



Sinonasal Rhabdomyosarcoma Metastasis in Bilateral Multiple Extraocular Muscles: A Case Report and Brief Literature Review

부비동과 비강 내 횡문근육종의 양측 다발성 외안근 전이: 증례 보고와 문헌고찰

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Isolated metastasis in the extraocular muscle (EOM) is uncommon, while metastases in bilateral multiple EOMs is even rarer. Rhabdomyosarcoma (RMS) is a rare soft-tissue malignancy that usually occurs in the pediatric population and is one of the primary malignancies of isolated EOM metastasis. Here, we present a case of sinonasal RMS metastasis to multiple bilateral EOMs along with a brief review of 10 previously reported cases of RMS metastasis in EOMs.

Index terms Extraocular Muscles; Metastasis; Rhabdomyosarcoma; Magnetic Resonance Imaging

INTRODUCTION

Metastatic tumor of the orbit is uncommon, accounting for 4% to 14.7% of all orbital tumors, while isolated metastasis to the extraocular muscle (EOM) is even rarer, affecting only 5% of metastatic orbital tumor (1).

Rhabdomyosarcoma (RMS) is a rare soft-tissue malignancy which occurs often in the pediatric population. The incidence is only 0.4414 per 100000 children per year, although it is the most common mesenchymal tumor in children (2). Although RMS is rare disease, it is one of the primary tumors of isolated metastasis to the EOM (1). According to Leung et al. (1), the most common primary tumors of isolated metastasis to the EOM were melanoma (22%), breast cancer (15%), and carcinoid tumor (14%), while RMS accounts for 6.5% of primary tumors of isolated metastasis to the EOM. There

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have only been 10 scattered case reports of RMS metastasis to the EOM and no summative study. Further, there is a lack of literature detailing radiologic findings.

Thus, the purpose of this article is to report a case of sinonasal RMS metastasis to bilateral multiple EOMs and to briefly review 10 previously reported cases of RMS metastasis to the EOMs. With the literature review, we expect some distinctive features of RMS metastasis to EOMs apart from that of other tumors.

CASE REPORT

In August 2019, a 25-year-old woman presented to our clinic with a seven-day history of blurred vision, ophthalmalgia, and periorbital swelling. She was diagnosed with stage 4, group IV alveolar-type RMS in the bilateral paranasal sinuses and nasal cavities on July 2016 and had undergone a combination chemotherapy [cyclophosphamide, vincristine, doxorubicin, dacarbazine (CyVADIC) and zoladex] and radiation therapy. Despite the multimodal treatment, the disease had progressed and provoked multifocal distant metastases in the lymph nodes, soft tissue, and bone.

On physical examination, the right eye showed limited mobility and mild proptosis. MRI revealed multiple variable-sized discrete oval masses in the bilateral medial and inferior rectus muscles and left superior oblique muscle, with the largest being in the right medial rectus muscle (Fig. 1A–D). The lesions showed mild enhancement and high signal intensity on T2-weighted image. The margins of the lesions with orbital fat were well-defined. (Fig. 1A–D). Where specified, muscle bellies were involved and tendinous portions were spared (Fig. 1A). There were no abnormal findings in other orbital structures, including the globe, optic nerve, orbital fat, and lacrimal gland.

Metastases were most likely suggested and she was received radiation therapy in the right eye. A week after the completion of radiation therapy, the clinical symptoms were somewhat improved. Follow-up enhanced brain CT, performed three months later, showed decreased thickening of the involved medial rectus muscle in the right eye (Fig. 1E). However, the patient died of multiple metastatic disease in November 2019, three months after the EOM metastases were diagnosed.

