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Case Report

Mediastinal small cell carcinoma with a metastasis to the orbit: A rare carcinoma with an unusual metastatic progression

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Abstract

Extraocular muscle (EOM) is a rare site for orbital metastasis. We presented a case of solitary EOM metastasis from mediastinal small cell cancer (MSCC) for the first time. A 49-year-old man presented with hoarseness. Thorax computed tomography (CT) revealed a mediastinal mass. A fine-needle aspiration biopsy (FNAB) confirmed the diagnosis of MSCC. The patient staged as limited-stage MSCC with a positron emission computed tomography (PET-CT). The patient received radical chemo-radiotherapy (CRT). PET-CT showed a complete response after CRT. Afterward, the patient presented with double vision and a headache. Brain magnetic resonance imaging (MRI) demonstrated a 2 cm metastatic lesion at the left inferior rectus muscle. A 30 Gy palliative RT was applied. The full regression of the mass was achieved 3 months after the palliative RT. Although solitary EOM metastasis is rare, the timing of accurate diagnosis and appropriate treatment can help to preserve the patient's vision and relieve complaints related to the mass.

Keywords:
Helical tomotherapy, mediastinal small cell cancer, orbital metastasis, radiotherapy, small cell cancer

Introduction

Small cell carcinoma (SCC) is a highly aggressive malignancy that predominantly arises from the lungs. However, this cancer can also occur not only in the lung but also in other organs. Extrapulmonary SCC (EPSCC) is a rare malignancy accounting for only 2.54% of all SCCs. The mediastinal SCC (MSCC) is a subgroup of EPSCC. It is characterized by the presence of lesions in the mediastinum without any pulmonary origin.[1-3]

Orbital metastasis is a relatively uncommon presentation for malignancies and occurs up to 7%.[4] The cancers that most commonly metastasize to orbit are breast (53%), prostate (12%), and lung cancers (8%).[5,6] Herein, we report a case of 49 years old man, who presented with the metastatic progression of a primary MSCC after the complete response to the concomitant chemoradiation therapy (CRT). This case is the first reported case for orbital metastasis of MSCC in the literature.

Case History

A 49-year-old man presented with hoarseness. Physical examination was regular, but vocal cord examination revealed paralysis on the left side. Thorax computed tomography (CT) showed

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a mediastinal mass. A fine-needle aspiration biopsy (FNAB) was performed for the diagnosis. The hematoxylin and eosin staining showed cells with increased mitotic activity of 12 times the size of the mature lymphocyte and in some places containing crushing artifact. Immunohistochemical staining showed positivity for pan-cytokeratin, thyroid transcription factor-1 (TTF-1), CD 56, chromogranin, synaptophysin, and neuron-specific enolase (NSE) and negativity for CD 68 and leukocyte common antigen (LCA). The Ki-67 proliferative index was 99%. On the basis of these findings, the diagnosis of small cell cancer was confirmed [Figure 1]. Positron emission tomography (PET-CT) and magnetic resonance imaging (MRI) of the brain were performed for staging, and there were no primary or metastatic lesions in the body except the mediastinal conglomerated lymph node. Therefore, the patient was diagnosed as a limited-stage MSCC [Figure 2].

The patient received 56 Gy (28 fractions) radiotherapy (RT) to the mediastinal mass and bilateral supraclavicular regions. The concomitant CT regimen was cisplatin 75 mg/m^2/1 day, etoposide 100 mg/m^2/3 days every 21 days. After completing radical CRT, CT was completed in four cycles. After CT was completed, the patient was screened with a brain MRI. Since no metastatic mass was detected, 25 Gy (10 fractions) prophylactic cranial irradiation was performed by a linear accelerator.

PET-CT revealed a complete response at three months after radical CRT. Three months after the proven complete response on PET-CT, the patient presented with double vision and headache. Diplopia, exophthalmos, and reduced vision were present during the ophthalmological examination. Brain and orbital MRI demonstrated a 2 cm metastatic lesion at the left inferior rectus muscle [Figure 3]. Liver, and adrenal metastases, and multiple intra-abdominal metastatic lymph nodes were detected in the re-staging PET-CT.

