

Orbital liposarcoma: a retrospective, single-center study of thirteen patients

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Abstract

• **AIM:** To explore the clinical and pathological characteristics of thirteen patients with orbital liposarcoma.

• **METHODS:** The clinical history data of thirteen patients diagnosed as orbital liposarcoma at Beijing Tongren Hospital, from 2006 to 2021 were collected and analyzed. The data includes age, gender, affected orbital side, course of disease, status of disease (primary or recurrent), clinical manifestations, preoperative visual acuity, operative treatment, the relations between liposarcoma and surrounding tissue, longest diameter of liposarcoma, histological subtype, immunohistochemical indicators, follow-up treatment and prognosis.

• **RESULTS:** The initial symptoms are diverse. Proptosis is the most frequent chief complaint and the others included vision loss, epiphora, diplopia, and eyelid palpable mass. Results of imaging examination [computed tomography (CT) or magnetic resonance imaging (MRI)] showed orbital mass. In terms of treatment, 10 patients received tumor resection, and the mean longest diameter of the tumor was 3.39 ± 1.36 cm. The other 3 patients had optic nerve invaded, so they received orbital exenteration. Pathological examination results confirmed the diagnose of liposarcoma for 13 patients. Six patients displayed as myxoid type, and three patients in each type of dedifferentiated and well-differentiated type. One patient was verified as pleomorphic,

which was a rare type of liposarcoma. All of the patients showed Vimentin positive, and most showed CD34 and S-100 positive. Besides, four patients showed smooth muscle actin positive. All thirteen patients were alive.

• **CONCLUSION:** Orbital liposarcoma is a rare disease and it has no specific clinical manifestation. The diagnosis of liposarcoma should be considered when proptosis and orbital mass occurred in orbit. It is recommended to perform pathological examination to achieve early detection and early treatment.

• **KEYWORDS:** liposarcoma; orbital tumor; orbital mass; proptosis

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INTRODUCTION

Liposarcoma is rare in all neoplasm malignancies. Most of the liposarcoma are located in the deep soft tissue, such as retroperitoneum and mesenteric region, while less than 5% occur in the head and neck region^[1-3]. Furthermore, the occurrence of orbital liposarcoma is extremely rare. In the largest study population of 318 patients, who suffered head and neck liposarcoma, derived from the National Cancer Institute^[4], surprisingly, the study did not demonstrate any case of orbital tumors. Approximately 40 cases of primary orbital liposarcoma have been reported in the previous English literature^[5-15]. However, they scatteredly reported the clinical history, manifestation, characteristics, and histological subtypes of orbital liposarcoma. Owing to the invasiveness and the poor prognosis of orbital liposarcoma, early detection and treatment become extremely important. However, the nonspecific clinical manifestation of orbital liposarcoma makes the diagnosis highly challenging. From this, we aimed to conduct a study to gain a thorough understanding of the characteristics of orbital liposarcoma.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the ethics review committee of Beijing Tongren Hospital and was

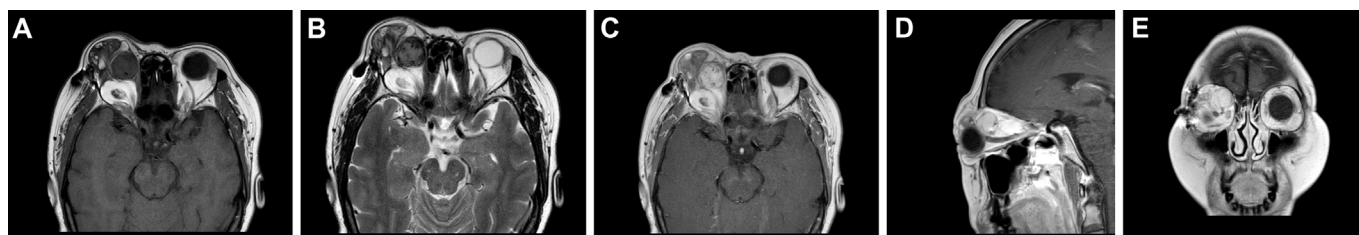


Figure 1 MRI image of orbital liposarcoma MRI: Magnetic resonance imaging.

conducted in accordance with the Declaration of Helsinki. Telephone follow-up was performed in December 2021, and informed consent was obtained from all patients.

