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Aggressive Orbital Dedifferentiated Liposarcoma With Osseus Components in a Young Woman

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Abstract

Background/Aim: Dedifferentiated liposarcoma (DDLS) is a rare but aggressive subtype of liposarcoma that arises in soft tissues. In orbital liposarcoma, malignant transformation from well-differentiated to DDLS typically takes at least a year. We herein report a case of a young female with an aggressive DDLS, that developed from an orbital lipoma within one year.
Case Report: A 25-year-old woman presented with left upper eyelid swelling. MRI revealed abnormal adipose tissue in the medial orbit. The excised tissue was diagnosed as an orbital lipoma. The eyelid swelling recurred three months later, and the orbital tumor enlarged. An additional resection was performed, which again revealed a lipoma without malignant features. Three months later, the swelling worsened, and tumor resection confirmed well differentiated liposarcoma with a Ki-67 labeling index of 10%. Two months later, CT imaging depicted calcified lesions within the tumor. The patient subsequently underwent orbital exenteration followed by proton beam radiation. Histopathological examination of the exenterated tissue revealed DDLS with extensive osseous components. The Ki-67 labeling index exceeded 50%.
Conclusion: Ocular oncologists should pay attention to the possibility of rapid malignant transformation in DDLS in primary orbital liposarcoma.

Keywords: Dedifferentiated liposarcoma, orbit, histopathology, orbital exenteration, Ki67.

Introduction

Liposarcoma is a rare non-epithelial malignant tumor of the orbit, which is commonly classified into four subtypes: myxoid, pleomorphic, well-differentiated, and dedifferentiated. Dedifferentiated liposarcoma (DDLS) is a highly aggressive subtype of liposarcoma characterized by a transition from a well-differentiated lipomatous

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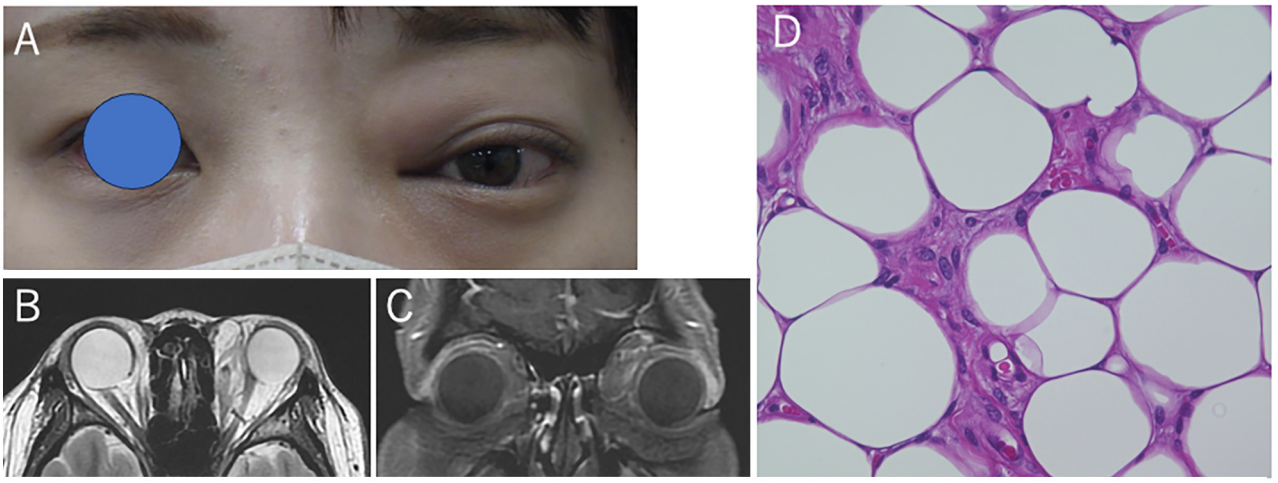

Figure 1. *Initial clinical presentation, magnetic resonance imaging (MRI) with T2-wieghted image (B), T1 weighted MRI with gadolinium enhancement (C), and histopathology of the orbital tumor. Mild swelling of the left eyelid with a palpable subcutaneous soft mass of unclear margins (A). T2-weighted MRI showing a heterogenous orbital mass with iso-intensity (B), similar to orbital fat. There was no enhancement within the lesion (C). Histopathological analysis of the incisional biopsy demonstrating abundant mature adipocytes without cellular atypia (D).*

component to a non-lipogenic one (1). Treatment options include local tumor resection combined with radiotherapy, and in severe cases, orbital exenteration (2). DDLS has been shown to arise from well-differentiated liposarcoma, with transformation usually occurring over one to several years (3).

