

CASE REPORT

Myxoid/round cell conjunctival liposarcoma. A case report

STELA GIURI¹⁾, M. RAICA²⁾, M. MUNTEANU³⁾¹⁾*"Dr. Giuri Stela" Private Medical Office, Timisoara*²⁾*Department of Histology,
Angiogenesis Research Center Timisoara*³⁾*Department of Ophthalmology**"Victor Babeş" University of Medicine and Pharmacy, Timisoara***Abstract**

Purpose: To present a rare case of conjunctival myxoid liposarcoma, subtype round cells, that had a seven years follow up. **Clinical observation:** A 61-year-old female patient presents with a palpable, non-painful tumor, on the superior temporal bulbar conjunctiva of the right eye. The initial examination detects a fleshy tumor, orange in color, under the superior temporal bulbar conjunctiva, as well as two oval-shaped hyperpigmented conjunctival lesions, near the limbus at 10 o'clock, causing moderate blepharoptosis. Vision was normal, there was no diplopia, proptosis, afferent pupillary defect or lymphadenopathy; there was no orbital involvement in MRI. An isolated 15/15 mm tumor, with no connections with the eye socket, was excised. Histopathology revealed a poorly differentiated myxoid liposarcoma. Five recurrences occurred, of which four were treated by local excision and the last required exenteration. Repeat histopathology detects lipoblasts, small round cells, with immunohistochemistry positive for CD34, S100 and vimentin. The last two rapidly evolving and large recurrences, as well as pulmonary metastasis and finally death of the patient, underlined the aggressive character of round cell conjunctival liposarcoma. **Conclusions:** Conjunctival myxoid liposarcoma is characterized by numerous local recurrences, but the speed of the succession and volume of the recurrences may suggest a change in the underlying histopathological aspect, that is definitory for the therapeutical and prognostic approach of the case.

Keywords: conjunctival tumors, myxoid/round cell liposarcoma.

Introduction

Myxoid liposarcoma is a malignant tumor of primitive mesenchymal lipoblasts, characterized by signet ring lipoblasts, myxoid stroma, undifferentiated small round cells, and a well-developed vascular network. Myxoid liposarcoma subtype with round cells is less common, and liposarcoma with pure round cells is very rarely. Liposarcoma is frequently mixed, with round cells and myxoid components in different proportions. The elective site of liposarcoma is the lower extremities and the retroperitoneum, primary or metastatic orbital liposarcoma is extremely rare [1]. We only found one case of conjunctival myxoid/round cell liposarcoma published in the literature [2]. We report a case of myxoid/round cell conjunctival liposarcoma with aggressive evolution.

Patient, Methods and Results

The patient, a 61-year-old female, was complaining about a mass in the external third of the right eye that appeared eight months before. At first examination (in 2000), we found a tumor mass of the bulbar conjunctiva, orange-red with a gelatin-like consistency, localized supero-temporally, and two distinctive, slightly pigmented, juxtalimbal lesions. Visual acuity was normal and unmodified until the last recurrence. The patient did not display proptosis, eye movement limitations, satellite adenopathy, or orbital involvement in MRI. Wide excision of the tumor mass, with no orbital extension, was performed.

Five other local recurrences were found and treated surgically over seven years of evolution. The macroscopic aspect of the tumor changed over the years, from a smooth orange-red, slightly prominent formation to a fleshy, dark red, prominent tumor with exulcerated areas and bleeding surface (Figure 1). The juxtalimbal lesions, that were never excised, progressed from hypopigmented slightly prominent, poorly delimited areas to hyperpigmented prominent well-delimited lesions, rapidly growing over the last year, turning into red-brown fleshy lesions (Figure 2).

At the time of the last recurrence, a large infiltrative mass is found, and the patient underwent orbital exenteration followed by skin graft of the orbital cavity. Six months later the patient died after being diagnosed with right pulmonary metastasis with aggressive evolution despite chemotherapeutic treatment.