Patients This was a retrospective, single-center, and clinical study. We retrospectively gathered and analyzed medical health records of all patients with orbital liposarcoma from the database of Beijing Tongren Hospital, Capital Medical University from 2006 to 2021. The diagnosis of liposarcoma was confirmed by two professional pathologists.

Clinical Data Collection General information was obtained from the medical records review, including data of age, sex, affected orbital side, disease course, disease status (primary or recurrent), clinical manifestations, and preoperative visual acuity. Visual acuity was observed by logMAR visual chart and reported with the 5-grade notation of the standard logarithmic visual acuity chart (visual acuity=5-logMAR). The visual acuity lower than 4.9 was regarded as vision loss. We collected the data of therapy, including operative treatment, relationship between liposarcoma and the surrounding tissue (optic nerve, striated muscle, and orbital bone), longest diameter of the liposarcoma, histological subtype (myxoid, dedifferentiated, well-differentiated, and pleomorphic), immunohistochemical indicators [Ki-67, Vimentin, CD34, smooth muscle actin (SMA), and S-100], follow-up treatment, and prognosis.

Operative Treatment and Follow-up Treatment All patients received operative treatment once they were diagnosed with an intraorbital tumor. The operative treatment included tumor resection and orbital exenteration. Two professional ophthalmologists decided the operation plan. Orbital exenteration should be performed once the tumor invaded the surrounding tissue. The incisions were designed depending on the tumor size, such as conjunctival incision combined with lateral cantholysis, eyebrow arch skin incision, and double-eyelid skin incision. For medium-sized and well-defined tumors, tumor resection would be performed. For large or aggressive tumors involving the optic nerve, enucleation is the most common surgical option.

Follow-up treatment mainly includes radiotherapy, depending on the invasiveness and metastasis of liposarcoma. Common methods were radioactive seed implantation and external gamma radiation therapy. The appropriate radiation range was chosen according to the pathological type of the tumor

and the extent of tumor involvement. All the radiotherapy for liposarcoma patients were performed by radiologists.

RESULTS

Preoperative Demographics and General Information of Patients with Liposarcoma Overall, 13 patients had orbital liposarcoma and received surgical treatments at Beijing Tongren Hospital, Capital Medical University. Details of patients' demographics and general information were shown in Table 1. Magnetic resonance imaging (MRI) images of one patient were shown in Figure 1. Up to December 2021, all 13 patients were alive. Some of them kept regular return visit and the others were confirmed by telephone follow-up.

Mean age of patients was 45.2 ± 17.44 y (range 19–81y). In terms of sex and laterality, female patients outnumbered male patients, and oculus dexter outnumbered oculus sinister. Mean duration of the disease course was 10.7 ± 9.8 mo (range 1–36mo). Twelve patients had a primary diagnosis of liposarcoma, and one patient had liposarcoma in the groin approximately 3 years ago. Moreover, proptosis was the most frequent chief complaint in all the patients, and some of the cases were complicated with epiphora (case No.5), and diplopia (cases No.3 and No.10). Additionally, two patients had an eyelid palpable mass as well (cases No.1 and No.2). In our study, patients whose preoperative visual acuity was lower than 4.9 comprised 69.2% of the total cases.

Intraoperative and Postoperative Information of Patients with Liposarcoma All the patients underwent an operation and two professional ophthalmologists decided the operation plan. Ten patients received tumor resection, and attempts were typically made to excise the entire suspicious lesion during the operation (Figure 2A). After the operation, eight patients received radiotherapy, including radioactive seed implantation and external gamma radiation therapy (Figure 2B). As for the rapid development of surgical technique and radiotherapy, only three patients received orbital exenteration.

