American Journal of Ophthalmology Case Reports 33 (2024) 101983

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

A case of primary orbital liposarcoma with dedifferentiated transformation from a well-differentiated form

Mika Tanabe [a,*], Hiroshi Yoshikawa [a], Masatoshi Fukushima [a], Masahiro Mizoguchi [b], Masato Akiyama [a,c], Yuhei Sangatsuda [b], Fumiya Narutomi [d], Koh-Hei Sonoda [a]

[a] Department of Ophthalmology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[c] Department of Ocular Pathology and Imaging Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[d] Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

ARTICLE INFO

Keywords:
Primary orbital liposarcoma
Dedifferentiated liposarcomas
Well-differentiated
Transitioning
Orbital exenteration

ABSTRACT

Purpose: Primary orbital liposarcomas are rare. To the best of our knowledge, only four cases of primary dedifferentiated liposarcomas of the orbit have been reported. Furthermore, there have been no reports of primary orbital liposarcomas transitioning from a highly differentiated to a dedifferentiated form. Here, we report a case of primary orbital liposarcoma that was well-differentiated at the time of initial resection at our hospital but had dedifferentiated on recurrence 10 years after the initial resection.

Observations: The patient was diagnosed with an inflammatory mass after an initial tumor resection by a previous physician at age 52. Thereafter, there were four recurrences (first to fourth recurrences), and the patient underwent five surgeries and radiotherapy. For the fifth recurrence, he first visited our hospital at age 64 and was diagnosed with a well-differentiated liposarcoma after undergoing tumor resection. When the tumor recurred 9 years later (the sixth recurrence), it was well-differentiated. When the tumor recurred (the seventh recurrence) six months after surgery at the age of 73 years, the patient underwent orbital exenteration because of rapid tumor growth, and pathological examination showed that the tissue had changed to a dedifferentiated liposarcoma.

Conclusions and Importance: Primary well-differentiated orbital liposarcoma may transform to a dedifferentiated form over time. The risk of dedifferentiation at recurrence should be considered in developing a treatment plan, even if the initial pathology is a well-differentiated liposarcoma.

1. Introduction

Liposarcoma is a malignant tumor that develops in adipocytes and accounts for 20 % of soft-tissue sarcomas in adults with a predilection for the extremities and retroperitoneum.[1] Liposarcomas of the orbit are rare. Liposarcomas are classified into well-differentiated, myxoid, pleomorphic, myxoid pleomorphic, and dedifferentiated.[2,3] To the best of our knowledge, only four cases of primary dedifferentiated liposarcomas of the orbit have been reported.[4–7] Furthermore, there have been no reports on the transformation of liposarcoma from a well-differentiated to a dedifferentiated type. Here, we present our experience with a patient with primary orbital liposarcoma that was well-differentiated at the time of initial resection at our hospital but later transformed to a dedifferentiated liposarcoma at the time of recurrence.

2. Case report

A 52-year-old man visited another hospital for left eyelid swelling and decreased vision and underwent tumor resection in the same year. An inflammatory mass was diagnosed based on pathology, which showed fibrous tissue with mild lymphocytic infiltration.

Five years later, at the age of 57 years, the tumor recurred and was resected again. The tissue was similarly fibrous. However, the patient underwent radiotherapy with 30 Gy to the ocular region because of recurrence. He subsequently had three recurrences and underwent repeated resections by his previous physician over six years.

At the age of 64 years, the patient relapsed for the fifth time and was subsequently referred to the Department of Ophthalmology, Kyushu University Hospital, for an initial consultation to discuss diagnosis and

* Corresponding author. Department of Ophthalmology, Kyushu University Graduate School of Medical Sciences, 3-1-1, Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan.
E-mail address: tanabe.mika.722@m.kyushu-u.ac.jp (M. Tanabe).

https://doi.org/10.1016/j.ajoc.2023.101983
Received 14 July 2023; Received in revised form 7 December 2023; Accepted 21 December 2023
Available online 26 December 2023

treatment.

