



Recurrent primary orbital well-differentiated liposarcoma /atypical lipomatous tumor: A rare case report with six-year follow-up

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ABSTRACT

Purpose: We report a case with over 6 years of follow-up for well-differentiated liposarcoma or atypical lipomatous tumor (WDL/ALT).

Observations: Over a 6-year time course, a patient with a recurrent right orbital mass was biopsied/debulked four times. It was not until the fourth biopsy that a diagnosis of WDL/ALT was obtained. Throughout the time course, the patient maintained good vision and there has been no evidence of dedifferentiation or metastasis thus far.

Conclusions: The diagnosis of WDL/ALT should be considered in the cases of a recurrent orbit mass when pathology continually shows nonspecific fibrofatty tissue with chronic inflammatory changes.

1. Introduction

Liposarcoma is the most common soft tissue sarcoma in adults. The majority of liposarcomas occur in the limbs and retroperitoneal space.¹ Orbital involvement is rare. The typical presentation of an orbital liposarcoma is painless progressive proptosis due to intraconal or extraconal involvement.² Well-differentiated liposarcoma or atypical lipomatous tumor (WDL/ALT) is the most common subtype of liposarcoma, characterized by local aggressive behavior and very low metastatic potential unless the cells dedifferentiate.³ We present a patient with localized orbital WDL/ALT with over six years of follow-up at our institution with multiple biopsies for multiple episodes of tumor regrowth.

2. Clinical course

The patient is a 39-year-old female with no significant past medical history who first presented to our clinic for a second opinion regarding a recurrent right orbital mass. She had initially developed subacute proptosis of her right eye and binocular diplopia three years prior. She had already undergone an anterior orbitotomy with biopsy followed by strabismus surgery shortly after at an outside facility. Pathology from the biopsy performed prior to presentation to our institution was reported as benign glandular tissue consistent with lacrimal gland with only mild chronic inflammation.

Upon initial evaluation, she was noted to have no compromise to her vision. She had a best corrected visual acuity (BCVA) of 20/20 in both eyes, full color vision in both eyes, no relative afferent pupillary defect, and no visual field defects in either eye. Her exam was significant for right-sided proptosis (25mm on the right compared to 18mm on left by Hertel) and a −2 limitation of supraduction in the right eye. Magnetic resonance imaging (MRI) of the orbits demonstrated a right intraorbital mass that was closely associated with the superior and lateral rectus muscles (Fig. 1).

After discussing the risks, benefits, and alternatives with the patient, she decided to proceed with a repeat orbitotomy for biopsy and debulking of the mass. During the procedure, the mass was dissected off the superior and lateral recti and appeared to have been removed in its entirety except for a small defect in the outer “capsule” (possibly due to the prior biopsy). Pathology of the mass was interpreted as pleomorphic lipoma with focal mild lymphoid follicular hyperplasia. Repeat MRI six months after the second orbitotomy showed that the orbital mass was smaller in size but still with residual tumor in the superior aspect of the orbit along the superior rectus. During the postoperative period, the patient maintained good vision, full color vision, and full visual fields in both eyes.

The patient returned two years later. She presented again with worsening right-sided proptosis (23mm on the right compared to 15mm on left) without visual compromise. Repeat MRI of the orbits showed an increase in the size of the mass with associated proptosis and

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enhancement of the mass. The decision was made to proceed with a 3rd debulking of the mass to primarily improve the patient's proptosis. Pathology of the specimen showed fat lobules and striated muscle separated by dense connective tissue with mild chronic inflammation. Flow cytometry was unremarkable. After the surgery, the patient maintained good vision, full color vision, and full visual fields in both eyes. The patient developed worsening right hypotropia and esotropia for which she underwent left inferior oblique and medial rectus recession along with right inferior rectus recession, lateral rectus resection, and superior rectus resection.

One year following her third orbitotomy, MRI of the orbits redemonstrated an ill-defined enhancing lesion within the superior anterior aspect of the orbit with secondary proptosis. There were also areas of nodular enhancement along the lateral aspect of the lesion. At this time, the patient was stable morphometrically and the decision was made to repeat imaging and follow-up in six months.

