European Journal of Ophthalmology / Vol. 13 no. 1, 2003 / pp. 108-112

SHORT COMMUNICATION

Case report

Liposarcoma metastatic to the orbit

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PURPOSE. *To describe a patient with liposarcoma metastatic to the left orbit.*
METHODS. *A 72-year-old man was admitted with diplopia and proptosis of the left eye. Previously, a retroperitoneal liposarcoma had been surgically removed followed by postoperative radiation. Visual acuity was normal. There was proptosis of the left eye, increased retrobulbar resistance and reduced mobility. Trans-septal orbital biopsies showed liposarcoma. The patient was initially treated with prednisolone and later received radio- and chemotherapy. Despite treatment he lost vision of the left eye and died a few months later.*
RESULTS. *Histological examination of the orbital tumor revealed a spindle-cell liposarcoma similar to the primary tumor of the retroperitoneum.*
CONCLUSIONS. *Liposarcoma metastatic to the orbit is rare, but should be suspected in a patient with proptosis caused by a space-occupying lesion and a history of liposarcoma. (Eur J Ophthalmol 2003; 13: 108-12)*

KEY WORDS. *Liposarcoma, Orbit, Metastasis, Ultrasonography, Histology*

Accepted: July 1, 2002

INTRODUCTION

Liposarcomas are among the most common adult soft tissue sarcomas in the body. Usually they arise from the deep soft tissue of the extremities or the retroperitoneum. Despite the high content of fat in the orbit, both benign and malignant tumors of adipose tissue are extremely rare at this site (1-3). Up till now no large series studying the clinicopathologic features of primary orbital liposarcomas have been published. Liposarcoma metastatic to the orbit is even more rare and only a few cases have been described (4-8). This report adds a new case to the literature and discusses symptoms, imaging, histology and treatment of this rare tumor.

Case report

Clinical history

In 1997 a 72-year-old man was referred to this hospital because of diplopia and proptosis of the left eye, increasing over one and a half months. Two years earlier a large retroperitoneal tumor (Fig. 1a) adjacent to the spleen and left kidney had been surgically removed. Postoperatively, external beam radiation therapy of 66 Gy was administered to the area of resection.

On admission the corrected visual acuities were 6/4.5 and 6/6. There was proptosis of the left eye with marked, predominantly inferior, chemosis. Hertel exophtalmometry values were 18-26/110 mm. There was a painless increase of retrobulbar resistance and a firm mass could be palpated in the inferolateral quadrant of the left orbit. The eye appeared slightly displaced and mobility was markedly restricted. Pupillary reflexes, visual field examination by tangent screen and Ishihara color plate testing were all normal. The same held for slitlamp of the globe and ophthalmoscopic evaluation. In particular there was no evidence of blurred disc or other fundus signs of external pressure. Intraocular pressure (IOP) of the left eye by Goldmann applanation tonometry was elevated (16/36 mmHg).

On B-scan a well-demarcated elongated tumor in the inferotemporal part of the orbit was seen.