We herein report the case of a young patient with aggressive DDLS, which rapidly developed from an orbital lipoma in less than a year, ultimately necessitating orbital exenteration.

Case Report

A 25-year-old female presented with left eyelid swelling without pain. A subcutaneous soft mass with unclear margins was palpable (Figure 1A). There were no abnormalities of extraocular movements. Magnetic resonance imaging (MRI) with T2-wieghted imaging revealed a heterogenous orbital mass with iso-intensity (Figure 1B), resembling orbital fat, without enhancement in the lesion (Figure 1C). An incisional biopsy was conducted, which confirmed the presence of mature adipocytes without cellular atypia (Figure 1D), leading to a diagnosis of orbital lipoma. However, three months later, she suffered from recurrent left eyelid swelling (Figure 2A). The eyelid skin was reddish. A slightly elastic, hard mass was palpable beneath the eyelid skin. T2-weighted MRI depicted a heterogenous ill-defined adipose tissue mass in the medial-superior orbit (Figure 2B), with gadolinium-enhanced T1-weighted MRI showing enhancement around the tumor (Figure 2C). A second orbital biopsy was conducted, revealing yellowish tissue macroscopically (Figure 2D) and mature adipocytes without cellular atypia histopathologically (Figure 2E). Immunoreactivity for MDM2, a specific marker for liposarcoma, was negative in the excised tissue (Figure 2F), confirming the diagnosis of orbital lipoma once again. After the biopsy, the eyelid swelling rapidly recurred with pronounced eyelid redness. Since inflammatory reactions were suspected, 200 mg of systemic soluble prednisolones were administered; however, the patient's symptoms did not improve (Figure 3A). At six months after the initial biopsy, MRI with gadolinium enhancement demonstrated a mixture of markedly enhanced and non-enhanced regions within the lesion (Figure 3B). Positron-emission tomography/computed tomography (PET-CT) showed no abnormal