Usually, malignancies with aggressive behavior would involve the surrounding tissue. According to the operative recordings, we found that striated muscle was more likely to be invaded. Furthermore, 15.4% and 7.7% of tumors involved the orbital bone and optic nerve, respectively (Figure 2C). Tumor size was another factor that might affect the prognosis. The mean longest diameter of liposarcoma was 3.39 ± 1.36 cm, which

Table 1 Details of 13 patients with orbital liposarcoma

No.	Age (y)	Sex	Affected orbital side	Disease course (mo)	Disease status	Clinical manifestations	Visual acuity	Operative treatment	Follow-up treatment	Relations between liposarcoma with surrounding tissue	Longest diameter of liposarcoma (cm)	Histological subtype	Immunohistochemical indicators				
													Ki-67	Vimentin	CD34	SMA S-100	
1	51	F	OS	1	Primary	Eyelid palpable mass	1	Tumor resection	Radioactive seed implantation	Orbital bone	1.8	Myxiod	60%	+	+	+	+
2	44	M	OD	16	Primary	Eyelid palpable mass	5.1	Orbital exenteration	External gamma radiation therapy	Optic nerve	6	Dedifferentiated	1%	+	+	-	+
3	81	M	OS	12	Primary	Proptosis & diplopia	4.9	Tumor resection	Radioactive seed implantation	/	2.8	Myxiod	/	/	/	/	/
4	36	F	OD	2	Primary	Proptosis	4.85	Tumor resection	External gamma radiation therapy	/	5	Pleomorphic	70%	+	+	-	+
5	61	F	OS	10	Primary	Proptosis & epiphora	4.9	Tumor resection	External gamma radiation therapy	/	2.8	Well-differentiated	1%	+	+	+	+
6	19	F	OD	12	Primary	Proptosis	5	Tumor resection	/	Striated muscle	/	Myxiod	3%	+	-	-	+
7	24	F	OD	36	Primary	Proptosis	4.8	Tumor resection	No follow-up treatment	Striated muscle	/	Dedifferentiated	100%	/	+	+	+
8	63	M	OS	12	Primary	Proptosis	4.7	Orbital exenteration	No follow-up treatment	Optic nerve	3.5	Myxiod	5%	+	/	-	+
9	36	F	OD	9	Primary	Proptosis	3.8	Orbital exenteration	External gamma radiation therapy	Optic nerve	4	Well-differentiated	5%	+	+	-	-
10	57	F	OD	24	Primary	Proptosis & diplopia	3	Tumor resection	No follow-up treatment	Striated muscle	2	Dedifferentiated	3%	+	+	+	+
11	34	M	OD	1	Primary	Proptosis	4.85	Tumor resection	External gamma radiation therapy	Orbital bone	4	Myxiod	40%	+	-	-	+
12	50	M	OS	8	Secondary	Proptosis	3.5	Tumor resection	/	Striated muscle	/	Myxiod	/	/	/	+	-
13	32	F	OD	6	Primary	Proptosis	3.3	Tumor resection	External gamma radiation therapy	Striated muscle	3.5	Well-differentiated	20%	/	+	-	-

OD: Right eye; OS: Left eye; SMA: Smooth muscle actin.