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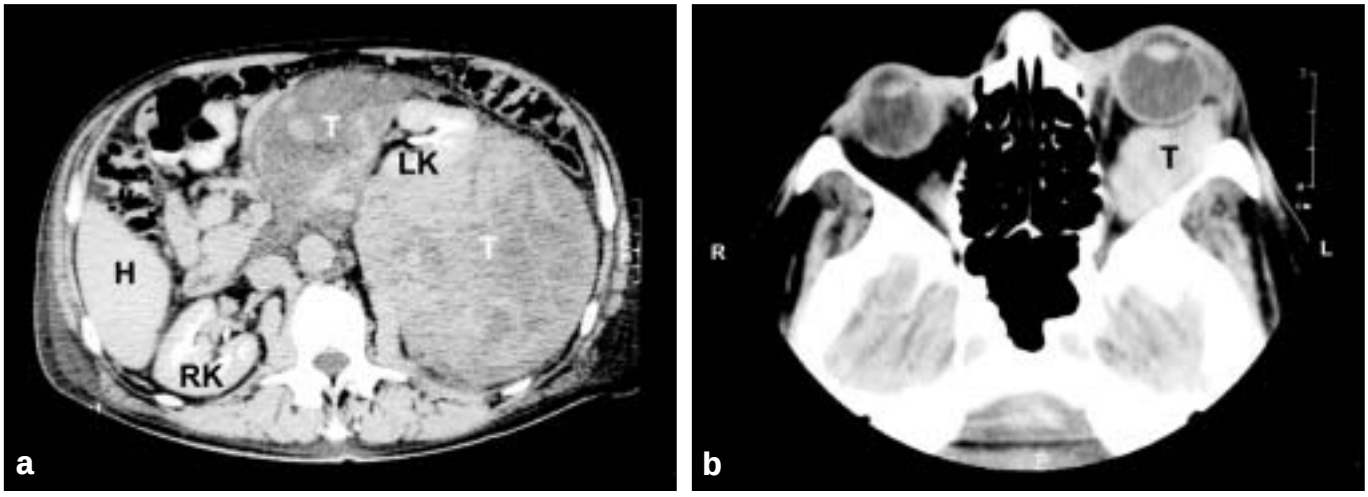

Fig. 1 - a) *CT scan of the abdomen showing the large retroperitoneal tumor (T) displacing the left kidney (LK). The right kidney (RK) and liver (H) are intact.* **b)** *Axial CT scan showing the retrobulbar tumor (T) in the left orbit.*

The tumor filled the space between the lateral and inferior rectus muscles. The internal acoustic structure of the tumor was homogeneous with low overall reflectivity, as confirmed by A-scan (Fig. 2).

Subsequent computer tomography (CT) of the left orbit showed a 2 x 3.5 x 3 cm demarcated retrobulbar mass lying inferotemporally in close relation to the lateral rectus muscle, slightly displacing the optic nerve and pushing the eye forward (Fig. 1b). There was no evidence of erosion of the bony walls.

Four trans-septal orbital biopsies were taken under local anesthesia. The patient was treated with high prednisolone doses (100 mg per day) and external beam radiation therapy with a total dose of 30 Gy to the left orbit. He subsequently received two cycles of chemotherapy (ifosfamide). CT scan at this time showed recurrence of the retroperitoneal tumor, but no metastases outside the orbit.

Vision decreased during treatment due to compression of the optic nerve and disc edema. The proptosis responded well to the treatment, but vision was lost over three months.

Seven months after biopsy the patient died in a nursing home. No autopsy was done.

Histological procedures

One of the orbital biopsies was frozen, sectioned and stained with oil red O and Sudan black B.

The other specimens were fixed in 4% buffered formaldehyde and embedded in paraffin. Sections were cut at 3 µm and mounted on glass slides. The sections were stained with hematoxylin-eosin (HE), periodic acid-Schiff (PAS), hematoxylin-phloxine-saffron (HPS), alcian blue, luxol-fast blue and Gordon & Sweets' method for reticular fibers. Immunohistochemical reactions were done using the streptavidin-biotin method (Boenisch 1989). The procedure included microwave oven processing. The following commercial antibodies were applied: S-100 (code no.Z0311, Dako A/S), vimentin (clone Vim 3B4, lot. no.83275620-06, Boehringer Mannheim GmbH), desmin (clone D33,code no. M0760, Dako A/S), CD34 (anti-HPCA-1, cat. no. 347660, Becton Dickinson), smooth muscle actin (SMA) (clone:1A4, code no. M0851, Dako A/S), CD117 (clone 104D2, DAKO A/S), myoglobin (code no. A 0324, Dako A/S).

Negative controls were run without the primary antibody.

