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Case Report

Osimertinib-induced rapid regression of large metastatic tumor to the pituitary in a patient with lung adenocarcinoma

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ABSTRACT

Background: Metastatic nonsmall cell lung cancer (NSCLC) to the pituitary (NSCLC-PitM) is rare and often presents with visual field deficits. Surgical resection for the decompression of the optic apparatus has been the treatment of choice in such cases. Osimertinib is a third-generation tyrosine kinase inhibitor (TKI) approved for the treatment of patients with NSCLC with an epithelial growth factor receptor (EGFR) mutation though its role in the treatment of NSCLC-PitM that remains unclear. We present a case of NSCLC-PitM with optic chiasm compression and visual deficits that were successfully treated with osimertinib alone without surgical intervention.

Case Description: A 43-year-old male presented with pleuritic chest pain, fatigue, and visual deficits found to have NSCLC and a sellar mass with suprasellar extension and optic chiasm compression. Visual field testing demonstrated associated visual field deficits. Molecular testing was positive for EGFR exon 19 deletion. The patient was started on osimertinib with complete resolution of pituitary lesion and visual deficits at 4 weeks.

Conclusion: Osimertinib is a third-generation EGFR-TKI that has demonstrated promising results among patients with metastatic EGFR-mutated NSCLC. While surgery is the mainstay of treatment in patients with a sellar mass, optic compression, and visual deficits, those with EGFR-mutated NSCLC-PitM may benefit from early initiation of such systemic therapies, rather than surgical intervention, with good ophthalmologic results.

Keywords: Nonsmall cell lung cancer, Osimertinib, Pituitary metastasis, Visual outcomes

INTRODUCTION

Metastatic pituitary tumors are a rare entity comprising only 1–2% of all metastatic lesions. They often signal late stage disease with a median survival time after diagnosis of 10–13 months.[5] Recent advances in the development of immunotherapies targeting specific oncogenic molecular markers have led to improved progression free survival. Osimertinib is a relatively new third-generation tyrosine kinase inhibitor (TKI) that is approved for treatment of nonsmall cell lung cancer (NSCLC) harboring a gain of function mutation in the gene coding for the epithelial growth factor receptor (EGFR).[7,11] Metastatic NSCLC to the pituitary (NSCLC-PitM) presents unique clinical challenges as treatment paradigms are not well defined and the choice of initial

treatment modality may require balancing the symptoms of local mass effect with treating the systemic disease. Surgical intervention has been prioritized when clinical evidence of mass effect on critical structures such as the optic nerves and chiasm are present for fear of worsening or irreversible damage.[5] As such, little is known regarding the response of NSCLC-PitM to systemic therapy as first-line treatment. We present a case of a patient with metastatic NSCLC who presented with acute visual symptoms and was found to have a large sellar mass with significant compression of the optic chiasm. He was immediately treated with osimertinib which resulted in complete regression of the pituitary tumor burden in 4 weeks and resolution of visual symptoms.

CASE DESCRIPTION

A 43-year-old male nonsmoker presented with pleuritic chest pain, fatigue, decreased vision, and urinary frequency. Chest computed tomography revealed a right upper lobe lung mass. Positron emission tomography scan revealed additional hypermetabolic foci within the spine and ribs. Percutaneous needle biopsy of the pulmonary lesion was consistent nonsmall cell lung adenocarcinoma. Molecular testing demonstrated EGFR exon 19 deletion. Magnetic resonance imaging (MRI) of the brain revealed a sellar mass with suprasellar extension and compression of the optic chiasm [Figure 1a and b]. Ophthalmologic evaluation demonstrated associated visual field deficits [Figure 2a and b]. Pituitary function testing was significant for adrenal insufficiency. The patient was subsequently started on hydrocortisone.

Multidisciplinary discussion between neurosurgery, oncology, and ophthalmology considered the differential diagnosis of pituitary macroadenoma versus metastatic disease to the pituitary. The patient was initiated on osimertinib therapy with the standard dose of 80 mg oral dose daily with a plan for close monitoring of symptomatic worsening and re-imaging at 4–6 weeks to evaluate for response and surgical resection of the lesion if necessary.