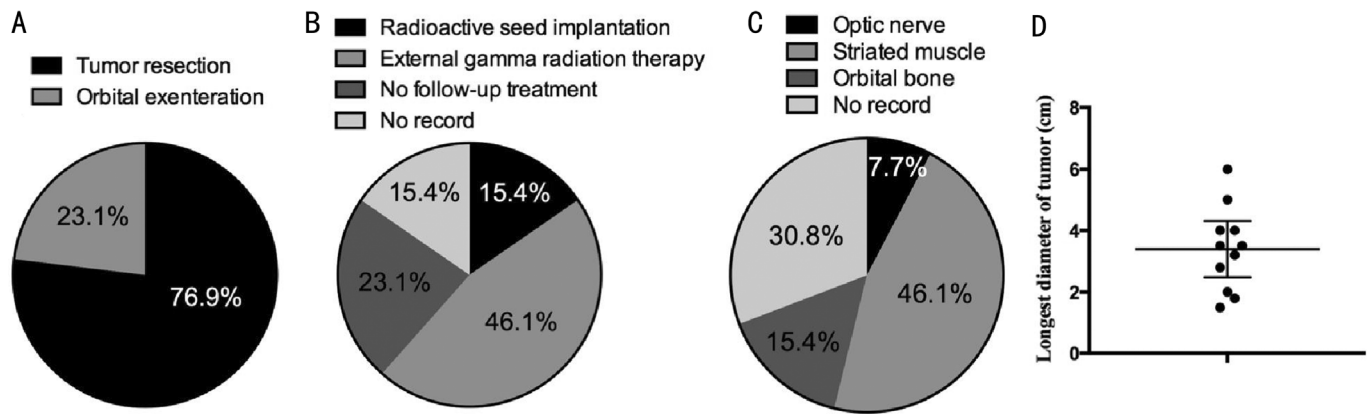


Figure 2 Intraoperative and postoperative information of patients with liposarcoma A: Surgical technique; B: Follow-up treatment; C: Surrounding tissue invaded by the tumor; D: Longest diameter of the tumor.

ranged from 1.5 to 6.0 cm (Figure 2D).

Histopathological Characteristics of Patients with Liposarcoma Histopathological analysis is the “gold standard” method for tumor diagnosis. All of 13 patients were examined by histopathology, and the results of all patients suggested liposarcoma (Figure 3). Six patients had a myxoid type, and there were several three patients had the dedifferentiated and well-differentiated types. Only one patient was verified to have a rare type of liposarcoma as pleomorphic subtype (Figure 4A). Furthermore, all the patineds also detected immunohistochemical indicators. The results of Ki-67 detection in immunohistochemical analysis are shown in Figure 4B. All of the patients were positive for Vimentin, and most of the patients were positive for CD34 and S-100. Moreover, SMA expression was positive in four patients and negative in six patients (Figure 4C).

DISCUSSION

Despite the abundance of fat in the orbit, orbital liposarcoma rarely occurs. The first description of orbital liposarcoma was given by Strauss appeared in 1911^[7]. Only nearly 90 cases globally were reported in the literature. One study reviewed seven orbital liposarcoma patients gathered from two American hospitals, while others reported almost individual cases. Thus far, none of the studies have summarized pathonomia, such as age, sex, and disease course. We retrospectively analyzed 13 patients with orbital liposarcoma who received treatments in the Department of Ophthalmic Oncology in Beijing Tongren Hospital in the recent 15y, *i.e.*, from 2006 to 2021. In our study, we found that liposarcoma tends to occur in middle-aged and elderly patients. In our study, we found out that the mean age of onset was 45.2 years old, and 8 patients, approximately 61.5% were middle-aged adults (30–60 years old). Furthermore, in terms of sex and laterality, female patients outnumbered male patients, and oculus dexter outnumbered oculus sinister. The mean duration of the disease course was 10.7mo. And our results showed that 12 of the 13 patients had a primary

