Case Report

Primary dedifferentiated liposarcoma of the orbit, a rare entity: Case report and review of literature

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Abstract

Head and neck liposarcomas are rare entities accounting for less than 5% of all liposarcomas. The primary orbital location is even rarer, with about 40 cases described in the English literature. According to the widely accepted classification of Enzinger and Weis there are 5 histologic variants of liposarcomas: well differentiated, myxoid, dedifferentiated, round cell, and pleomorphic. The first two are considered low-grade and display a favourable prognosis (>90% 5-year DSS and OS), whereas the dedifferentiated, round cell, and pleomorphic are defined high-grade and burdened with poorer prognosis (5-year DSS ranging 45–73%). Dedifferentiated liposarcomas (DDL) of the head and neck region are exceedingly rare, therefore there are scattered and contrasting data regarding their clinical history, treatment modality, and prognosis. We presented a case of DDL arising in the orbit (fourth case of primary orbital DDL described), free from disease after 5-year follow-up. Clinical history, treatment, and characteristics of the presented case were described and discussed in the light of how reported in the literature, in the attempt to bring further insight in the nature and management of this rare pathological entity.

Keywords: Dedifferentiated liposarcoma, Head and neck, Orbit

Introduction

Sarcomas are rare neoplasms representing less than 1% of all malignancies; of those, liposarcoma (LS) is one of the most common soft tissue sarcomas occurring in adults (about 20% of all sarcomas). Most of liposarcomas are located in deep soft tissue of lower extremities, retroperitoneum and mesenteric region; while less than 5% occur in head and neck region. According to the World Health Organization classification of soft tissue tumours, and the classification of Enzinger and Weis, five categories of liposarcomas are recognised: well differentiated, myxoid, dedifferentiated, round cell and pleomorphic. In this report, we present a case of dedifferentiated liposarcomas (DDL) arising in the orbit. Treatment, clinical, and prognostic aspects of this rare tumor are discussed in the light of our experience and compared with how reported in the literature.

Case report

Informed consent for publication of pertinent medical history and explicative photos has been obtained from the patient. Because of its retrospective nature, the study did not require approval from the REB of our Institution.

A 47-years-old Caucasian man was referred to our clinic with chief complaint of swelling of the upper left eyelid. At
the physical examination the patient had a nodular, round, well-defined, not painful mass of the upper eyelid of about 2.5 cm of diameter inducing palpebral ptosis and reduction of the OS visual field (Fig. 1a). Clinical differential diagnosis included inflammatory disease (e.g. orbital pseudotumor), lacrimal gland tumor, orbital tumor NOS. CT and MR scan with contrast were performed showing a solid neoplasm located in the supero-external quadrant of the orbit with intra-orbital extension, involving the upper eyelid; the mass showed brisk enhancement after contrast, undefined margins with aspect of erosion/reabsorption of the superior and lateral bone walls of the left orbit (Fig. 1b). Pathological findings on incisional biopsy indicated a lipomatous tumor with malignant features.

The patient underwent composite left orbital exenteration including the superior and inferior eyelids in continuity with the lateral pillar and wall of the orbit (Fig. 1c). The periorbit adjacent to the orbital roof seemed clinically intact and was therefore kept as superior limit of resection. The bone of the orbital roof and superior aspect of orbital rim, which was in intimate contact with the tumor, was drilled using a round burr to obtain further free margin of resection, even though it did not show obvious clinical signs of erosion/infiltration. Frozen sections of the resection margins returned as free of neoplastic infiltration. The surgical defect was filled using the ipsilateral temporalis muscle flap (TMF) harvested and transposed anteriorly through the trans-orbital retrograde approach previously described.15

Pathology report on the permanent specimen showed mixoid liposarcoma with areas of pleomorphic sarcoma of high grade with rhabdomyosarcoma-type cells. These findings were confirmed by positive immunostaining for myosin, desmin, caldesmon, vimentin, and S100 protein.

The aggressive nature of the tumor and the close margins of resection advocated adjuvant radiotherapy treatment; accordingly, the surgical bed was irradiated by intensity modulated radiotherapy (IMRT) at the dose of 64 Gy. Regular follow-up was scheduled without evidence of recurrent disease at 60 months post adjuvant treatment (Fig. 1d).

Discussion

Sarcomas of the head and neck region represent rare pathology in adults (accounting for 2–10% of all cancers), while they are more frequent in the pediatric population (35%).1,2 Head and neck liposarcomas (HNLS) account for less than 5% of liposarcomas3 and 2–9% of all sarcomas arising in the region.4–12 The rarity of HNLS is clearly demonstrated by the small number of cases reported in the major series, such as the 30 cases in 60-year timeframe of MD Anderson Cen-
ter, and the 9 cases reported in the 30-year interval series of Mayo Clinic. The orbital location of liposarcomas is extremely rare with around 40 cases reported in English literature, mainly in form of case-report or small series widely scattered with respect to clinical history, presentation and histological subtype. In the largest study population of 318 HNLS derived from the register of Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, the distribution for primary site was: subcutaneous tissue of face, neck and scalp, oral cavity, skin, salivary glands, and upper aerodigestive tract in decreasing order of frequency; surprisingly the study did not report any case of orbital location, confirming the extreme rarity of this subgroup of HNLS.

