the pituitary gland ☆

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ABSTRACT

Pituitary metastasis (PM) is rare occurrence and accounts for <1% of all intracranial metastatic lesions. In this study, we highlight the importance of considering atypical sites for lung adenocarcinoma metastasis by presenting a case of a 54-year-old male who was diagnosed with PM 15 months after being diagnosed with stage IV lung adenocarcinoma with metastasis to the spine, pelvis, left frontal lobe, and right occipital lobe. He was on a prolonged course of chemotherapy during those 15 months and received palliative radiation for his brain metastasis with subsequent remission after 5 months following his initial diagnosis. The pituitary lesion was picked up as an incidental finding on a routine staging magnetic resonance imaging (MRI) 10 months after his brain metastasis remission. The patient successfully underwent trans-sphenoidal pituitary lesion resection. This case emphasizes the importance of routine surveillance and examination of atypical sites of metastasis even in patients undergoing a prolonged course of chemotherapy.

Introduction

Lung adenocarcinoma is one of the leading causes of cancer-related deaths in North America [1]. It is the most common subtype of cancer diagnosed in nonsmokers and represents about 40% of all lung cancers [1]. The most common sites of metastatic spread of lung adenocarcinoma are nervous system (47%), bone (39%), and other parts of the respiratory system (22%) [2]. The most common areas for lung adenocarcinoma metastasis in the brain were the left frontal lobe (53%), cerebellum lobe (56%), and the right frontal lobe (48%) [3]. Metastasis to the pituitary gland is an extremely rare finding accounting for <1% of intracranial metastatic lesions [4]. Patients with metastasis to the pituitary are typically asymptomatic and die prior to diagnosis, but can rarely present with symptoms such as visual disturbance, fatigue, diabetes insipidus, and headaches [4,5]. Symptoms are reported in <20% of the cases [4].

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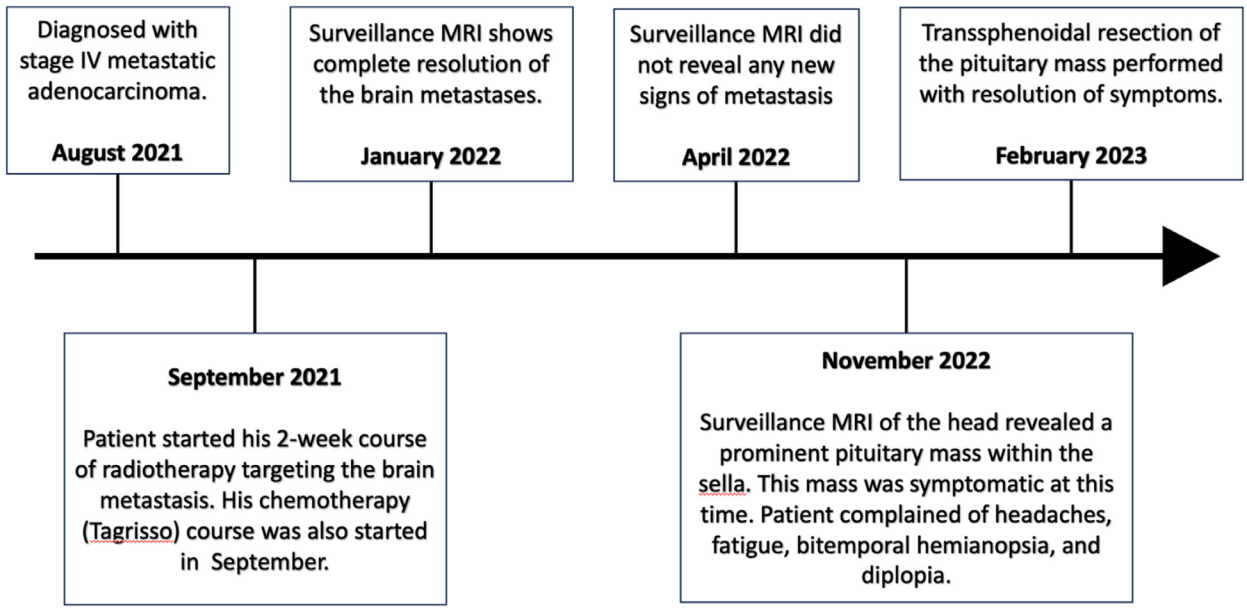

Fig. 1 – The timeline of events in the patient's care starting from his initial diagnosis in August 2021.