Visual field examination 1 week after osimertinib initiation was grossly stable with possible slight worsening. Repeat MRI 4 weeks after osimertinib initiation demonstrated complete resolution of the pituitary lesion. Repeat visual field testing found improvement in the previous deficit [Figure 2c and d].

DISCUSSION

With the emergence of targeted genetic therapies we have seen an improvement in our ability to treat NSCLC. One particular class of immunotherapy that has shown success in improving survival is the EGFR-TKIs. In individuals with NSCLC containing mutations in the gene coding for EGFR, EGFR-TKIs are able to block the cellular signal cascade from initiating by binding to the adenosine triphosphate (ATP) binding site of the receptor. First and second-generation EGFR-TKIs target mutations on exons 19 and 21 (Del19 and L858R), but rapidly induce resistance as a result of further

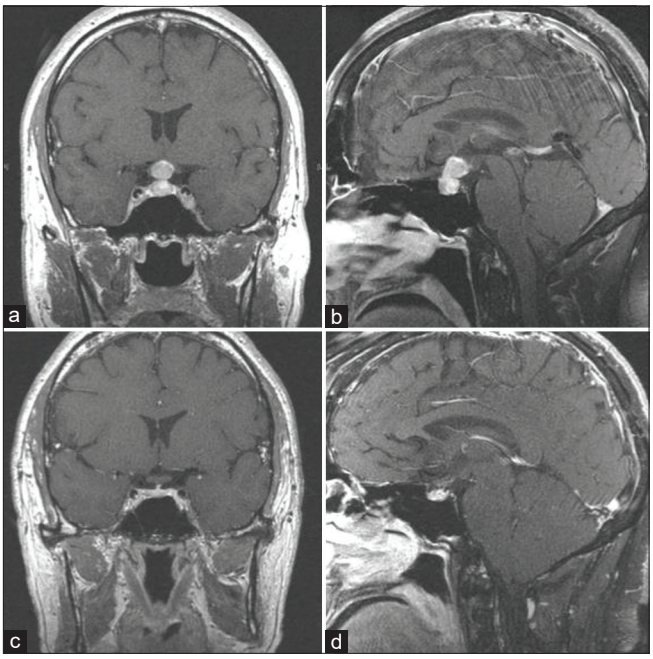

Figure 1: (a) Pretreatment coronal and (b) sagittal-contrasted magnetic resonance imaging (MRI) demonstrating sellar and suprasellar enhancing lesion with compression of the optic chiasm. (c) Posttreatment coronal and (d) sagittal contrasted MRI demonstrating complete resolution of pituitary lesion.

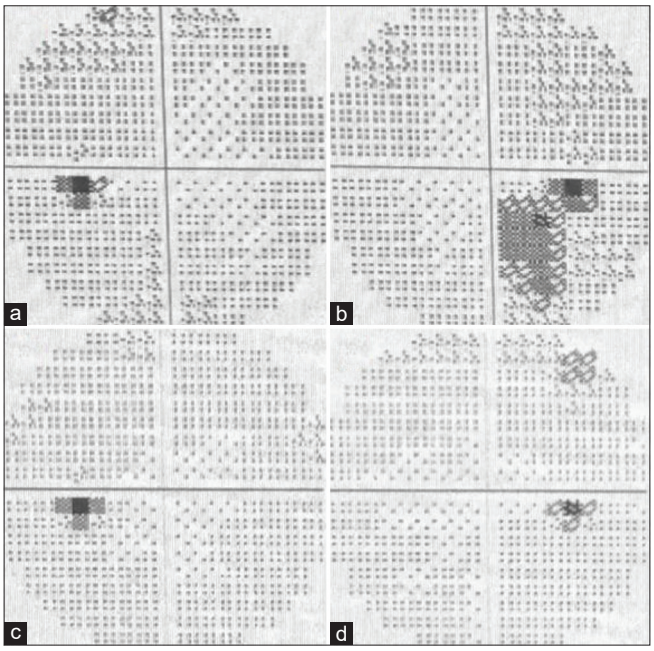

Figure 2: (a) Initial left and (b) right visual fields demonstrating visual field deficit. (c) Left and (d) right visual fields 4 weeks after initiation of osimertinib demonstrating significant improvement.