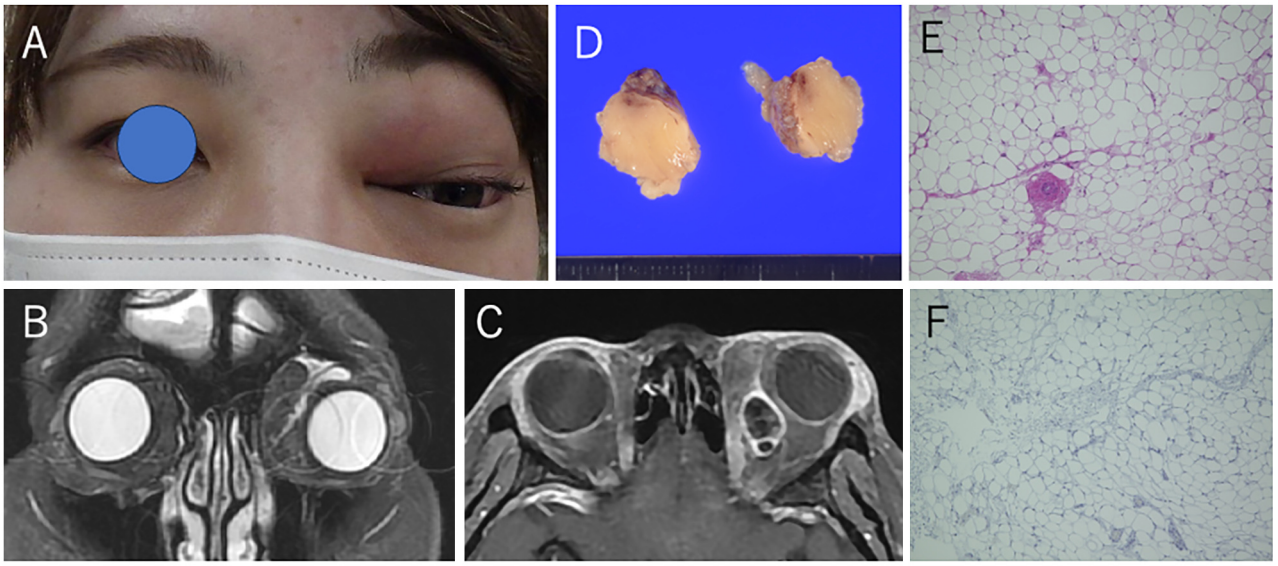

Figure 2. *External photograph (A), T2-weighted magnetic resonance imaging (MRI) (B), gadolinium-enhanced T1-weighted MRI (C), macroscopical findings of the excised tumor (D), HE staining of the excised tumor (E), and immunoreactivity for MDM2 (F) obtained three months after the initial presentation. The patient experienced recurrent left eyelid swelling (A). T2-weighted MRI depicted a heterogenous orbital mass in the medical-superior orbit (B). Gadolinium-enhanced T1 showed some enhancement around the tumor (C). Macroscopically, the cut section of the excised tumor appeared yellowish (D). Histopathologically, the tumor tissue composed of mature adipocytes without cellular atypia (E). Immunoreactivity for MDM2, a specific marker for liposarcoma, was negative in the excised tissue (F).*

findings except for the left orbit. A third excision of the tumor was conducted. Macroscopical findings of the excised tumor revealed a grayish solid tumor (Figure 3C). Histopathological findings demonstrated that there were lots of stromal areas including cellular components, where the areas of mature fat tissues were marginally intermingled (Figure 3D). At a high magnification, the cellular components were composed of atypical stromal cells with bizzarro nuclei (Figure 3E) and lipoblasts containing a markedly foamy cytoplasm (Figure 3F; arrow). There were no osseus components in the specimens. Immunohistochemical examination revealed that the tumor cells were positive for MDM2 (Figure 3G), Cdk4 (Figure 3H), and S100. Ki67-labeling index was approximately 10%. The excised tumor was pathologically diagnosed as well-differentiated liposarcoma. Despite being informed of the diagnosis, the patient initially hesitated to undergo orbital exenteration. However, subsequent orbital CT scans revealed high-intensity lesions in the left orbital tumor, suggestive of osseus components (Figure 4A), and malignant transformation to DDLS was clinically suspected. MRI revealed high enhancement, mostly in the tumor sites without osseus components (Figure 4B). The cancer board in Hokkaido University Hospital recommended orbital exenteration followed by proton beam radiation. The patient eventually accepted the recommended therapy about eight months after the initial biopsy. Orbital exenteration was performed with pedicled temporoparietal fascia flap and free skin grafts, followed by proton beam radiotherapy with a total dose of 70 Gy. Macroscopical findings of the exenteration revealed marked bone tissues within the tumor (Figure 4C, asterisk). Histopathology of the exenteration tissues demonstrated that there were markedly immature osseus components (Figure 4D, asterisks) admixed with atypical oval or spindle tumor cells without typical lipoblasts (Figure 4E), where MDM2 immunoreactivity was positive. Ki67-labeling index was over 50% in the tumor cells (Figure 4F). Finally, the tumor was diagnosed as DDLS. There was no recurrence or distant metastasis six months after surgery.