Case report

The patient is a 54-year-old male with a known diagnosis of metastatic non–small-cell lung cancer. The timeline of the events following his diagnosis is provided in Fig. 1.

The course of events leading up to the diagnosis of pituitary metastasis

At the time of the patient's diagnosis of stage IV lung cancer in August of 2021, a nuclear medicine full body scan with single-photon emission computed tomography was conducted which revealed metastatic disease involving the thoracic vertebrae and the right acetabulum superiorly. Furthermore, an MRI of the head with contrast showed 2 circumscribed enhancing gray-white matter junction masses posterior left frontal lobe and right occipital lobe measuring 7 mm and consistent with metastasis. It was planned for the patient to undergo hypofractionated stereotactic radiotherapy (HSRT) to the brain and receive urgent inpatient chemotherapy (carboplatin-pemetrexed). Targeted chemotherapy with Tagrisso was started a week later after molecular testing revealed he had an epidermal growth factor receptor (EGFR) exon 19 deletion.

MRI of the head was repeated in January and April of 2022, which revealed that the previous metastatic sites treated with radiation had completely resolved with no new metastases or suspicious enhancements. The patient denied any headaches, nausea, or visual deficits. It was determined there was no need for radiotherapy, but he continued to be followed by medical oncology.

However, restaging of his chest and abdomen in January and April of 2022 showed progression of the metastatic disease but the patient denied major symptomatic changes such as worsening back pain or disease progression. Therefore, no significant changes were made to his treatment plan and he continued with his chemotherapy regimen.

Pituitary metastasis discovered on routine surveillance

On a routine surveillance MRI conducted on November 2022, there was a suprasellar mass visualized with the involvement of the entire length of the pituitary stalk (Fig. 2). The lesion was enhancing and measured 1.5 × 2.7 × 1.9 cm in the anterior-posterior (AP), transverse (TV), and craniocaudal (CC) dimensions, respectively. This is in contrast to a normal pituitary which does not exceed 10 mm in the craniocaudal dimension. Furthermore, instead of a normal concave superior margin of the pituitary, Fig. 2B shows a convex superior margin (shown by the tips of the white arrows). There was a suspected invasion into the sella turcica surrounding the pituitary gland which appears of reduced enhancement. There was no extension through the sellar floor or into the sphenoid sinus, however, there was a mild obliteration of the suprasellar cistern and mild indentation of the inferior aspect of the optic chiasm. The lesion was inseparable laterally from the medial aspects of the cavernous sinuses and cavernous portions of the internal carotid arteries without frank invasion or encasement. The lesion was also inseparable from the anterior aspect of the infundibular and optic recesses of the third ventricle.

The patient was clinically assessed 8 days after the pituitary mass was visualized on the MRI. He complained of headaches, fatigue, bitemporal hemianopsia, and diplopia. His lab investigations revealed undetectable levels of ACTH (<0.7 pmol/L), cortisol (37 nmol/L), low LH and FSH (<0.30 IU/L and <1.0 IU/L, respectively), low testosterone (<0.4 nmol/L), low TSH (0.13 mIU/L), and low free T3 (18 pmol/L) and T4 (3.8 pmol/L). The patient also became hyponatremic with sodium levels at 123 mmol/L. His prolactin level was 14 ug/L thus ruling out the possibility of prolactinoma. He was started on