DISCUSSION

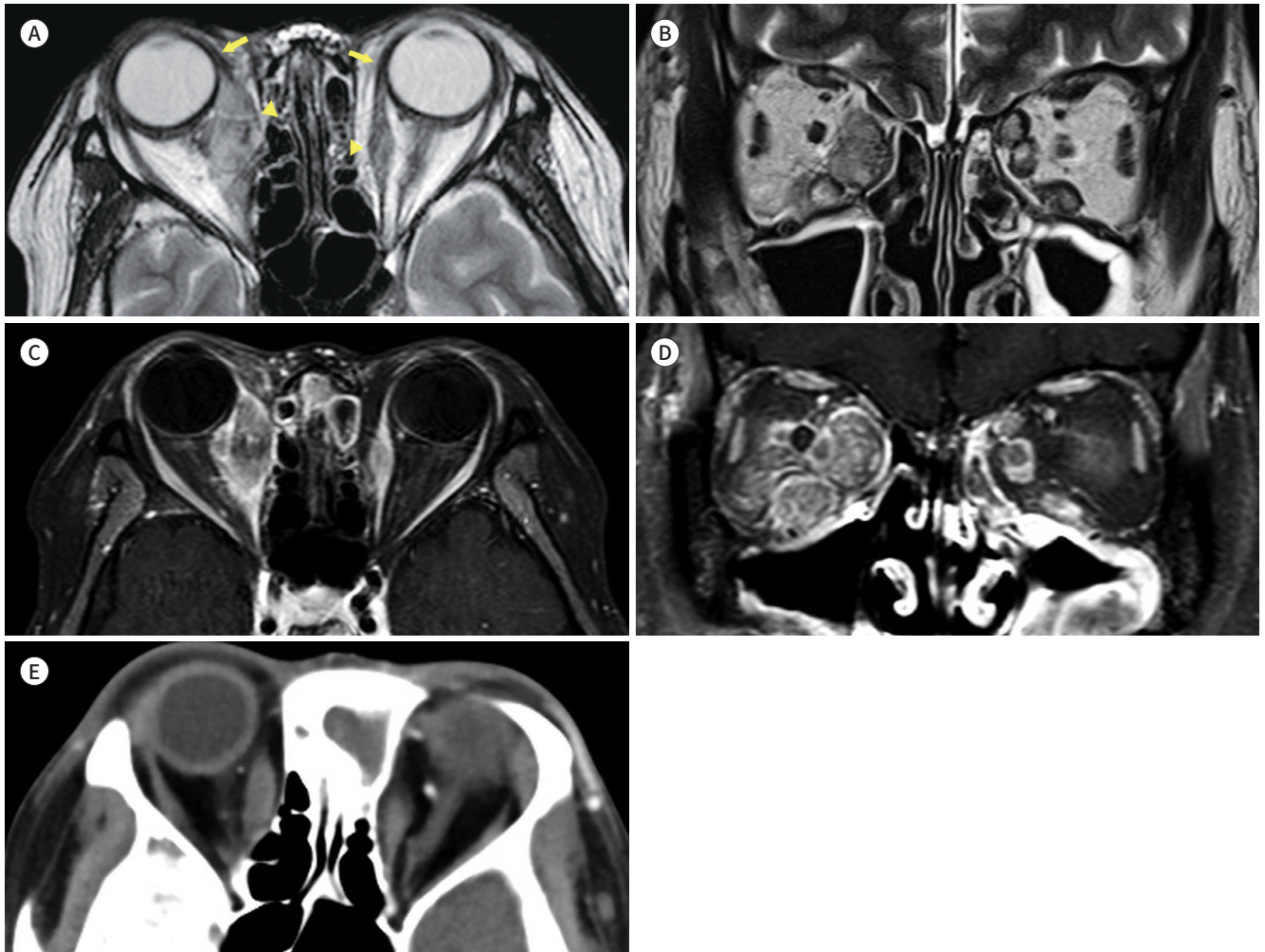
A literature search was undertaken in the electronic databases PubMed, Koreamed, and Google Scholar using the terms “rhabdomyosarcoma,” “metastatic,” and “extraocular muscle” or “orbit.” Ultimately, this search methodology identified 10 cases of RMS metastasis to the EOMs. For the total of 11 cases, including the present case, we reviewed the patient demographics, clinical manifestations, characteristics of primary RMS, survival time, features of EOM metastasis, and radiologic findings (Supplementary Table 1 in the online-only Data Supplement).

Among the 11 cases, the mean age was 22 years old, and six patients (54.5%) were women and five patients (45.5%) were men. The most common clinical symptoms were pain and proptosis in six patients (54.5%) and five patients (45.5%), respectively, while some patients also

Fig. 1. Sinonasal rhabdomyosarcoma metastasis to bilateral multiple extraocular muscles in a 25-year old woman.