The specimen was fixed in buffered formalin at pH 7.2 for 24 hours and embedded in paraffin, according to the standard histological procedure. Five-µm thick sections were stained with Hematoxylin–Eosin–Safran and Gömöri's trichromic methods for the pathological diagnosis. Additional slides were prepared for immunohistochemistry. In brief, after dewaxing and hydration, slides were submitted to antigen retrieval in buffer citrate pH 7.2, endogenous peroxidase was blocked with 3% hydrogen peroxide and incubated with the primary antibody for 30 minutes. We used the working system labeled Streptavidin–Biotin complex and the final product of reaction was made evident with 3,3'-diaminobenzidine

in brown. The panel of primary antibody included vimentin (clone V9), S100 protein (polyclonal) and CD34 (Qbend10). All reagents were from Dako (Glostrup, Denmark).

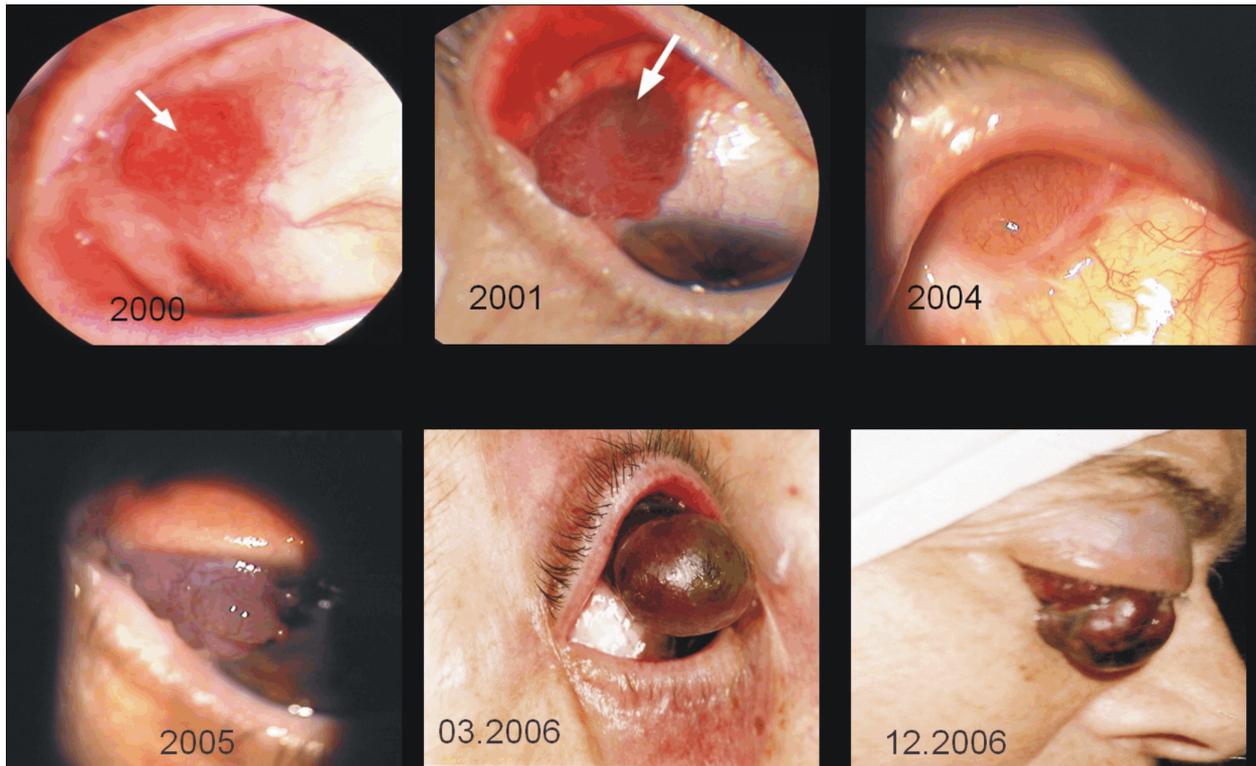


Figure 1 – Clinical evolution of tumor mass (2000–2006).