RESULTS

Gross examination

The retroperitoneal tumor removed in 1996 measured 30 x 26 x 13 cm, completely surrounding but not invading the left kidney. It was nodular, yellow to gray

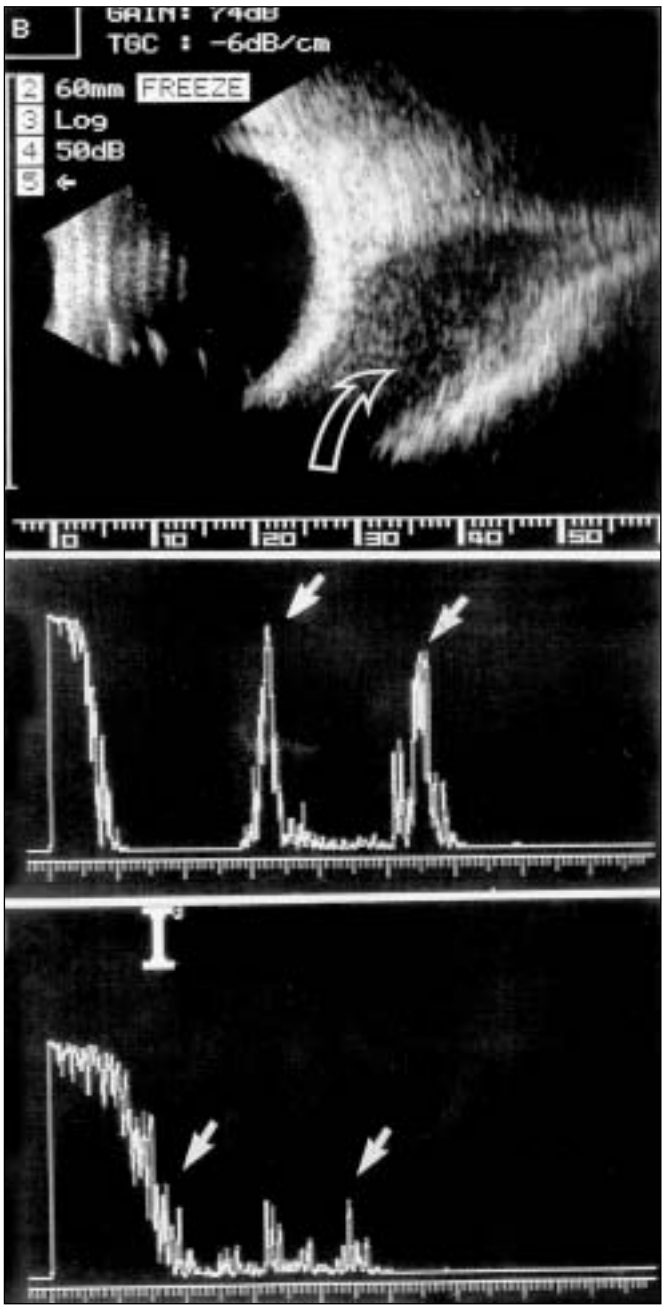

Fig. 2 - *Ultrasound imaging of the retrobulbar tumor in the orbit when first seen in the eye clinic. A fairly homogeneous low-reflecting tumor (curved arrow) is seen behind the posterior eye wall on B-scan (at top) and A-scan (middle, between arrows). Bottom: an inferotemporal parabulbar antero-posterior A-scan (at tumor sensitivity) shows a low-reflecting tumor pattern (between arrows) behind the normal high anterior orbital tissue echoes.*

or brown and partly myxoid with minor hemorrhages and necrosis centrally. The four orbital biopsies each measured approximately 3 x 3 x 3 mm.

Microscopic examination

The microscopic picture of the primary retroperitoneal tumor was heterogeneous showing smaller areas with atypical fatty tissue, a dominant myxoid component with varying cellular pleomorphism, and highly cellular foci with spindle cells (Fig. 3a), the latter with many, often atypical mitoses.