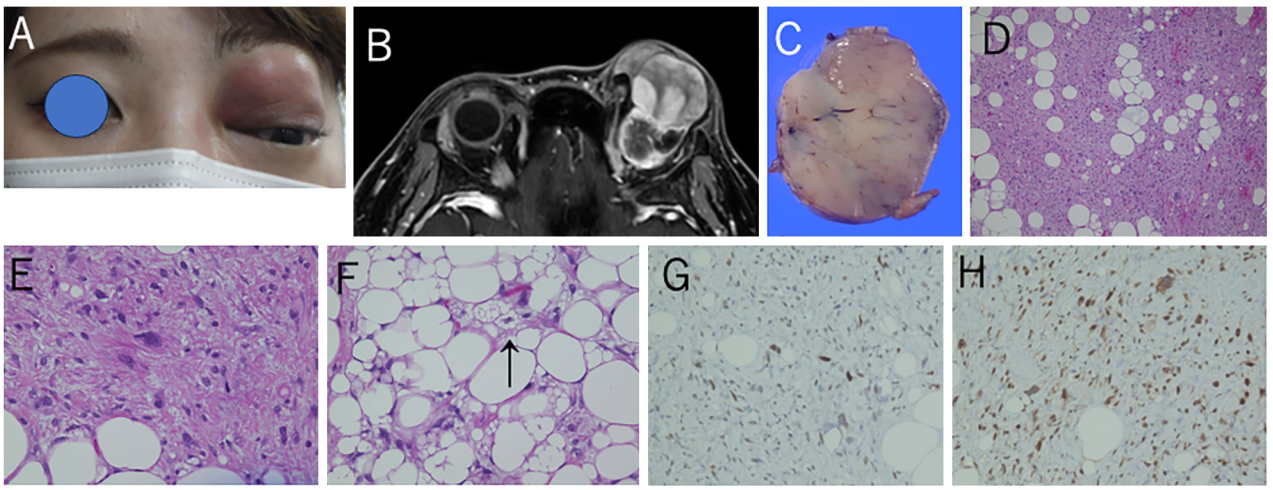

Figure 3. *External photograph (A), gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) (B), macroscopical findings of the excised tumor (C), HE staining of the excised tumor (D-F), and immunoreactivity for MDM2 (G) and Cdk4 (H) obtained six months after the initial presentation. The left eyelid swelling rapidly recurred, with marked redness (A). MRI with gadolinium enhancement demonstrated a combination of markedly enhanced and non-enhanced areas within the lesion (B). Macroscopic examination of the excised tumor revealed a grayish solid tumor (C). Histopathological findings demonstrated numerous stromal areas with cellular components, with mature fat tissues intermingled (D). At a high magnification, the cellular components included atypical stromal cells with bizarre nuclei (E) and lipoblasts containing a markedly foamy cytoplasm (F; arrow). Immunohistochemical examinations revealed that the tumor cells were positive for MDM2 (G), and Cdk4 (H).*