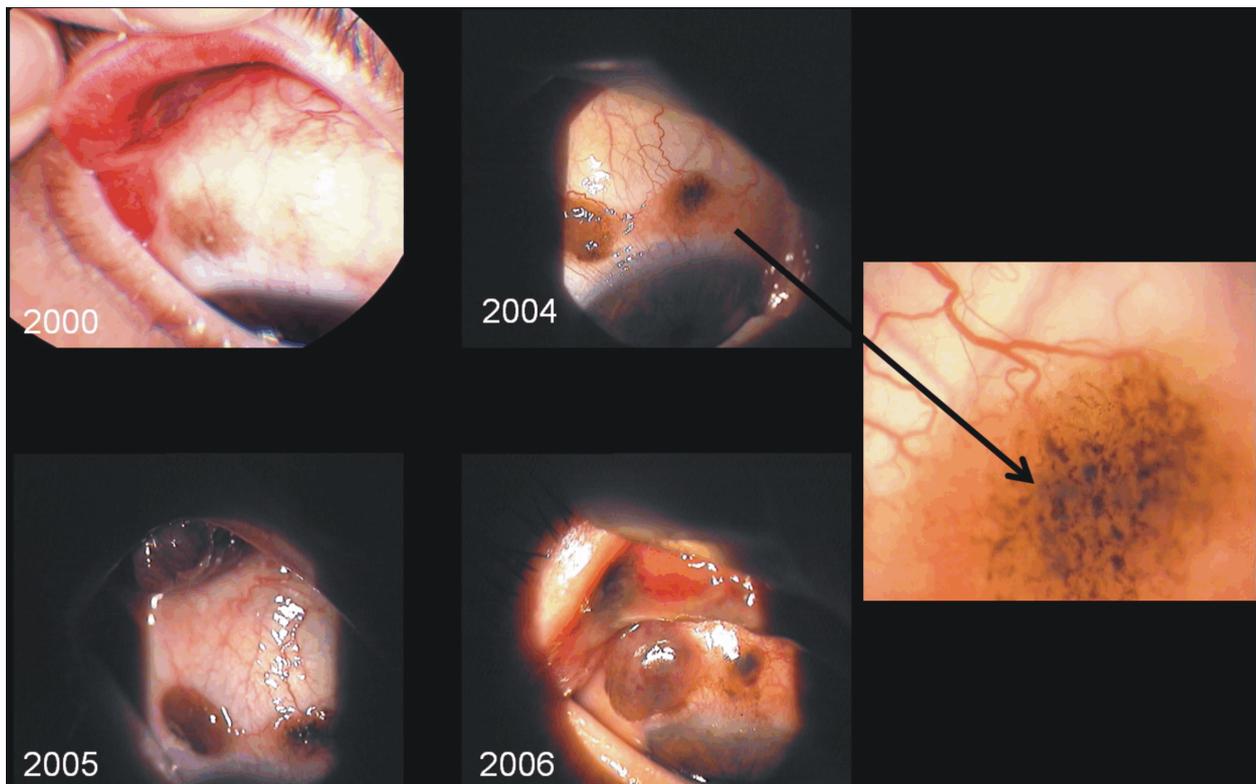


Figure 2 – Clinical evolution of juxtalimbal tumor mass (2000–2006).

The microscopic examination revealed a solid and diffuse proliferation of tumor cells, more or less differentiated toward the adipose line. Tumor cells were medium in size or large, with severe nuclear atypia and in the cytoplasm of majority, there were notices lipid droplets (Figure 3). A significant number of neoplastic

cells showed marked hyperchromasia and atypical mitosis (Figure 4). The mesenchymal nature of the proliferation was demonstrated by the strong expression of vimentin in the cytoplasm of virtually all tumor cells (Figure 5). The diagnosis of liposarcoma was further confirmed by the expression of S100 protein, with intense reaction

particularly at nuclear level (Figure 6). A rich vascular network in the tumor area was demonstrated with anti-

CD34, supporting the aggressive behavior of this tumor (Figure 7).