Immunohistochemically, S-100 stained atypical lipocytes/-blasts in the low-grade areas, while CD34, apart from demonstrating a branching capillary pattern by staining endothelium, decorated the spindle cell component. Some of the spindle cells also reacted with desmin while alpha smooth muscle actin and CD117 were negative. The picture was interpreted as a so-called dedifferentiated liposarcoma, characterized by low-grade areas with more or less abrupt transition to a medium or high-grade spindle cell component.

The orbital biopsies (Fig. 3b) showed spindle cells and scattered vacuolated lipoblasts. Mature univacuolated adipocytes were seen and in general the tumor appeared well-differentiated. In the frozen section some of the intracellular vacuoles stained positive with oil red O, but negative with Sudan black B. The spindle cells reacted with vimentin, but were S-100 negative. Scattered spindle cells reacted with CD34. This picture was consistent with a liposarcoma metastatic to the orbit.

DISCUSSION

Judging from the literature liposarcoma metastases to the orbit are extremely rare, despite the fact that liposarcoma is generally considered to be among the more common soft tissue sarcomas of adult life (2, 5, 9). The primary tumors occur most commonly in the thigh and the retroperitoneum. Liposarcoma is mainly a tumor of adult life, with a peak incidence between 40 and 60 years of age and there is a slight male preponderance. Recurrence is common in deep-seated liposarcomas of all types, presumably because of the difficulty of complete surgical excision.

The histological type is related to the overall recurrence: recurrent tumors usually have a cell type similar to the primary neoplasm, or a more anaplastic type (5). Enzinger and Weiss (2) divided liposarcoma into five