At the time of presentation to our hospital, his best-corrected visual acuity was 20/20 for the right eye and 20/63 for the left eye. The intraocular pressures of the right and left eyes were 13 and 19 mmHg, respectively. Additionally, his left eye was deviated inferiorly and had an impairment of supination. The cornea was transparent, the lens had mild opacity, and mild pallor of the left optic nerve papilla was observed on slit-lamp examination. Magnetic resonance imaging (MRI) showed a mass in the lacrimal gland area extending to the optic nerve within the muscle cone (Fig. 1), with a low signal on T1-weighted imaging, moderate signal on T2-weighted imaging, and uniform strong enhancement on gadolinium contrast imaging. The FDG-PET findings showed accumulation consistent with an orbital tumor (standardized uptake value [SUVmax] = 6.25) with no evidence of extension outside the orbit. The tumor was subsequently surgically removed through a bone window. Pathological examination revealed that the tumor was a well-differentiated liposarcoma (Fig. 1).

He discontinued his medical visits because his symptoms had ceased. Nine years passed without recurrence; however, at the age of 73 years, the patient returned with a mass in the supranasal area of the left orbit. Repeat MRI revealed a mass extending deep into the orbit. Repeat surgery was performed via a frontal bone incision extended nasally, and the mass was removed from the orbit and nasal cavity using a transcranial approach. The tumor was well-circumscribed and subtotally resectable. The pathology of the excised tumor was similar to that of a well-differentiated liposarcoma (Fig. 2). Six months after surgery, a lesion suspected to be recurrent developed on the nasal side of the orbit and grew rapidly. Two months later, the mass extended deep into the orbit with an anteroposterior diameter of 3.5 cm, compressing the optic nerve. The gadolinium contrast on MRI was more strongly enhanced relative to those of previous images (Fig. 3). Orbital exenteration was performed, but the patient underwent postoperative intensity-modulated radiation therapy with 60 Gy/30 Fr because of suspected positive margins at the orbital apex. Pathology examination of the resected tumor showed proliferation of atypical spindle-shaped cells with hyperchromatic nuclei accompanied by fibromyxoid stroma. Unlike previous findings, a diagnosis of dedifferentiated liposarcoma was made because differentiation into fat was unclear, and immunostaining was positive for CDK4 and MDM2 (Fig. 3). We found no recurrence on CT at 18 months postoperatively. CT at 1 year and 7 months postoperatively showed lesions in the left orbital apex, left cavernous sinus, and mid-left temporalis muscle, which were considered recurrent. Chemotherapy was considered but not performed aggressively administered due to the postoperative sinusoidal syndrome, cerebral infarction, and general condition of the patient. The patient was transferred to another hospital for palliative care.