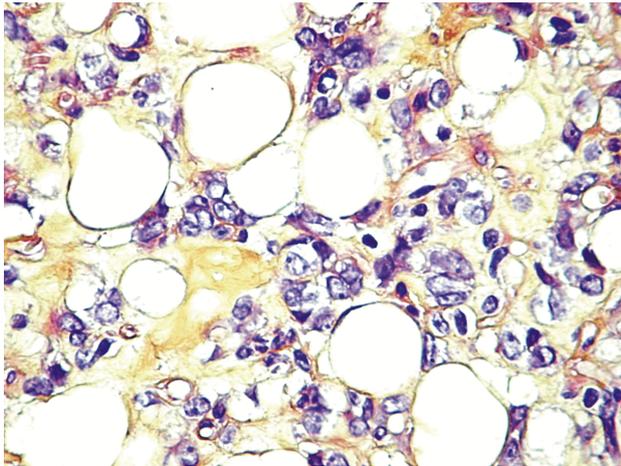


Figure 3 – Proliferation of tumor cells containing lipid droplets in the cytoplasm. Hematoxylin–Eosin–Safran, $\times 400$.

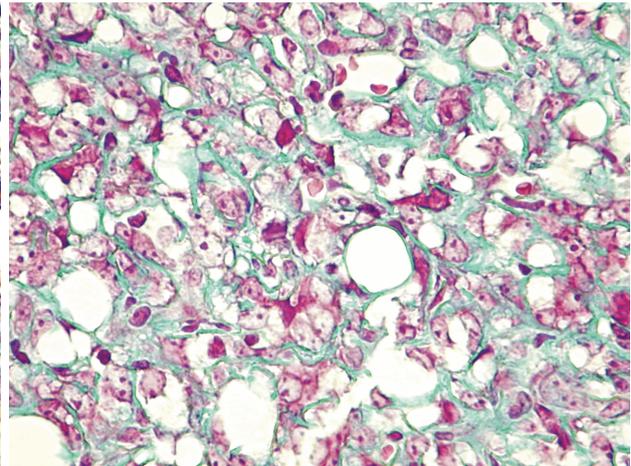


Figure 4 – Severe nuclear atypia and atypical division in tumor cells. Gömöri's trichromic method, $\times 400$.

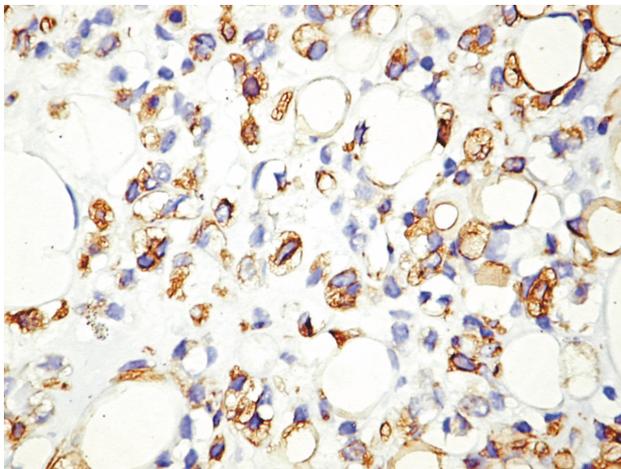


Figure 5 – Strong positive reaction for vimentin in neoplastic cells. Anti-vimentin, $\times 400$.

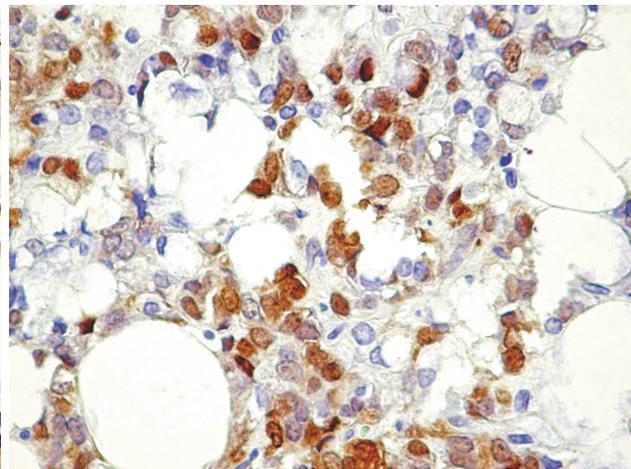


Figure 6 – S100 protein in liposarcoma tumor cells, with preferential nuclear expression. Anti-S100 protein, $\times 400$.