mutation on the ATP binding site. Resistance typically occurs in 8–12 months, 50% of which are due to mutations on exon 20 (T790M).[2] Osimertinib is a third-generation EGFR-TKI that was approved in 2017 to treat individuals with EGFR T790M-mutated NSCLC showing improved survival as a second-line treatment in those who have developed resistance to earlier generation EGFR-TKIs when compared to standard second-line platinum-based therapy. It has also been used effectively as a first-line treatment compared with earlier generation EGFR-TKIs. Importantly, this benefit extended to those with central nervous system (CNS) involvement as well.[7,11]

CNS involvement in metastatic disease is not uncommon, occurring in 20–40% of patients with systemic malignancies.[9] By contrast, metastatic disease to the pituitary gland is uncommon occurring in only 1–2% of these patients. Lung cancer is a leading site of primary malignancy for pituitary metastasis. Diagnosis of NSCLC-PitM represents a late stage in this disease with a median time of survival after diagnosis of 10–13 months, and 26% survival at 2 years.[5] Despite advances in our ability to treat the systemic disease burden in individuals with NSCLC, the local effects of NSCLC-PitM can make its treatment challenging. The most common manifestations of pituitary metastasis are often neurologic and endocrinological in nature due to mass effect on local structures with 49% presenting with visual symptoms, 38% with panhypopituitarism, and 38% with diabetes insipidus.[5,10] Surgical decompression has been favored over initiation of systemic therapy over fears of irreversible deficits caused by continued mass effect and potential pseudoprogression.[1,5,8] As a result, little is known about the response of NSCLC-PitM's to EGFR-TKIs. Whether NSCLC-PitM that presents with optic nerve or chiasm compression and visual symptoms can be effectively treated with EGFR-TKIs that remain to be determined. Fan *et al*. reported a case of Del19 NSCLC-PitM that presented with a visual field deficit and panhypopituitarism that completely resolved 5 weeks after initiation of osimertinib.[4] In that case, while surgical intervention was not pursued, osimertinib was only initiated when the lung and sellar lesions demonstrated progression 8 months after the patient received three cycles of carboplatin and pemetrexed. Furthermore, visual outcomes were not reported though endocrine defects were noted to persist despite resolution of the mass. Megyesi *et al*. similarly reported a case of T790M-mutated NSCLC-PitM that fully responded to osimertinib, though they did not report the time period to resolution or if there were any pre- or post-operative visual symptoms.[6]

Our report is the first to demonstrate the feasibility of treating NSCLC-PitM presenting with signs and symptoms of optic compression with osimertinib. In this case, by initiating EGFR-TKI therapy, we were able to address his systemic disease and potentially the pituitary lesion. Should the pituitary lesion be an adenoma, early initiation of therapy and reduction of systemic tumor burden potentially minimizes perioperative morbidity for subsequent resection. On the other hand, if it is a NSCLC-PitM, in which it ultimately proved to be, it may be treated concomitantly, obviating the need for surgical intervention. Of note, we did observe possible slight worsening of the patient's vision after initiation of osimertinib that may be further evidence of pseudoprogression that Okauchi *et al*. had noted.[8] Overall, the robust response of CNS disease to osimertinib, as seen in prior studies, is in line with preclinical animal studies that demonstrate good blood brain barrier (BBB) penetrance of the drug.[3] Furthermore, given the lack of BBB and rich vascular supply of the pituitary gland, it may be expected that the response of NSCLC-PitM to treatment may be enhanced.

While limited to one case, this report may serve as a framework for treating patients with EGFR-mutated NSCLC-PitM who present with optic nerve or chiasm compression and visual symptoms. We believe that it is reasonable to initiate EGFR-TKIs with close monitoring for progression of symptoms and follow-up imaging at 4 weeks. This patient will require continued close monitoring for possible recurrence of his sellar lesion.

CONCLUSION

Patients with EGFR-mutated NSCLC metastasis to the pituitary may be considered for EGFR-TKI therapy prior to surgical intervention even in the setting of visual deficits.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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