The progression treatment was started with the second-line CT due to the excessive tumor burden in the body. After two cycles of topotecan application, the patient underwent a simulation CT for palliative RT and then immobilized with a thermoplastic mask (type-S thermoplastic-based system CIVCO, Civco Medical Solutions, Kalona, IA, USA). CT images were taken with 3-mm slice thickness with a contrast agent. Gross tumor volume (GTV) was contoured with the help of the MRI. The optic nerves, chiasm, bilateral lenses, globes, brain, brainstem, and pituitary gland were delineated as organs at risk (OAR). A 3-mm planning target volume (PTV) margin was given to the GTV. Helical tomotherapy (HT) plans were made with the intensity-modulated RT (IMRT) technique in the Hi-Art HT planning system (Accuray Inc., Madison, USA) [Figure 4]. Biological equivalent doses (BED) for 2 Gy of all OARs were calculated to prevent morbidity related to the visual pathways in the patient who underwent total cranial irradiation previously. The maximum permitted doses of OARs were considered according to the quantitative analysis of normal tissue effects in the clinic (QUANTEC) dose limits. A 30 Gy (10 fractions) palliative RT

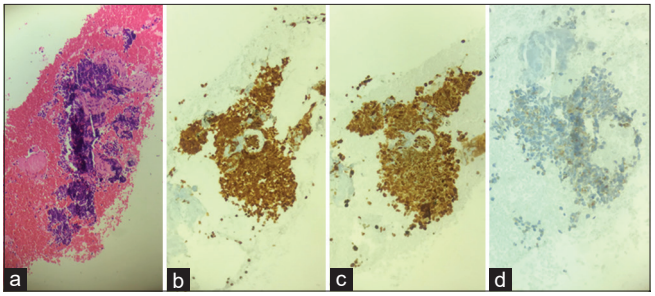


Figure 1: The pathological findings of the fine needle aspiration cytology (FNAC) from the mass. (a): Hematoxylin and eosin staining; (b): Nuclear positivity in TTF-1 and increased proliferative index in Ki-67; (c): Cytoplasmic staining with CD 56; (d): granular positivity with pan-cytokeratin

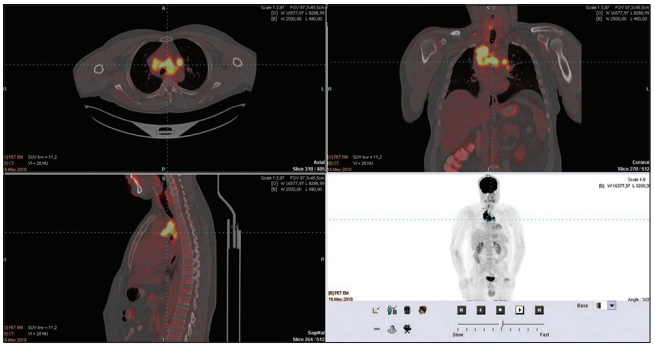


Figure 2: PET-CT revealing the presence of primary mediastinal mass



Figure 3: MRI revealing the presence of metastatic lesion

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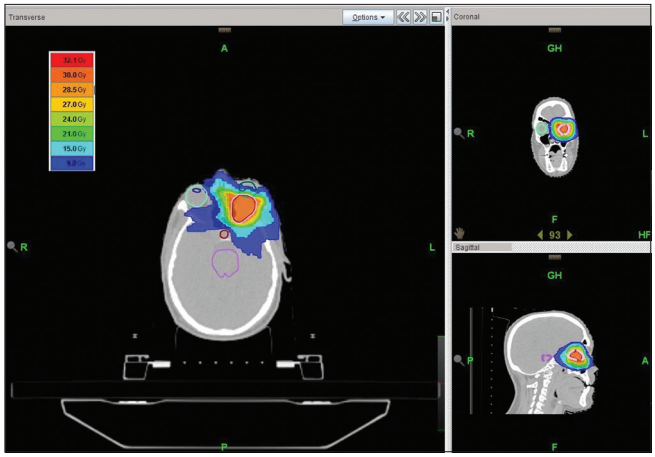


Figure 4: RT dose distribution of the tomotherapy plan

was applied by using 6 MV X-ray beams and image-gated RT (IGRT). At the end of RT, a rapid relief was obtained in the patient's symptoms. MRI after RT revealed >50% response [Figure 5]. The full regression of the mass was achieved at 3 months after palliative RT. The patient continues chemotherapy for other metastases.