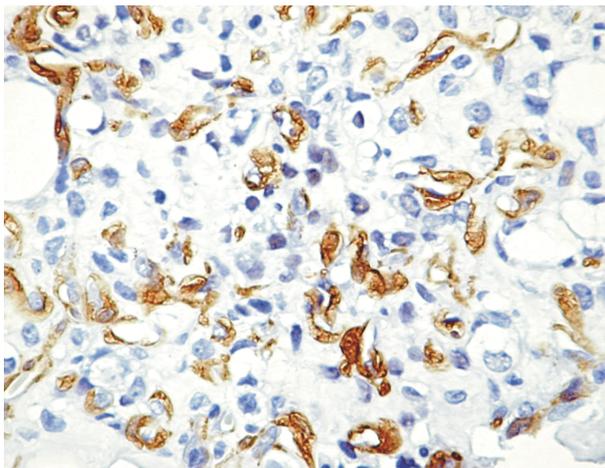


Figure 7 – Numerous small and irregular microvessels in the tumor area of liposarcoma. Anti-CD34, $\times 400$.

Discussion

Histologically, liposarcomas are subtyped into five variants: well-differentiated, myxoid, round cell, dedifferentiated and pleomorphic [3].

Myxoid liposarcoma is a common liposarcoma subtype, which has the tendency to local recurrences and a low degree of malignancy. Some of these tumors have a histological progression towards round cell liposarcoma with rapidly aggressive evolution and frequent metastasis. The malignant tumor originates from the primitive mesenchymal lipoblasts, which during their evolution replicate the development of adipose fetal tissue. Because of this, the structure of liposarcoma contains lipoblasts, pro-lipoblasts (spindle cells), undifferentiated round cells and occasionally brown malignant adipose cells.

Structurally, the tumor contains myxoid areas (reduced cellularity and myxoid stroma rich in hyaluronic acid), transitional areas (with evidence increasing of cellularity) and areas with very numerous undifferentiated round cells where the myxoid stroma is reduced or absent. Increase in the proportion of undifferentiated round cells over 5% is a determinant of evolution and prognostic [4]. Other unfavorable prognostic factors that increase the risk of local relapses and the risk of metastasis are: degree of cellularity, tumor differentiation score, mitotic index, necrosis degree and overexpression of p53 [5].

After excision of the tumor, local relapses rate is 50–70%. Lymphatic metastases are rare, hematogenous pulmonary metastasis is common.

Favorite location of myxoid liposarcoma is in the lower limbs and retroperitoneal region, head and neck localizations are relatively rare, only less than 100 cases have been reported in the literature. In the ocular area were reported less than 40 primitive orbital liposarcomas [6–9], despite the high content of fat in the orbit, and some orbital metastases with origin in retroperitoneal or inferior limb [5, 10, 11].

Miyashita K *et al.* [2] reported a case of myxoid liposarcoma with origin in bulbar conjunctiva, no connection with orbital tissue. In our case, we followed the primary tumor and “satellite” juxtalimbal conjunctival lesions uncertain significance, which is interpreted as local extensions, local metastases or multiple separate tumors.

Cytogenetic exam reveals specific re-arrangement, t(12;16)(q13;p11) translocation, and hybrid gene TLS(FUS)/CHOP that resulted encodes an aberrant transcriptional regulator involved in adipocytes differentiation [12, 13].

Myxoid liposarcoma’s transformation into the highly malignant round cell type is achieved by acquiring genetic and epigenetic random additional alterations that are clinically characterized by early recurrence, rapid increase of tumor volume and macroscopic changes [14].