At the next visit, the patient reported worsening orbital pain, proptosis, and diplopia. The patient still had good vision without evidence of optic nerve compromise. However, the eye was noted to be more proptotic (26 mm on the right compared to 17 mm on left) with hypoglobus of the right eye. MRI showed increased size of the mass with significant mass effect on the right lateral and superior rectus muscles. The decision was made once again to undergo orbitotomy for debulking. During the procedure, the mass was noted to be firmly adherent to the adjacent superior and lateral rectus muscles and the optic nerve. Due to the posterior extension and adherence to the optic nerve, the lesion was removed subtotally. This 4th biopsy, was interpreted as WDL/ALT.

Given the patient's multiple recurrences and final diagnosis of WDL/ALT, the idea of exenteration versus close monitoring was introduced. The patient was referred to another institution for a second opinion. Given her good visual function and low risk of metastasis potential, the patient elected to continue close observation.

3. Results

The first biopsy performed in our facility in 2016 was large (2.5 and 2.2 cm). The cut surfaces were yellow lobulated adipose tissue with no discrete alteration. Microscopic findings showed a few circumscribed areas of fibrosis containing lymphocytic infiltration with occasional lymphoid follicles, many plasma cells, and a few eosinophils. Fibroadipose stroma near the inflammatory infiltrates contained a few atypical cells featuring markedly enlarged nuclei in a myxoid background. Immunohistochemistry (IHC) stains showed that the large atypical cells were negative for S100 but positive for CD34. The lymphoid cells in the follicles stained for both CD3 and CD20 with CD20 showing more diffuse positive staining in the extrafollicular areas. Occasional plasma cells stained for IgG4 with an IgG4/IgG ratio of 18.3% (greater than 40% is required for the diagnosis of IgG4-related disease). A diagnosis of pleomorphic lipoma with focal mild lymphoid follicular hyperplasia was rendered.

The most recent specimen that was obtained in 2021 consisted of

three fibrofatty nodules that were 2.0, 3.0, and 3.5 cm in their greatest dimension. Histopathology revealed fibroadipose tissue which was scattered throughout the specimen with some myxoid changes (Fig. 2A–B). Fibrous tissue interdigitated between adipocytes and fat lobules with embedded atypical cells (Fig. 2C). Fibrous regions contained chronic inflammation in the background, which was exuberant in some regions. IHC of Ki-67 identified only very rare dividing cells, representing <1% of the total atypical cells present (Fig. 2D). Fluorescent in situ hybridization (FISH) of MDM2 gene on chromosome 12q15 versus chromosome enumeration probe on the same chromosome (CEP12) was amplified with a MDM2/CEP12 ratio of 9.63 (Fig. 3). This supported the diagnosis of WDL/ALT. Flow cytometry showed a mild kappa light chain excess among polyclonal B lymphocytes but no definite monoclonal population. This further ruled out the lymphoid background as being a hematolymphoid malignancy.

4. Discussion

Liposarcoma accounts for 15%–25% of all sarcomas and is the most common sarcoma of adults. According to the World Health Organization (WHO), liposarcomas are categorized into four subtypes—well-differentiated liposarcoma/atypical lipomatous tumor (WDL/ALT), myxoid/round cell, dedifferentiated, and pleomorphic types.³ Liposarcoma is extremely rare in the orbit, reported as less than 0.4% (six cases) of all orbit tumors (1795 cases) from a single institutional experience between 1948 and 1997⁴ - less than 1% of all liposarcoma cases.² So far, less than 70 primary orbital liposarcoma cases have been reported and less than 30 of them have been the WDL/ALT subtype, slightly more than myxoid/round cell type.^{5–11} Although WDL/ALT is considered to have the least potential to metastasize among all subtypes of liposarcomas, local invasion or recurrence have been reported.^{2,5,6,11,12} Only four of 29 cases in the literature have been followed up for at least six years as in our current case. Three out of four of these cases had local recurrence.^{2,12,13}