Discussion

The incidence of primary tumors that metastasize to the orbit is ~7%.[4,5] Metastases are delivered to the orbital tissues by a hematogenous route, and many of them target the bony wall of the orbit. Extraocular muscle metastases (EOM) are rare and constitute only 9% of the orbital metastasis.[7]

Case reports on EOM reported that the majority of these metastases were detected at the time of diagnosis.[8-10] In some cases, as in our case, these metastases are detected during the systemic progression.[4] The inferior rectus muscle is the muscle with the lowest incidence of EOM. The most affected muscles are the medial, lateral, and superior rectus muscles.[7] Abnormal eye position (65%), proptosis (63%), increased orbital pressure (54%), diplopia (54%), and limited ocular motility (52%) are the 5 most frequent clinical manifestations.[11] These lesions are well-defined, fusiform, or round masses with heterogeneous and minimal enhancement on the MRI.[10] In our case, a mass limited EOM was observed with similar image features. In more advanced cases, invasion and destruction of the orbital bony structures and eyes can be seen.[12]

The diagnosis is established by history, physical examination, and orbital imaging (primarily orbital MRI), and can be confirmed by either open biopsy or FNAB. The biopsy can be performed from the mass in cases without a history of primary malignancy.[10] A primary mass or another site of metastasis, which

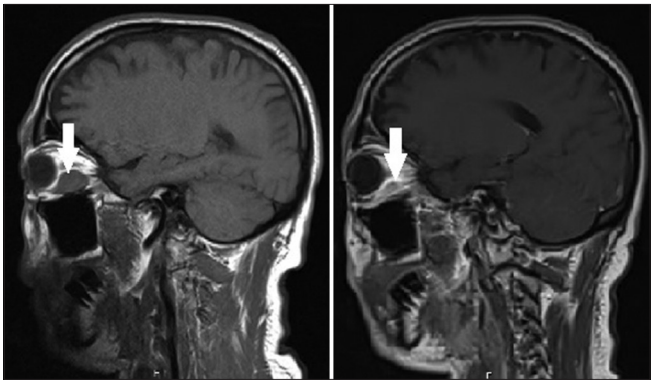


Figure 5: MRI showing the response to RT

is more accessible and safer for tissue diagnosis, can be detected in screening tests.[4,8,10] In our case, since there was a primary malignancy history and widespread metastatic disease was detected in the re-staging PET-CT, a biopsy was not required for diagnosis.

Rapid diagnosis is vital in preserving the patient's visual functions. Therefore, radiation oncology, oncology, radiology, ophthalmology, and pathology departments should work together in diagnosis. Radiotherapy, chemotherapy, surgical excision, and hormonal therapy are treatment options. The treatment approach is selected based on the histology, cancer stage, and the location and extent of the orbital mass.[4] In our case, the treatment was started with systemic chemotherapy due to the widespread tumor burden in the body. CT has shown curative effects in most cases, but RT may be the mainstay treatment for orbital metastasis because the response rate is up to 79%.

Moreover, RT can save visual quality in 80% of the cases.[13] The standard dose of RT is 30-50 Gy, which should be administered carefully to prevent radiation-induced side effects.[12] Ophthalmic side effects of radiation include optic neuropathy, corneal scarring, and retinopathy. Our case had previously received 25 Gy in total cranial irradiation. Palliative RT dose could not be increased to >30 Gy, especially for the protection of optical pathways. Also, RT was applied with the IGRT technique to reduce set-up errors and treatment-related morbidity.

Orbital metastases represent stage 4 malignancy because they are associated with the hematologic spread and are usually associated with poor prognosis. The mean survival time was reported as 20 months after the diagnosis. Primary lung cancer patients have the shortest survival time (mean, 46 months) after orbital metastasis.[5] Our case is progression-free for orbital mass for nine months after RT and has no visual complaints.

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Conclusion

We presented here a case of solitary EOM from MSCC. To our knowledge, this is the first reported case of a primary MSCC with an orbital metastasis. Although solitary EOM metastasis is rare, the timing of accurate diagnosis and appropriate treatment can help to preserve the patient's vision and relieve complaints related to the mass.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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