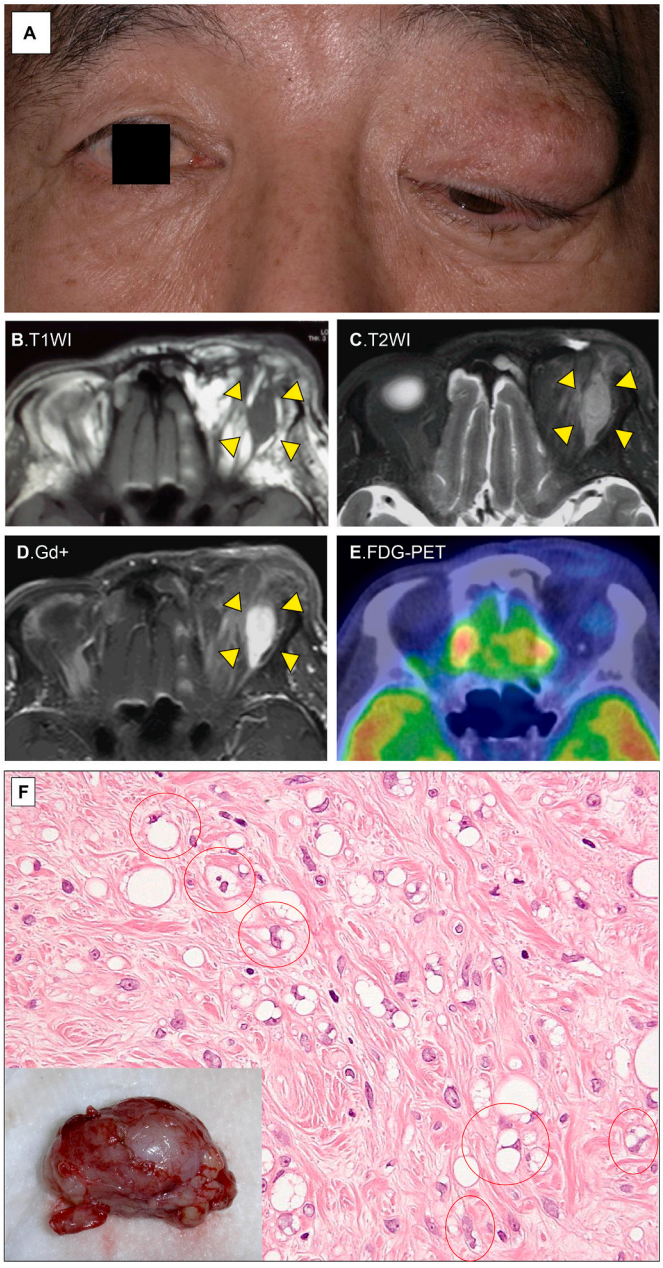

Fig. 1. Clinical, imaging, and histopathology findings at the time of the first visit at the age of 64 years. The patient's left eye shows exophthalmos and inferior deviation (panel A). Magnetic resonance imaging shows a mass in the lacrimal gland area and aurally on the optic nerve within the orbital muscle cone, with low signal on T1-weighted images (panel B), moderate signal on T2-weighted images (panel C), and uniform strong enhancement with gadolinium contrast (panel D). ^{18}F-fluorodeoxyglucose positron emission tomography findings show accumulation consistent with an orbital tumor (standardized uptake value [SUVmax] = 6.25), with no metastasis outside the eye (panel E). Specimen and histopathology findings (panel F) reveal a hard and elastic tumor. The section shows a proliferation of atypical spindle cells, adipocytes, and lipoblasts with hyalinized or myxomatous stroma. Lipoblasts are indicated by red circles. These atypical cells were positive for CDK4 and CD34 and focally positive for MDM2. Pathology first diagnosed the tumor as a differentiated liposarcoma.

3. Discussion

Liposarcoma is a type of sarcoma that arises from soft tissues such as subcutaneous tissue and muscle. It is the most common type of soft-tissue sarcoma.

The 2020 World Health Organization soft-tissue classification system identifies five distinct liposarcoma subtypes, as discussed above.[3] Myxoid pleomorphic liposarcoma is a recently defined subtype of liposarcoma that preferentially involves the mediastinum in young patients and shows mixed histological features of conventional myxoid liposarcoma and pleomorphic liposarcoma. Previous reports have shown that primary orbital liposarcomas are predominantly myxoid and well-differentiated.[8] The pathology of well-differentiated liposarcomas is characterized by an increase in the number of mature adipocytes and various lipoblasts. In contrast, dedifferentiated liposarcomas present different histology characterized by a few mature adipocytes and highly dysmorphic cells.

Well-differentiated and dedifferentiated liposarcomas share a known amplification of 12q13-15.[9] Recently, it was reported that the addition of a *DNM3OS* fusion gene and other genes may transform a well-differentiated liposarcoma into a dedifferentiated liposarcoma.[10] Dedifferentiated liposarcoma has the clinical characteristics of high malignancy, frequent local recurrence, and metastasis.[11] In the present