A-D. Axial (**A**) and coronal (**B**) T2 weighted images show variable-sized discrete masses in the bilateral medial and inferior rectus muscles and left superior oblique muscle with high signal intensity. The lesions are confined to the muscle bellies (**A**, arrowheads), sparing the tendinous portions (**A**, arrows), and show well-defined margins with orbital fat. Axial (**C**) and coronal (**D**) fat-suppressed enhanced T1 images demonstrate mild enhancement of the involved muscles with slightly hypo-signal intensity relative to the normal extraocular muscles.

E. About two months after the completion of radiation therapy on the right eye, follow-up enhanced brain CT shows decreased thickening of the right medial rectus muscle.



complained of periorbital swelling, restricted eye movement, diplopia, and blurred vision.

The most common primary site of RMS was the sinonasal region in five cases (45.5%), with other primary sites being the perineum and scrotum, orbit other than the EOM, and calf. The alveolar type was the most common histologic subtype, accounting for nine cases (82%), while only two cases (18%) were the embryonal type. In nine cases (82%), patients had pre-existing metastatic lesions at the time of diagnosis of EOM metastasis. Six among the total of 11 patients were reported to have died by the end of the case report; the mean survival time of these six patients was 4.6 months, ranging from two months to 8.6 months.

In EOM metastasis, bilateral involvement was observed in nine cases (82%). Among them, two cases (3, 4) initially showed unilateral involvement but then progressed to bilateral metastases according to follow-up imaging studies. Unilateral involvement was reported in two

cases (18%) and each case had single-muscle metastasis.

We reviewed the radiologic imaging findings and radiologic reports in all 11 cases, of whom four underwent CT, five underwent MRI, and two cases underwent both. MRI and CT revealed round or oval-shaped discrete masses in the EOM muscle belly. The involved EOMs were described as exhibiting “discrete thickening,” “mass-like enlargement,” “muscle belly thickening,” or “fusiform enlargement.” Where specified, in all but two cases, muscle bellies were involved while sparing the tendinous portions. In one case, it was not known whether the tendon was involved, while in another case (5), it was mentioned that tendinous portions were diffusely involved, although consistent images were not contained. The margins of the lesions were well-defined with orbital fat. However, in one case (3), the lesions were described as provoking extensive muscle swelling with infiltrative spread to the posterior orbit, although consistent images were not contained in the paper. Lesion enhancement was evaluated by comparing the signal intensity or density of the lesion with that of normal EOM. Six cases showed slight hypo-signal intensity or hypodensity and one case showed iso-signal intensity and isodensity, which is defined as less and equal enhancement of involved EOMs relative to normal EOMs. Four cases could not be evaluated due to an absence of enhanced images or poor image quality.

RMS is a rare soft-tissue malignancy thought to arise from pluripotent mesenchymal cells and which occurs often in the pediatric population. The incidence is only 0.4414 per 100000 children per year, although it is the most common mesenchymal tumor in children (2). The head and neck region is the most frequently affected site at more than one-third of RMS (6). In the head and neck, sinonasal RMS is included in parameningeal subsite, along with the nasopharynx, infra-temporal fossa, pterygopalatine fossa, middle ear, and mastoid, and is well-known for carrying a worse prognosis (6).

Isolated EOM metastases are thought to represent haematogenous spread of malignancies, generally in an advanced stage, and confer a poor prognosis. In our case, the patient already had many sites of pre-existing distant metastasis when she was diagnosed with EOM metastasis. Also, in our literature review, nine of the 11 cases had pre-existing metastatic lesions. On histology, the alveolar type was more often than the embryonal type in nine versus two cases, even though the embryonal type is the most common histologic subtype of primary RMS. Alveolar RMS is seen more often in older children and has a worse prognosis (6). In view of these points, most cases appeared marked by very advanced disease with an expected poor prognosis; in fact, six cases were reported to have died by the end and their mean survival time was only 4.6 months.