Histopathologically, WDL/ALT usually presents as a relatively benign tumor composed of mature adipocytes with nuclear atypia. The morphological diagnosis of WDL/ALT sometimes can be challenging to differentiate from benign spindle cell/pleomorphic lipoma which characteristically has spindle cells or multinucleated floret cells.¹⁴ Although these cells are usually bland looking, lipoblasts and mitotic figures can be seen. "Ropey" collagen and mast cells are helpful diagnostic clues to favor spindle cell/pleomorphic lipoma. For morphologically challenging cases, IHC and cytogenetic studies such as FISH study are helpful. WDL/ALT and dedifferentiated liposarcoma are characterized by supernumerary ring and/or giant marker chromosomes containing amplified material in chromosome 12q14-15, leading to MDM2 and CDK4 overexpression.^{15,16} MDM2(+) and CDK4(+) by IHC and amplification of MDM2 by FISH are supportive of ALT/WDL diagnosis while excluding benign lipomatous tumors.^{16–18}

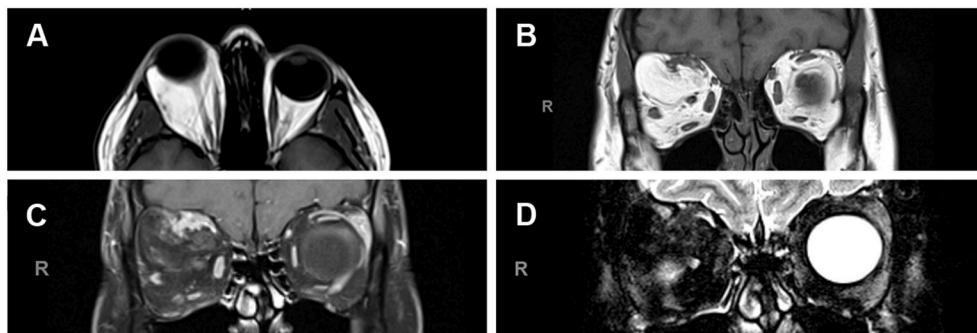


Fig. 1. MRI orbits with and without contrast from the first presentation to our institution. (A) T1 axial image with noted right sided proptosis and a mass measuring approximately 2 cm craniocaudad. (B) T1 coronal image with noted superior location of mass that measured 3cm transversely. Mass was inseparable from the superior rectus, adjacent to the lateral rectus, and touching the optic nerve. (C) T1 post-contrast image with noted minor component with enhancement. (D) T2 fat suppressed image with noted major composition of mass with fat.