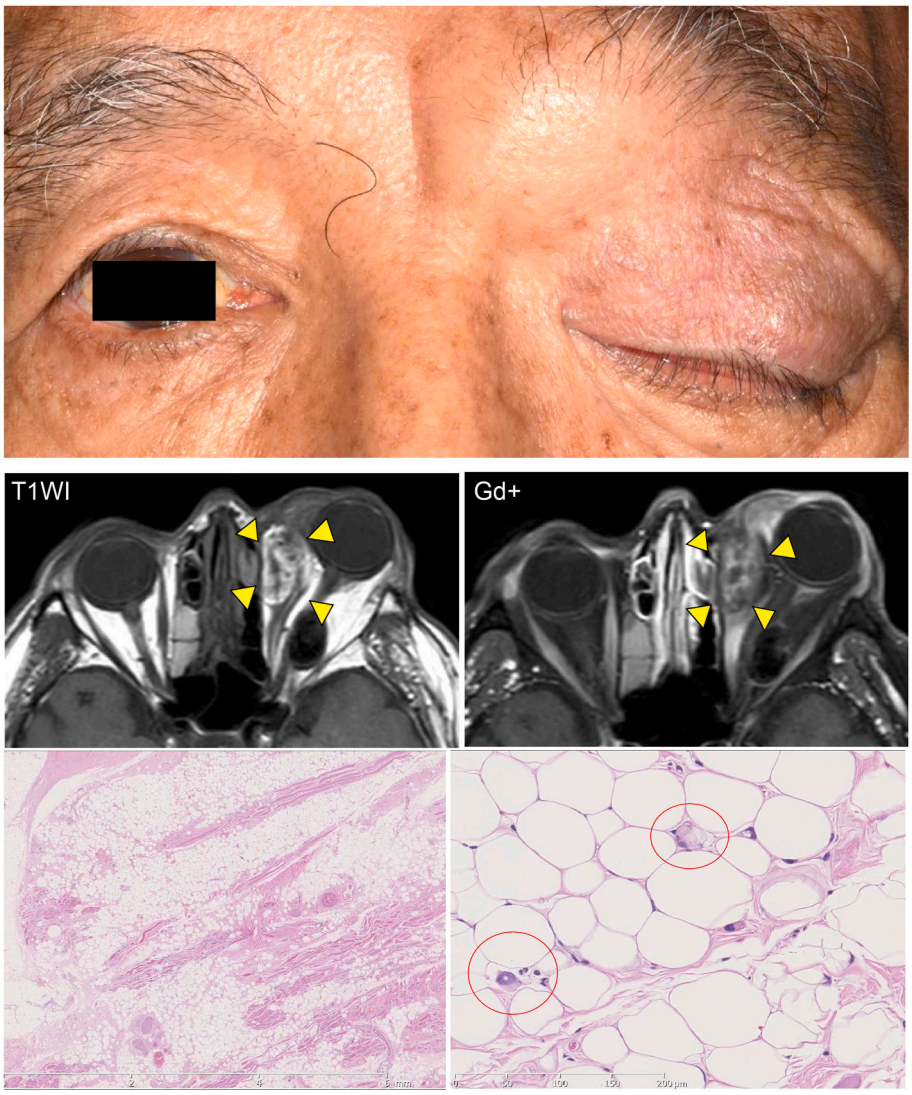

Fig. 2. Clinical, imaging, and histopathology findings at recurrence at the age of 73 years. A large, 2-cm mass was observed outside the muscular cone in the orbit, with an internal fatty component. Recurrence of liposarcoma was considered. The pathology of the excised tumor is similar to that of a well-differentiated liposarcoma. Lipoblasts are indicated by red circles.

case, the tumor was well-differentiated for 9 years and dedifferentiated at year 10. The recurrence duration was shortened from 9 years to 6 months, which may be related to the disease grade.

The patient underwent seven localized tumor resections, including those performed by other physicians. In this case, the tumor was resectable as a single mass, but negative margins were not achieved with all excisions. The tumors were difficult to treat due to repeated recurrences. We do not know if previous radiotherapy may have caused further dedifferentiation. A previous report also found recurrence in 8 of 12 patients who underwent local tumor resection.[12] In contrast, a study reported recurrence for only 1 of 11 cases initially treated with orbital exenteration,[11] suggesting that orbital exenteration is less likely to lead to recurrence. Additional therapy has not yet been established, but radiotherapy has been reported for dedifferentiated liposarcoma,[5,6,13] similar to the present case. Therefore, radiotherapy may be considered as an additional treatment to prevent recurrence.