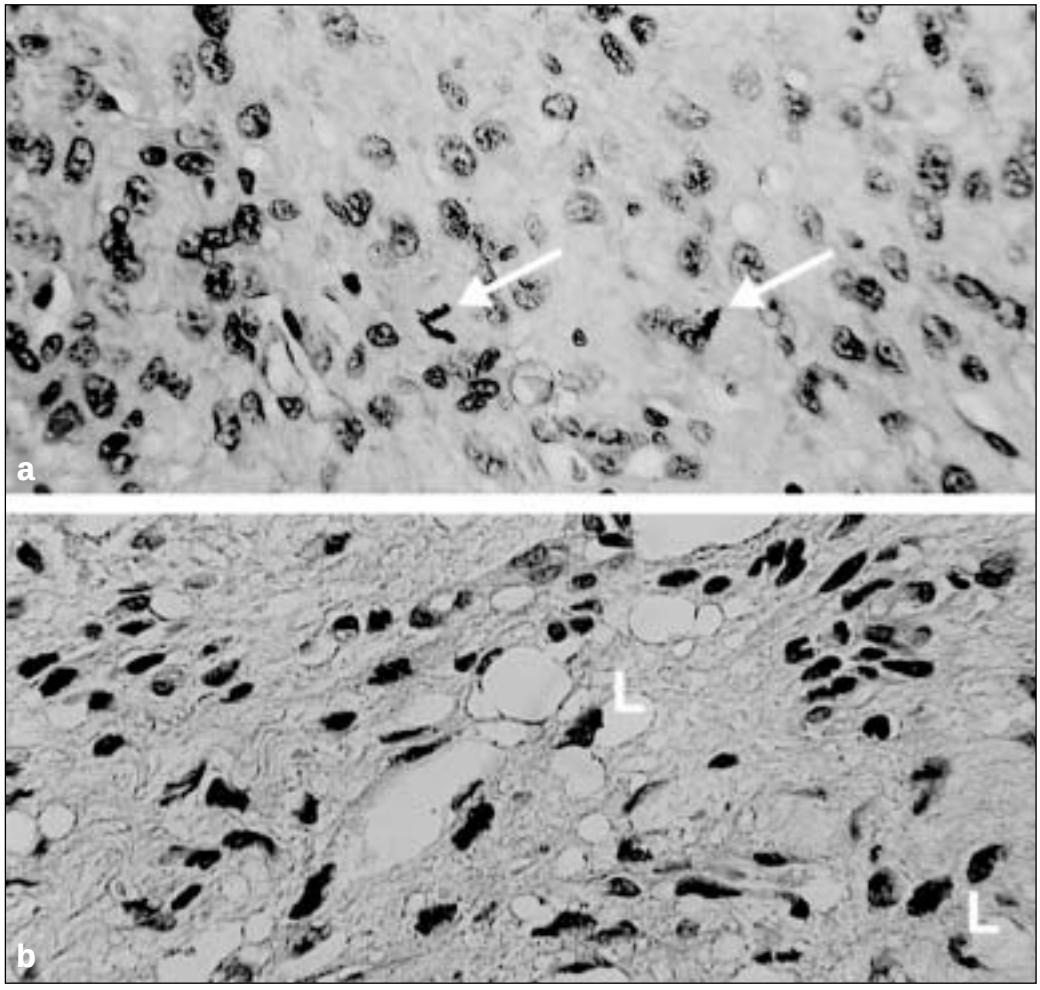

Fig. 3 - a) *Histological section of the retroperitoneal tumor showing pleomorphic and spindle shaped cells. Mitotic figures are seen (arrows) (HE, x 400).*
b) *The orbital tumor showing spindle cells and vacuolated lipoblasts (L) (HE, x 400).*

basic histological categories: 1) myxoid, 2) round cell, 3) well-differentiated (including atypical lipoma), 4) dedifferentiated and 5) pleomorphic. About half the cases are of the myxoid type, followed in frequency by well-differentiated, dedifferentiated, round cell and pleomorphic liposarcomas. Mixed forms with a combination of two or more histologic types are also found, with a frequency of about 5-10%.

The light microscopic differential diagnoses include undifferentiated sarcoma, malignant solitary fibrous tumor and some peripheral nerve sheath tumors that may become secondarily lipidized (9). However, only liposarcomas contain multivacuolated lipoblasts.

Histologically, metastatic tumors may recapitulate the appearance of the primary lesion, or may appear less differentiated (10). In the present case the orbital tumor appeared more well-differentiated than the retroperitoneal tumor. Therefore, the existence of two primary liposarcomas cannot be completely excluded. However, multicentricity in liposarcoma almost certainly reflects metastasis since most such patients develop disseminated disease (11).

Metastases from liposarcoma are found mainly in lungs, visceral organs, bone, serosal surfaces of the pleura, pericardium and diaphragm (2, 6). Orbital metastases are very rare. So few cases have been reported that typical histological and imaging features can hardly be applied (4-8). However, factors such as age, sex, site of primary tumor, symptoms, objective findings and therapy supported the diagnosis in our case.

Orbital tumors can in general present with a variety of symptoms like proptosis, diplopia, orbital or retroorbital pain, eyelid swelling, ptosis, visual loss and ophthalmoplegia (5, 7, 12, 13). The imaging tools to elucidate these tumors are CT, MRI and ultrasound. Together with the clinical picture these methods are

helpful indicators of the tumor but cannot give pictures pathognomonic for liposarcoma. The diagnosis must be based on histological examination of a biopsy (13). This statement is supported by Nasr et al (6), who showed that one of their two cases of orbital liposarcoma had ultrasonic reflectivity similar to a cavernous hemangioma. However, the other case gave the same low-reflecting pattern as our case.

In general the treatment of orbital tumors depends on the tumor type and location within the orbit and on the patient's general physical and ophthalmological condition. In the case of orbital liposarcoma metastasis, life expectancy is poor and the main goal of management is symptomatic relief by reducing pain and preserving vision (7).

The majority of experts recommend surgical excision of the tumor followed by postoperative radiation (2, 5, 9, 12, 14, 15). Exenteration of the orbit was considered in our patient, but was not done because of his weak general condition. Adjuvant chemotherapy has not yet gained any place in the treatment of liposarcoma and requires further study (2, 9, 12).

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