☒ Conclusions

A rare case of myxoid/round cells liposarcoma of the bulbar conjunctiva, with an evolution observed for seven years is presented and discussed clinically and histological. Speed development of local relapses and the emergence of large recurrence are clinical signs of underlying histopathological changes represented by increased numbers of undifferentiated round cell relative to myxoid component of the tumor.

Corresponding author

Mihnea Munteanu, Associate Professor, MD, PhD, Department of Ophthalmology, “Victor Babeş” University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041 Timișoara, Romania; Phone +40744–661 405, e-mail: mihneam1@gmail.com

Received: February 25, 2013

Accepted: July 22, 2013

References

- [1] Smith TA, Easley KA, Goldblum JR, *Myxoid/round cell liposarcoma of the extremities. A clinicopathologic study of 29 cases with particular attention to extent of round cell liposarcoma*, Am J Surg Pathol, 1996, 20(2):171–180.
- [2] Miyashita K, Abe Y, Osamura Y, *Case of conjunctival liposarcoma*, Jpn J Ophthalmol, 1991, 35(2):207–210.
- [3] Enzinger FM, Winslow DJ, *Liposarcoma. A study of 103 cases*, Virchows Arch Pathol Anat Physiol Klin Med, 1962, 335:367–388.
- [4] Antonescu CR, Tschernyavsky SJ, Decuseara R, Leung DH, Woodruff JM, Brennan MF, Bridge JA, Neff JR, Goldblum JR, Ladanyi M, *Prognostic impact of p53 status, TLS-CHOP fusion transcript structure, and histological grade in myxoid liposarcoma: a molecular and clinicopathologic study of 82 cases*, Clin Cancer Res, 2001, 7(12):3977–3987.
- [5] Fabi A, Salesi N, Vidiri A, Mirri A, Ferraresi V, Cognetti F, *Retroperitoneal liposarcoma with metastasis to both orbits: an unusual metastatic site*, Anticancer Res, 2005, 25(6C):4769–4771.
- [6] McNab AA, Moseley I, *Primary orbital liposarcoma: clinical and computed tomographic features*, Br J Ophthalmol, 1990, 74(7):437–439.
- [7] Jakobiec FA, Rini F, Char D, Orcutt J, Rootman J, Baylis H, Flanagan J, *Primary liposarcoma of the orbit. Problems in the diagnosis and management of five cases*, Ophthalmology, 1989, 96(2):180–191.
- [8] Lane CM, Wright JE, Garner A, *Primary myxoid liposarcoma of the orbit*, Br J Ophthalmol, 1988, 72(12):912–917.
- [9] Naeser P, Moström U, *Liposarcoma of the orbit: a clinicopathological case report*, Br J Ophthalmol, 1982, 66(3):190–193.
- [10] Hannachi Sassi S, Braham E, Bhouiri L, Mrad K, Abbes I, Driss M, Dhoub R, Jaafoura H, Bouguila H, Ben Romdhane K, *Orbital metastasis of liposarcoma*, J Fr Ophthalmol, 2007, 30(9):e28.
- [11] Tehrani AH, Heegaard S, Prause JU, Fledelius HC, Daugaard S, *Liposarcoma metastatic to the orbit*, Eur J Ophthalmol, 2003, 13(1):108–112.
- [12] Pedeutour F, Maire G, Sirvent N, *De la cytogénétique à la cytogénomique des tumeurs adipocytaires 2. Tumeurs adipocytaires malignes*, Bull Cancer, 2004, 91(4):317–323.
- [13] Aman P, Ron D, Mandahl N, Fioretos T, Heim S, Arheden K, Willén H, Rydholm A, Mitelman F, *Rearrangement of the transcription factor gene CHOP in myxoid liposarcomas with t(12;16)(q13;p11)*, Genes Chromosomes Cancer, 1992, 5(4): 278–285.
- [14] Mandahl N, *Soft tissue tumors: Liposarcoma / malignant lipomatous tumors*, Atlas Genet Cytogenet Oncol Haematol, 2000, <http://AtlasGeneticsOncology.org/Tumors/liposarc5029.html>.