4. Conclusions

Here, we report a case of primary liposarcoma of the orbit followed up for more than 20 years. This is the first report of a case of primary, well-differentiated orbital liposarcoma changing to a dedifferentiated form over time.

Thus, the possibility of dedifferentiation at recurrence should be considered in the treatment plan even if the initial pathology is well-differentiated liposarcoma.

Patient consent

This report does not contain any personal information. The study was approved by the Institutional Review Board of Kyushu University Hospital and Medical Institutions under the title "Retrospective Study of Ocular Tumors" (IRB: 30–343) and we have an explanatory consent document on our website (https://www.eye.med.kyushu-u.ac.jp/patient/clinicaltrial/pdf/35.pdf) and an opt-out option.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

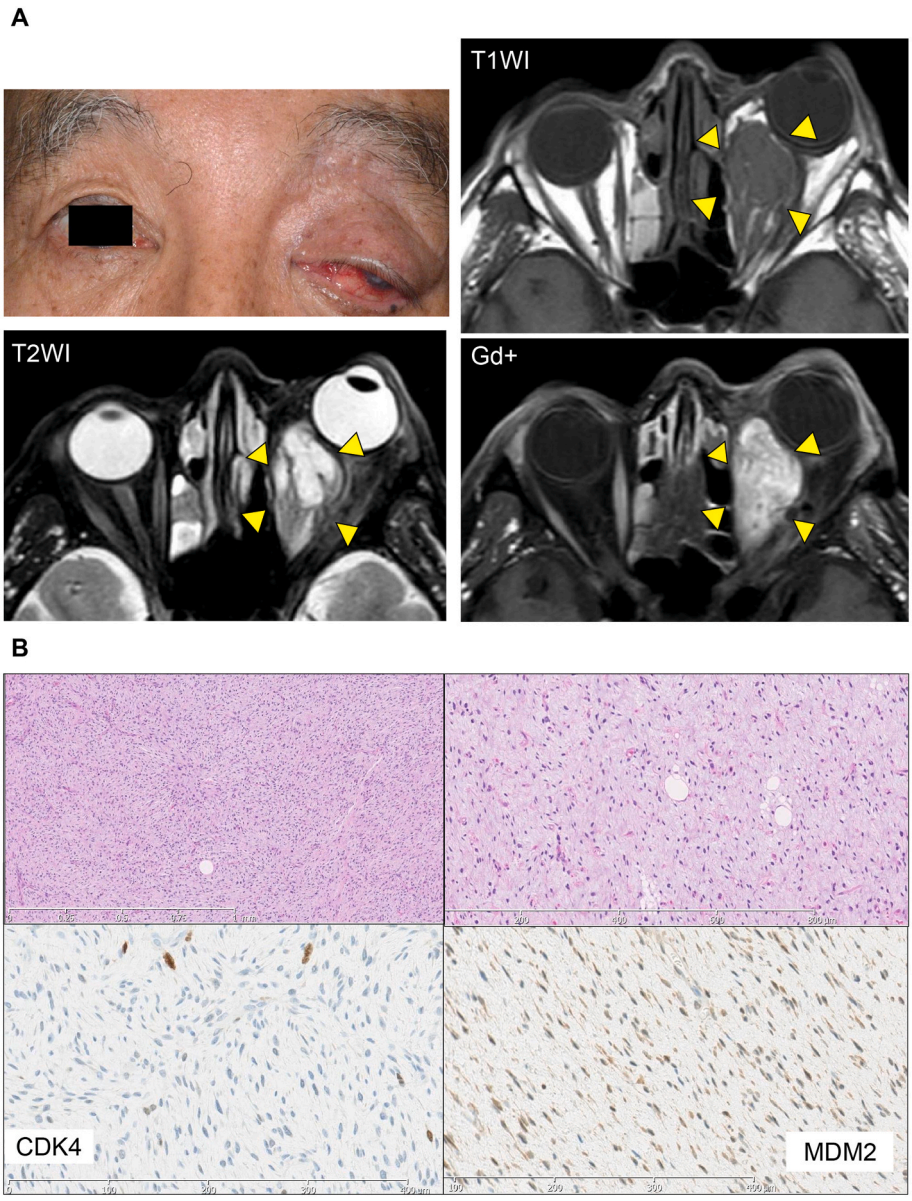

Fig. 3. A. Clinical and magnetic resonance imaging (MRI) findings at recurrence at the age of 74 years. The tumor extended deep into the orbit and had an anteroposterior diameter of 3.5 cm, compressing the optic nerve. Gadolinium contrast-enhanced MRI shows stronger enhancement than that at the last recurrence. **B. Histopathology findings at the age of 74 years.** Histopathological examination of the resected tumor shows proliferation of atypical spindle-shaped cells with hyperchromatic nuclei accompanied by a fibromyxoid stroma. Unlike previous findings, the differentiation into fat is unclear. Immunostaining shows positivity for CDK4 and MDM2. At this time, the diagnosis was dedifferentiated liposarcoma.

CRediT authorship contribution statement

Mika Tanabe: Writing – original draft. **Hiroshi Yoshikawa:** Conceptualization. **Masatoshi Fukushima:** Data curation. **Masahiro Mizoguchi:** Writing – review & editing. **Masato Akiyama:** Writing – review & editing. **Yuhei Sangatsuda:** Writing – review & editing. **Fumiya Narutomi:** Writing – review & editing. **Koh-Hei Sonoda:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