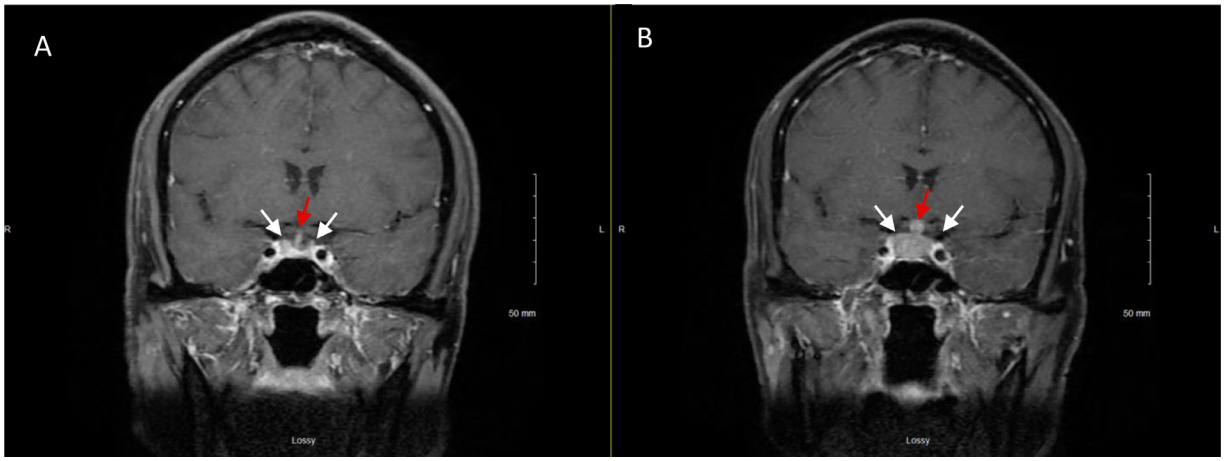

Fig. 2 – Normal staging MRI of the head conducted in April 2022 (A) compared to the staging MRI in November 2022 in which a pituitary lesion (white arrow) was first detected (B). The craniocaudal dimension of the pituitary measured 1.9 cm (B) compared to the normal pituitary (A). The superior margin of the pituitary appeared convex (B) compared to the normal MRI showing the concave superior margin (A). The transverse diameter of the infundibulum at the level of the optic chiasm measured 5.87 mm (B) compared to 2.05 mm in the normal MRI (A) (shown by the red arrows).

levothyroxine and exogenous cortisol. At this time, it was unclear whether this was a pituitary adenoma or metastasis from the lung adenocarcinoma. The patient was seen in the neurosurgery office and the option of trans-sphenoidal resection of the pituitary adenoma was discussed with the patient.

Trans-sphenoidal resection of the pituitary mass

In February 2023, the patient successfully underwent trans-sphenoidal resection of the pituitary mass without any complications. The pathology report from the resected tissue revealed poorly differentiated metastasis adenocarcinoma to the pituitary most consistent with lung origin. The MRI of the pituitary conducted 2 days after the operation showed a residual tumor measuring 1.7 × 2.9 × 1.3 cm (AP × TV × CC), however, the patient's visual deficits resolved (Fig. 3). It was planned for the patient to undergo further palliative radiation therapy for the residual tumor with 2000 centigray (cGy) in 5 fractions to shrink the tumor and prevent damage to the nerves. Currently, the patient is awaiting his first radiation treatment and is being followed by the endocrinology, ophthalmology, and cancer clinic. Following the radiation therapy, he has been scheduled for follow-ups for routine surveillance by medical oncology, radiation oncology, endocrinology, and neurosurgery with the goal of providing symptomatic relief. He has also been referred for an assessment by the palliative care team if the need for home palliation arises given his poor prognosis.