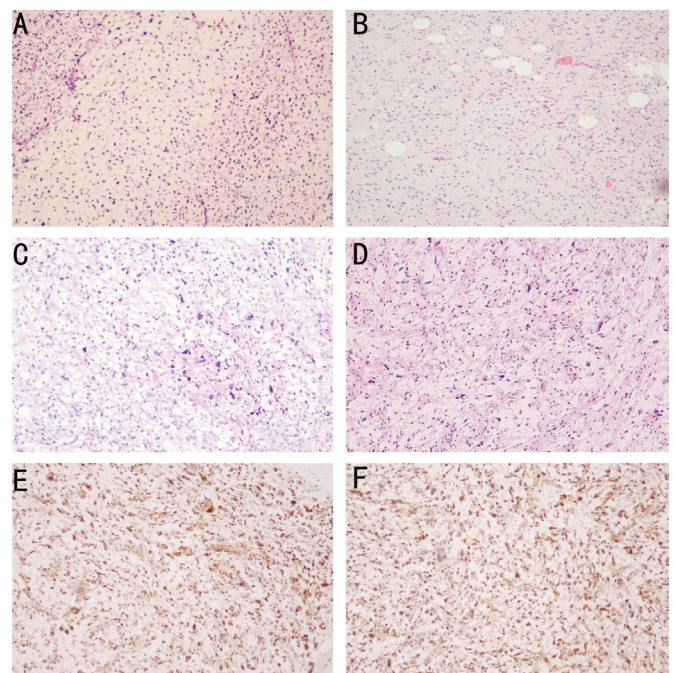


Figure 3 Histopathological image of each major tumor subtype of orbital liposarcoma (x100) A: Myxoid; B: Well-differentiated; C: Dedifferentiated; D: Pleomorphic; E: Expression of MDM-2; F: Expression of CDK-4.

diagnosis of liposarcoma, and only one patient was labelled as secondary liposarcoma. This patient found tumor in the groin 3 years ago, and in orbit this time. Both of the two tumor were confirmed by operation and pathology that the patient got liposarcoma. However, these features of orbital liposarcoma were found to be somewhat distinct from other liposarcoma. Alessandra reported that liposarcoma occurred most frequently in the age group of 40–60y individuals, and there were more male patients than female patients^[16]. These discrepancies might be related to racial and regional differences. The most common presenting symptom of orbital liposarcoma was proptosis, with or without pain. Zhang *et al*^[7] reported that the main clinical symptoms was proptosis (92.1%), diplopia (42.1%), vision loss (28.9%), and localized congestion (21.1%).

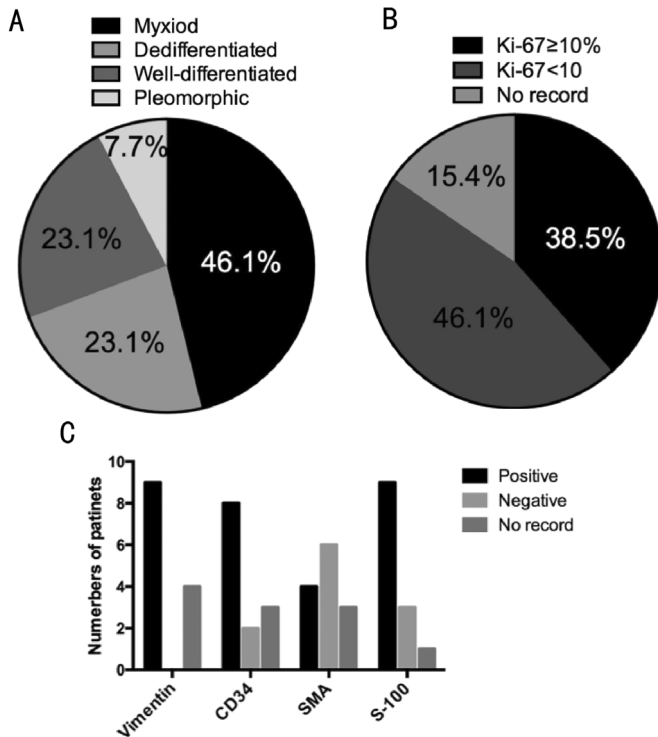


Figure 4 Histopathological characteristics of orbital liposarcoma A: Histopathological type; B: Expression of Ki-67; C: Expression of Vimentin, CD-34, SMA, and S-100.

Moreover, a few patients had pain, limited eye movement, and even smell or taste disorders. In our study, proptosis was the major clinical manifestation (11/13, 84.6%), and some of patients had complications such as vision loss, epiphora, and diplopia. The other 2 patients (2/13, 15.4%) also had eyelid palpable mass. This feature had never been reported in the past cases. In addition, as other types of orbital tumor, once the tumor implicated with the optic nerve, the visual acuity would be injured. In our study, four patients still had good visual acuity (No.2, 3, 5, 6). It indicates that in clinical practice, early diagnosis is difficult for nonspecific symptoms and signs of orbital tumor. Thus, imaging examination is important for diagnosis and visualization of the extent of the tumor and the relationship between the lesion site and adjacent structures.