Dedifferentiated liposarcoma (DDL) was first described in 1979 by Evans as a neoplasm having a well-differentiated lipomatous component associated with a nonlipogenic sarcoma. Genetic factors as well as traumas, and history of previous radiation has been indicated as possible co-factors inducing malignant transformation and/or progression toward higher grade forms. Systemic neurofibromatosis (von Recklinghausen syndrome) and genetic syndromes predisposing for cancer development (e.g. Li Fraumeni syndrome) were also associated with high grade liposarcomas.

Few authors have described DDL in head and neck region as parapharingeal space, cheek, tongue and parotid gland. As per the orbital location, only 40 cases of primary orbital liposarcoma have been reported so far, the majority of those being myxoid and well differentiated type; at the best of our knowledge, this is the fourth case of primary DLS localized in the orbit reported in the English literature (Table 1).

MRI is essential to the evaluation of lipogenic tumors. Radiologically, DDL should be suspected in case of tumors displaying coexistent areas of fatty and non-fatty solid components. Contrast enhancement depends on the level of de-differentiation. In DDL, enhancement is more intense in contrast with minimal contrast enhancement of well-differentiated liposarcomas. In our report the imaging confirmed the mixed lipomatous/solid component of the tumor and played a critical role in showing the aggressive nature of the mass.

The first choice of treatment is complete surgical removal. Because DDL have an aggressive behavior, with a local recurrence rate of 41%, disease specific (DS) mortality of 28%, and because the fascia surrounding the mass it is not a true capsule, recommendations are to keep surgical dissection with wide negative margins of at least 2 cm from the margin of the lesion, when feasible. Neck dissection is usually not required because of the extreme rarity of lymph node metastases. Despite the above mentioned recommendation, in surgical excision of head and neck DDL the concept of free margin cannot be based on the linear distance from the tumor (i.e. 2 cm of free margin) due to the intrinsic constraints of the region (maxillofacial skeleton) and the proximity with vital structures (orbital content, brain, major nerves and vessels), hence the ideal free margins must be tailored on each case based on the tumor location, extension, and the proximity to adjacent structures; in most cases the rule of 2 cm free-margin is not feasible, and other anatomical structures offering high resistance to progression of tumor (e.g. periosteum, bone, periorbit, dura mater) should be acquired as safe margin of resection. According to those principles in our case, where the mass was localized in the upper-outter quadrant of the orbit, the ocular globe was included in the volume of resection along with the lacrimal gland, and the lateral wall of the orbit; the periorbit was kept as safe superior margin, and the upper orbital wall was drilled to provide further resection-margin, although not macroscopically involved.

Davis and Dubin pointed out a possible role of adjuvant radiation therapy (RT) in reducing the rate of local recurrences. However, the effectiveness of adjuvant RT in treating liposarcomas and DDL in particular, is still controversial; several studies showed as adjuvant radiotherapy reduces the rate of local recurrence from 60% to 40%, but it does not modify the overall survival or the rate of metastasis. In our case adjuvant radiotherapy was warranted because of the aggressive histology pattern (high grade rhabdomyosarcoma and pleomorphic sarcoma) and the inability to obtain a wide resection margin. Chemotherapy (CT) has proven to be ineffective on DDL, while ifosfamide-based CT could be considered in histologic-type at higher risk of develop distant metastases (round cell and pleomorphic liposarcoma).

Prognosis of LSs is mainly dependent on the histological grade: low grade, well differentiated LSs having a 5-year disease specific survival (DSS) and overall survival (OS) of 90%, whereas high grade LSs (round cell, DDL and pleomorphic) have 5-year DDS ranging from 44% (DDL) to 59% (pleomorphic), and 75% (round cell).

Despite the intrinsic limits of a case report, our experience did provide some interesting hints: it confirmed the relatively younger age of insurgence of head and neck LSs in adults, and their favourable prognosis. However, in discordance of how reported in the Literature, where the majority of primary orbital LS where well differentiated, our case had high grade histology; the favourable prognosis displayed in our case, with a 5-year disease free survival, could be explained by the relatively young age of the patient and his good general health status, the low stage of disease, and the radical resection. In the instance, it was remarkable to notice that the oncologic parameters used for excision of head and neck epithelial malignancies (i.e. consider adequate margin of resection structures offering higher resistance to tumor progression, such as bone, periorbit etc.) can be applied in the surgical treatment of head and neck DDL. Regarding the treatment options, our experience confirmed the surgery as mainstay therapy for LS, with adjuvant radiation therapy in selected cases of high grade tumors with close margins of resection.

Primary DDL of the orbit is an extremely rare pathological entity. Despite the aggressive nature and the poor prognosis

Table 1.

| Author          | Year | No. of cases (DDL) | Features and location                       |
|-----------------|------|--------------------|---------------------------------------------|
| Cai et al.      | 2001 | 7 (1)              | >2 cm, right orbit, retrobulbar             |
| Henderson       | 2007 | 6 (1)              | Right orbit                                |
| Zhang et al.    | 2011 | 1                  | Right orbit, medial canthus                 |
| Torroni et al.  | 2015 | 1                  | 3 cm, left orbit, supra-7ateral             |

Cases of primary dedifferentiated liposarcomas (DDL) of the orbit reported in the recent English Literature.
reported in literature, the orbital location seems to offer better outcomes in terms of local control and survival, mainly because the early diagnosis at lower stage of disease. The mainstay factor to obtain a favourable prognosis is represented by the capacity of obtain a radical resection of the tumor. Based on our experience, the same oncologic parameters adopted for radical resection of other malignancies most commonly involving the head and neck region (i.e. epithelial carcinomas), should be applied for resection of this rare tumor.

Conflict of interest

The authors declare no conflict of interest in publishing the present manuscript.

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