Discussion

The metastasis to the pituitary is a unique phenomenon accounting for less than 0.4% of all intracranial metastatic lesions [4,6]. In comparison, the incidence of pituitary adenoma, which is the most common pituitary tumor in adults, is 14.4% and 22.5% in postmortem and radiographic studies, respectively [7]. The incidence of Rathke's cleft cyst, which is the most common sellar lesion, ranges between 13% and 33% [8]. The first case of pituitary metastasis was reported by L. Benjamin in 1857 where he identified melanoma spread to the pituitary during an autopsy [9]. Most cases of PM are asymptomatic and discovered during an autopsy or during end-stage malignant course [4]. The most common primary cancer responsible for PM is lung cancer accounting for 36.8% of the cases followed by breast cancer accounting for 22.9% of the cases [4,10,11]. Both, the anterior and the posterior lobes of the pituitary can be affected, however, involvement of the posterior lobe is more common and likely due to the direct contact with the adjacent dura and inferior hypophyseal arteries which branch from the internal carotid artery [11,12].

The differential diagnosis of intrasellar tumor includes meningioma, craniopharyngioma, aneurysm, hypophyseal adenoma, and Rathke's cleft cyst [13]. Primary carcinomas known to metastasize to the pituitary are from the kidney, prostate, and colon with an incidence of 3%-5% [6]. Other rare causes of metastasis include thyroid, pancreas, melanoma, hematological, and from unknown primary cancers [6]. Although most patients are asymptomatic when initially diagnosed, rare symptoms of PM include headache, visual disturbances, hypopituitarism, diabetes insipidus, nausea, vomiting, dizziness, fatigue, and weight loss [4,5,14]. In our case, the patient complained of headache, fatigue, diplopia, and bitemporal hemianopsia. Diabetes insipidus is a common symptom seen in patients with PM which may be used to distinguish PM from more common pathologies such as Rathke's cleft cyst or adenoma [15]. In adenomas, diabetes insipidus is reported in 1% of the cases and is typically a late finding [11]. Symptoms of hypopituitarism, headaches, or visual disturbances are less helpful in differentiating between PM and adenoma [11]. Elevated prolactin levels are indicative

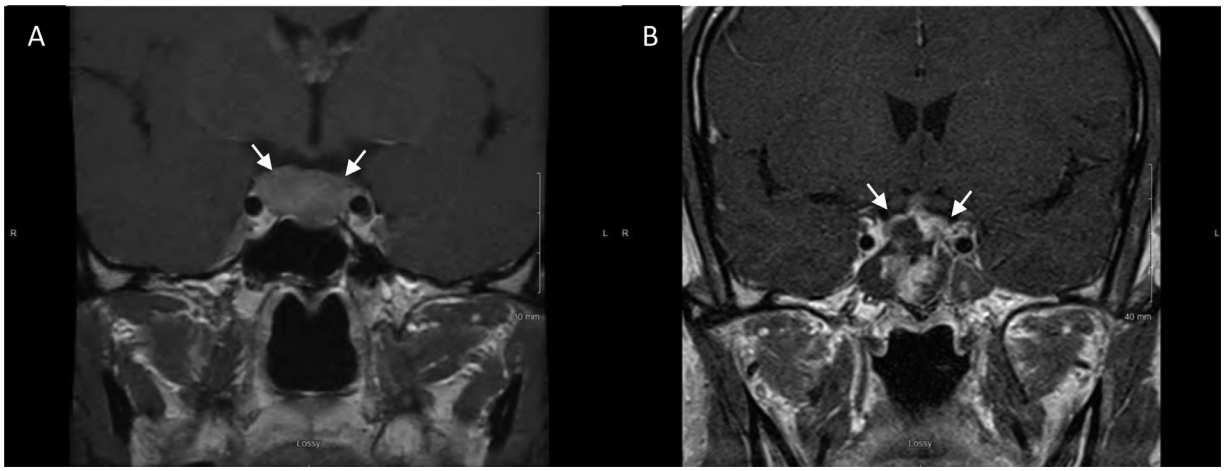

Fig. 3 – A dedicated MRI of the pituitary/sella (white arrows) was done to better characterize the pituitary mass pre-resection (A). (B) shows the MRI of the residual tumor post-resection.