At present, surgical resection is the primary and most effective method for treating orbital liposarcoma. Furthermore, in addition to resecting the tumor, surgery can also obtain histologic confirmation of the disease and help make plans for further treatments. Indeed, surgical resection with expanded margins admittedly improves survival and local control, but most of the orbital liposarcoma cannot be completely resected without damaging infiltrated structures, particularly the extraocular muscles^[17]. Conservative concepts recommend that invasive, dedifferentiated, and recurrent orbital liposarcoma is indicated to perform orbital exenteration. However, orbital exenteration is too traumatic and may lead to physical and mental disorders. With the development of surgical technique

and tumor radiotherapy, also more pinned importance to the ocular appearance, tumor resection with adjuvant radiotherapy is adopted by ophthalmologists in recent years^[17-18]. In our study, 6 patients had an aggressive tumor involving the striated muscle. Two and 3 patients had an aggressive tumor involving the orbital bone and optical nerve, respectively. Yet, only 3 patients who received orbital exenteration, and 2 of them received it a decade ago. Furthermore, 8 patients received adjuvant radiotherapy after surgery. Up to December 2021, all 13 patients were alive. As can be seen, the implementation of orbital exenteration declined with adjuvant radiotherapy. The differences in the long-term outcome between tumor resection and orbital exenteration need a longer observation period.

The World Health Organization recognizes four histologic types of orbital liposarcoma: myxoid, dedifferentiated, well-differentiated, and pleomorphic^[9]. Liposarcoma in the soft tissues accounts for 40%–50% of all liposarcoma subtypes^[17], and it is well correlated with orbital liposarcoma, as myxoid liposarcoma of the orbit is the most common histological type (55%)^[7]. In our study, 6 patients (46.1%) had the myxoid type, and 3 patients (23.1%) had dedifferentiated and well-differentiated types respectively. The pleomorphic subtype was a rare type of liposarcoma, and only 1 patient (7.7%) was verified to have the pleomorphic subtype. Myxoid and well-differentiated orbital liposarcoma have a relatively low aggressiveness, while the dedifferentiated and pleomorphic types usually behave aggressively with infiltration and distant metastasis^[9]. With the development of histopathology, diagnostic precision of liposarcoma may increase *via* modern immunohistochemical techniques, using antibodies against Ki-67, Vimentin, CD34, SMA, and S-100^[17]. Among these indicators, Ki-67 is a marker of cell proliferation, and a high expression level of Ki-67 implies enhanced proliferation of the tumor cells. It would stand to reason that a high Ki-67 could represent an aggressive tumor with poor outcome. Our study analyzed the Ki-67 proliferation index in those 13 cases, and 5 of 13 cases had a Ki-67 index of >10%. Furthermore, most of the patients were positive for Vimentin, CD31, and S-100, and all the indicators represent proliferation and malignancy of tumor cells. The prognosis of orbital liposarcoma depends on several factors, including histological type, grade of differentiation and tumor size. In our study, the mean longest diameter of the orbital liposarcoma was 3.39 cm (range from 1–6 cm). Up to December 2021, no distant metastasis occurred. Therefore, all the results together suggested that combined consideration of these factors would better predict the prognosis of orbital liposarcoma.

In conclusion, the occurrence of orbital liposarcoma is extremely rare, and the nonspecific clinical manifestation

makes diagnosis difficult. Through the summary and analysis of this article, we hope to deepen our understanding of the clinical and pathological characteristics of orbital liposarcoma. Orbital liposarcoma should be considered early in patients with unilateral proptosis, vision loss, ocular motility disorder, rapid disease progression, combined with their imaging features. Image examinations with computed tomography (CT) and MRI can reveal the location and infiltration of the tumor, but the primary means of diagnosis remains to be histopathological examination. Surgical resection should be performed with ample margins, and following radiotherapy can improve the prognosis and prolong survival, minimize the risk of tumor development, invasion and metastasis, and reduce the occurrence of complications such as exposure keratitis and orbital wall damage.

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