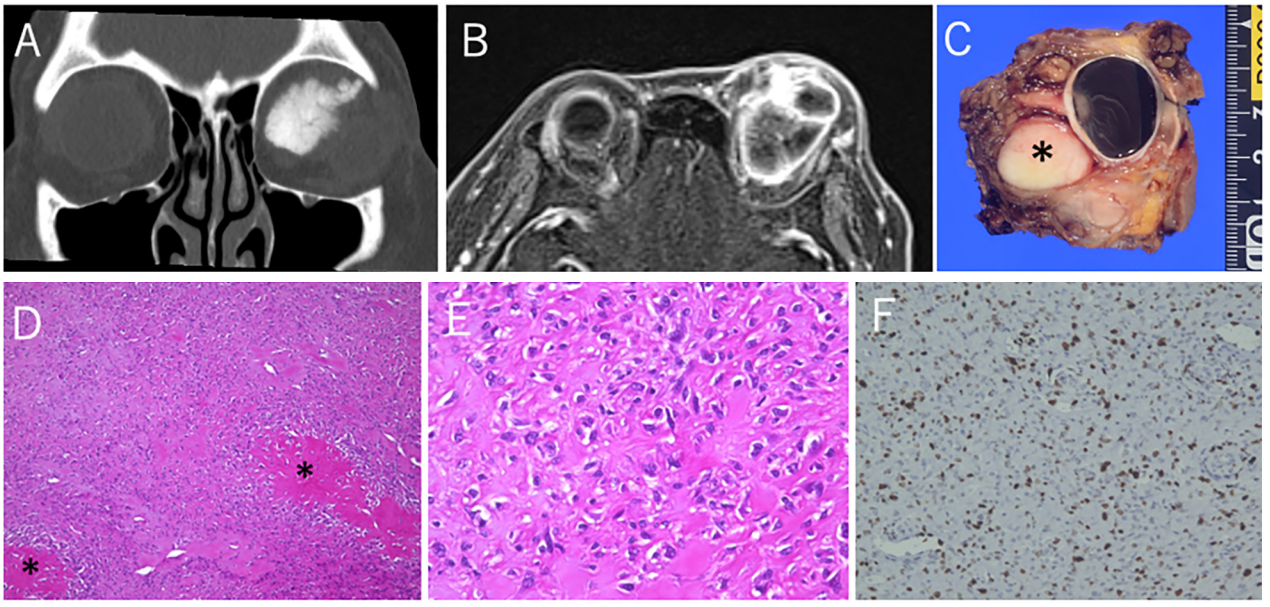

Figure 4. *Computed tomography (CT) (A), magnetic resonance imaging (MRI) (B), and macroscopical findings (C), HE staining (D, E), and Ki67 immunoreactivity (F) of the exenteration tissues obtained eight months after the initial biopsy. Orbital CT revealed that there were marked high intensity lesions in the left orbital tumor, suggestive of osseus components (A). MRI revealed high enhancement mostly in the tumor sites, with possible absence of osseous components (B). Macroscopical findings of the exenteration revealed marked bone tissues within the tumor (C, asterisk). Histopathology of the exenteration tissues demonstrated markedly immature osseus components (D, asterisks) mixed with atypical oval or spindle tumor cells (E). Ki67-labeling index exceeded 50% in the tumor cells (F).*

Discussion

This patient was initially diagnosed with an orbital lipoma, which transformed into DDLS within approximately eight months. So far, there have been at least 10 cases of well-differentiated orbital liposarcoma transforming into DDLS. The duration of the transformation was likely to be more than one year (3-5). Therefore, this case is quite unique because of its rapid malignant transformation compared to previous reported cases, emphasizing the need for ocular oncologists to remain vigilant for aggressive progression in primary orbital liposarcomas.

The ability to predict malignant transformation remains uncertain. While orbital CT scans can detect ill-defined adipose tumors, a retrospective observational study found calcifications in about one-third of orbital liposarcoma cases (2). The usefulness of CT scans for evaluating orbital DDLS is disputable; however, in this case, the CT scan detected osseus components in tumor tissues, when malignant transformation to DDLS was clinically suspected. Histopathologically, DDLS manifested increased relatively oval or spindle tumor cells with immature osseus components rather than typical lipoblasts. Therefore, orbital CT scan might aid in distinguishing DDLS from well-differentiated liposarcoma.

Gao *et al.* reported three cases of primary orbital DDLS in Chinese patients, aged 24, 57, and 44 years, including two females and one male (6). The disease course raged from 16 to 36 months. One patient required orbital exenteration. Ki-67 labeling index was 100% in one patient who underwent local resection, while the other two had had indices below10%. They suggested that a high Ki-67 labeling index is indicative of aggressive orbital liposarcoma (6). In this case, since rapid malignant transformation was suggested based on CT scan in addition to previous triple local resections, orbital exenteration was required to achieve complete resection of the tumor. The Ki-67 labeling index, which was 10% when well-differentiated liposarcoma was diagnosed, increased to over 50% upon confirmation of DDLS two months later. This significant increase aligned with the rapid malignant transformation and aggressive nature of DDLS.

Conclusion

This case highlights an extremely rapid transformation from orbital lipoma to DDLS within less than a year, necessitating aggressive treatment. Given the unpredictability of malignant transformation, clinicians should consider orbital CT scans and Ki-67 labeling indices as potential tools for early detection of aggressive behavior in orbital liposarcomas. Further studies are needed to better understand the progression and optimal management strategies for DDLS.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

SK observed the patient, wrote the entire manuscript and acquired clinical and pathological data. KM observed the patient, performed the reconstruction of the orbital exenteration, and revised the paper. NO made a pathological diagnosis, revised the paper and supervised pathological description. YS evaluated the clinical data and revised the paper. SI critically revised the paper.

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