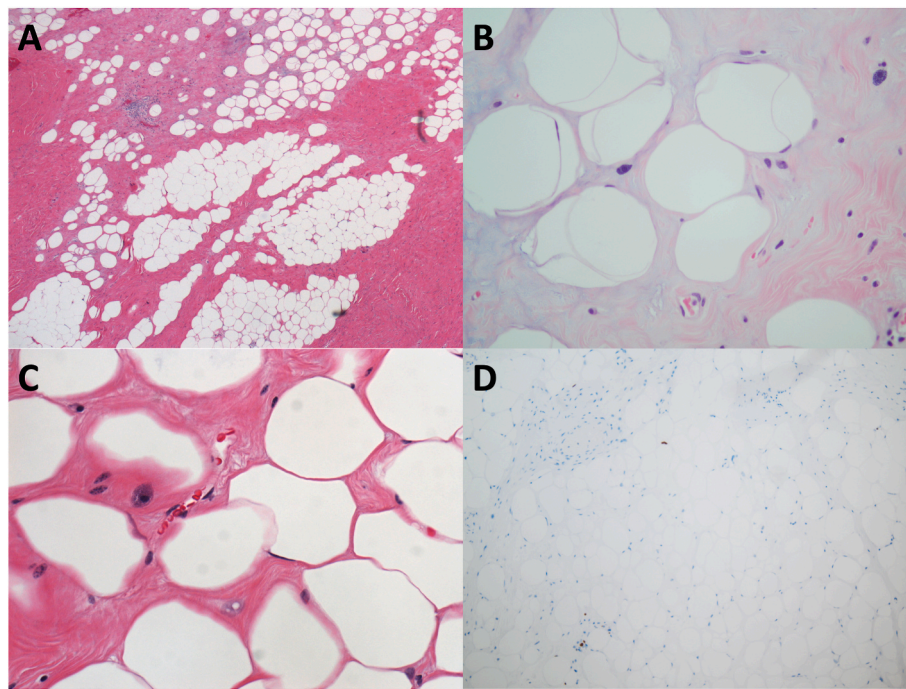


Fig. 2. Histopathology for the 4th biopsy showed that the recurrent mass consisted of adipose tissue mixed with thickened fibrous septa with increase cellularity (A, x40). The proliferation of adipocytes cells has atypical and hyperchromatic nuclei (B & C, x400) with occasional prominent nucleoli (C, x400). Myxoid change is also noted (A & B). IHC stain of Ki-67 proliferation index is less than 1% of cells (D, x100).

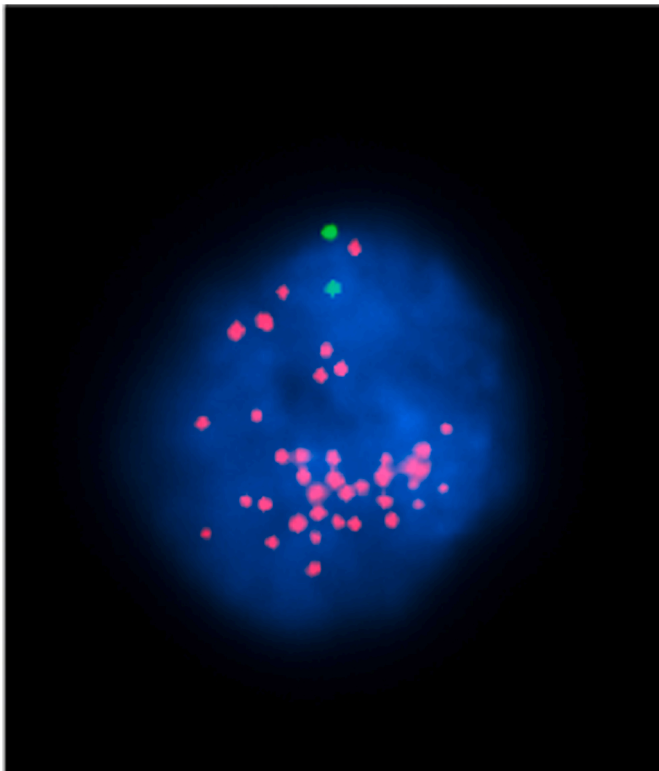


Fig. 3. FISH MDM2 (12q15) gene amplification was observed in the lesional cells (red). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

5. Conclusion

We have outlined a six-year clinical course of a patient with localized WDL/ALT of the orbit, the longest follow-up period documented for such a diagnosis. Throughout the patient's course, a recurrent right orbital mass was biopsied/debulked four times, and it was not until the fourth biopsy that a diagnosis of WDL/ALT was obtained. It is important to consider liposarcoma as an etiology of a recurrent orbital mass when pathology continually shows nonspecific fibrofatty tissue with chronic inflammatory changes. The addition of IHC looking for MDM2 and CDK4 positivity or FISH analysis for MDM2 amplification should be performed to aid in making the final diagnosis in challenging cases. The patient's vision was never affected throughout her clinical course and there has been no evidence of dedifferentiation or metastasis thus far. Definitive treatment for WDL/ALT is exenteration, but in a patient with good vision as in this case, it is reasonable to monitor closely with clinical exams and MRIs given the low incidence of local invasion and metastasis. It should be discussed with patients that there is a possibility for local recurrences of the tumor despite resection in cases where eye-preserving surgeries are performed. Referral to a regional cancer center is also reasonable to better inform the patient and surgeon regarding prognosis and potential therapies.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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