Usually, metastasis to the EOM occurs unilaterally and invades only one muscle (7). In contrast, interestingly, our review suggested the existence of a relatively high rate of bilaterality/multifocality (9/11 patients; 82%). This disproportionate bilaterality of RMS metastasis to the EOM was also mentioned in an article by Leung et al. (1), who suggested that carcinoid tumor and RMS are responsible for the majority of cases involving all EOM muscles. Although the pathophysiology is unclear, this may be associated with the fact that RMS is one of the most rapidly proliferating tumors and infiltrates adjacent tissue and distant organs easily (8).

Among radiologic findings, most lesions showed round or oval masses with less enhancement than normal EOMs, displayed well-defined margins with orbital fat, and were confined

to the muscle belly while sparing the tendinous portion. These findings are consistent with those of Gupta et al. (9), who reported cases of carcinoid tumor metastasis to EOMs. Among patients who show relatively “typical” findings on imaging, metastasis should be high in the radiologic differential, although bilaterality and symmetry of the lesions, especially in a patient with known RMS. An accurate radiologic diagnosis could reduce unnecessary tissue biopsy or invasive surgical procedures such as orbital exenteration.

However, in some cases, involved EOMs showed smooth thickening, rather than masses or nodular thickening, especially in the case of small lesions and on CT characterized by inferior soft-tissue resolution relative to MRI. Actually, some cases (3, 10) were initially misdiagnosed as thyroid-associated ophthalmopathy (TAO) among bilateral cases in our literature review. In TAO, not only EOM muscle enlargement but also increased orbital fat volume can be seen. In addition, the apparent diffusion coefficient (ADC) of the involved EOM is relatively high, which could be a differential point. According to Hassold et al. (4), affected EOMs with metastatic RMS showed high signal intensity on diffusion-weighted image ($b = 1000 \text{ s/mm}^2$) and low ADC value ranging from 0.5 to $0.9 \times 10^{-3} \text{ mm}^2/\text{s}$. This ADC value is lower than that of TAO with mean ADC value of $1.9 \times 10^{-3} \text{ mm}^2/\text{s}$. Therefore, ADC value of affected EOM can be one of differential points. The laboratory findings of thyroid hormones and thyroid-stimulating hormone level, and auto-antibody test should be evaluated also. Another differential diagnosis to be considered is immunoglobulin (Ig) G4-related disease, which can involve bilateral EOM muscles while sparing the muscle tendon. In IgG4-related disease, the lacrimal gland is primarily involved and concurrent salivary gland enlargement, infraorbital nerve enlargement, or paranasal sinus mucosal thickening may be differential points suggesting IgG4-related disease. Also, EOM lesions demonstrate low signal intensity on T2-weighted images due to fibrosis, while metastases usually provoke high signal intensity.

To summarize, regarding bilateral EOMs thickening in patients with RMS, if lesions appear confined to the muscle bellies with well-defined margins and less enhancement than the normal EOM, metastasis is more likely than other non-neoplastic diseases. Moreover, RMS metastasis to the EOM more frequently involved bilateral multiple EOMs.

SUPPLEMENTARY MATERIALS

The online-only Data Supplement is available with this article at <http://dx.doi.org/10.3348/jksr.2020.0045>.

Author Contributions

Conceptualization, J.J.H.; data curation, J.S.; formal analysis, all authors; funding acquisition, J.J.H.; investigation, J.S.; methodology, J.J.H.; project administration, J.J.H.; resources, J.S.; software, J.S.; supervision, J.J.H.; validation, J.J.H.; visualization, J.S.; writing—original draft, J.S.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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부비동과 비강 내 횡문근육종의 양측 다발성 외안근 전이: 증례 보고와 문헌고찰

지소현 · 장지혜*

고립성 외안근 전이는 매우 드물게 나타나며, 그중에서도 양측 다발성 외안근 전이는 더욱 드물다. 횡문근육종은 주로 소아에게 생기는 드문 연조직 악성 종양으로, 고립성 외안근 전이를 일으키는 원발암 중 하나로 알려져 있다. 이에 저자는 부비동에서 발생한 횡문근육종 환자에서 발견된 양측 다발성 외안근 전이의 한 증례를 보고하고, 이와 더불어 이전에 보고된 횡문근육종의 고립성 외안근 전이 10예에 대해 간략히 고찰하고자 한다.

원자력병원 영상의학과