of prolactinoma [11]. Moreover, infiltration of the tumor into the cavernous sinus can result in a unique constellation of neural deficits such as chemosis, proptosis, and ophthalmoplegia making the diagnosis of PM more likely over relatively common pathologies such as adenoma [15]. Metastasis from renal cell carcinoma more commonly involves the anterior pituitary (90%) (compared to diabetes insipidus (24%)) and visual field deficits are more common (82%) [15]. Characteristic radiological findings to distinguish meningiomas from other pituitary lesions include focal thickening of bone (hyperostosis), best seen on CT and linear enhancement along the dura (dural tail sign) [16]. A Rathke's cleft cyst is seen as a well-defined nonenhancing midline cyst within the sella arising between the anterior and intermediate lobes of the pituitary [17]. A rapidly growing sellar tumor, sudden onset of diabetes insipidus, ophthalmoplegia, and headaches in a patient over 50-year old, should strongly indicate PM [11].

While most cases of PM are diagnosed incidentally prior to receiving radiotherapy and chemotherapy, our case is unique because the patient had an intracranial metastasis to the pituitary after undergoing an initial course of radiotherapy for brain metastasis with complete remission. Moreover, the patient was already on chemotherapy when he was diagnosed with a pituitary mass. To the best of our knowledge, this is the first case showing lung adenocarcinoma metastasis in a patient with a prolonged course of chemotherapy and previous radiotherapy with complete intracranial metastatic remission. Our study highlights the importance of monitoring atypical sites of metastasis such as the pituitary gland in patients with lung adenocarcinoma with routine surveillance.

It can be difficult to differentiate pituitary adenoma from PM based purely on imaging [4]. The most sensitive imaging modalities for the radiological evaluation of pituitary masses are high-resolution CT and MRI [11]. A CT may show hyperdense or isodense mass, homogenously or inhomogeneously enhancing (if cystic degeneration, hemorrhage, or necrosis exists) [11]. MRI may show an isointense or hypointense mass on T1WI, with a usually high-signal intensity of the posterior lobe on T1WI [11]. Other findings include sellar bone erosion, nonhomogenous appearance, dumbbell-shaped pituitary gland due to the indentation of the diaphragm sellae, loss of posterior lobe bright spot, and rapidly growing lesion [4,11]. In this case, the MRI of the head showed a pituitary gland exceeding 10 mm in the craniocaudal dimension. Additionally, the superior margin of the pituitary appeared convex instead of the normal concave appearance. There was an invasion into the sella turcica.

The treatment of PM includes trans-sphenoidal surgical resection. Alternative treatment options include stereotactic sellar radiosurgery, a noninvasive and safe procedure preferred for patients with diffusely metastatic disease and short life expectancy [18]. Patients may also benefit from palliative radiation therapy postsurgery to prevent the recurrence of symptoms or treat the residual tumor [4]. Patients may also be referred to an endocrinologist for further monitoring and hormonal replacement. The patient in this study is currently planned to undergo radiation therapy with routine surveillance from the oncology, endocrinology, and neurosurgery teams.

The prognosis of patients with lung metastasis to the pituitary is poor with a median survival time ranging between 6 and 22 months (median of 12.9 months) [6,10]. Moreover, patients who are younger than 60 years of age, with primary sites other than lung or breast, and those who undergo surgical resection of the pituitary lesion have a prolonged survival [19]. Surgical resection and radiation can alleviate symptoms in about 50% of the patients [19]. Smaller volume of the lesions and a shorter interval between disease diagnosis and pituitary metastasis presentation is associated with longer survival [10].

In conclusion, this study highlights the importance of not overlooking atypical sites of lung adenocarcinoma metastasis such as the pituitary even in patients who have shown complete remission of brain metastasis and are on a prolonged chemotherapy regimen. Although patients with metastasis to the brain will ultimately have poor outcomes, there is still

a chance that palliative interventions can help prevent the worsening of symptoms (eg, vision loss, headaches, and fatigue) and improve their quality of life.

Patient consent

We confirm that informed consent was obtained from the patient for the publication of his case.

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