None.

References

1. Zhang JX, Ma JM, Wang NL. Dedifferentiated orbital liposarcoma, a case report. *Int J Ophthalmol*. 2011;4:452–453.
2. Yamazaki D, Ogihara N, Horiuchi T. Primary orbital dedifferentiated liposarcoma. *World Neurosurg*. 2020;139:604–607.
3. Sbaraglia M, Bellan E, Dei Tos AP, et al. The 2020 WHO Classification of Soft Tissue Tumours: news and perspectives. Pathologica. https://doi.org/10.32074/1591-951X-213.
4. Fay A, Dolman PJ. *Diseases and Disorders of the Orbit and Ocular Adnexa: Neoplastic Disorders*. Fay Dolman: Elsevier; 2016:358–359.
5. Fletcher CD, Unni KK, Mertens F. *World Health Organization Classification of Tumors, Pathology and Genetics of Tumors of Soft Tissue and Bone: Liposarcoma*. IARC Press; 2002:35–46.

6. Cai YC, McMenamin ME, Rose G, et al. Primary liposarcoma of the orbit: a clinicopathologic study of seven cases. *Ann Diagn Pathol*. 2001;5:255–266.
7. Saeed MU, Chang BY, Atherley C, et al. A rare diagnosis of dedifferentiated liposarcoma of the orbit. *Orbit*. 2007;26:43–45.
8. Madge SN, Tumuluri K, Strianese D, et al. Primary orbital liposarcoma. *Ophthalmology*. 2010;117:606–614.
9. Lee ATJ, Thway K, Huang PH, et al. Clinical and molecular spectrum of liposarcoma. *J Clin Oncol*. 2018;36(2):151–159.
10. Hirata M, Asano N, Katayama K, et al. Integrated exome and RNA sequencing of dedifferentiated liposarcoma. Nat Commun https://doi.org10.1038/s41467-019-13286-z.
11. Henricks WH, Chu YC, Goldblum JR, Weiss SW, et al. Dedifferentiated liposarcoma: a clinicopathological analysis of 155 cases with a proposal for an expanded definition of dedifferentiation. *Am J Surg Pathol*. 1997;21(3):271–281.
12. Madge SN, Tumuluri K, Strianese D, et al. Primary orbital liposarcoma. *Ophthalmology*. 2010;117(3):606–614.
13. Yamazaki D, Ogihara N, Horiuchi T, et al. Primary orbital dedifferentiated liposarcoma. *World Neurosurgery*. 2020;139:604–607.