

Radiotherapy in patients with solitary fibrous tumor of the orbit – a case report and literature review

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AUTHORS' CONTRIBUTION: (A) Study Design · (B) Data Collection · (C) Statistical Analysis · (D) Data Interpretation · (E) Manuscript Preparation · (F) Literature Search · (G) Funds Collection

SUMMARY

This article presents a rare case of solitary fibrous tumor (SFT) of the orbit. After a non-radical surgical procedure, the patient received stereotactic radiotherapy to the dose of 20 Gy with isodose of 100%. Thirty-six months later, progression in the form of a new cerebral metastatic lesion was detected. No local relapse or radiation complications were noted. The literature review analyzes clinical data, treatment methods and prognosis of all patients with orbital SFT reported in the literature.

Key words: radiotherapy, solitary fibrous tumor SFT

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Word count: 1934 **Tables:** 1 **Figures:** 5 **References:** 80

Received: 06.09.2016

Accepted: 12.10.2016

Published: 31.03.2017

INTRODUCTION

Up to 1994, solitary fibrous tumor (SFT) was believed to be extremely rare. After the publication of an article of Wester et al. [1], which appeared in 1994 and proposed a new method for SFT histological diagnosis, more case reports concerning this tumor appeared. It was reported to have occurred in various sites, but the orbit was one of the rarest locations [2,3].

This paper presents a literature review of publications available in the PubMed and Google Scholar databases, searched with the use of the following key words: *orbital solitary tumor* and *radiotherapy* as well as time descriptors: 1994–2015. This search yielded 119 case reports on orbital SFT [1,2,4–66].

CASE PRESENTATION

A white male, aged 51 years, was diagnosed due to left proptosis, which had been progressing for approximately 2 months and was accompanied by orbital mobility restriction, without pain or deteriorated vision.

MRI conducted on November 10 2011 revealed a solid–cystic tumor located medially in the superior and inferior quadrant of the left orbit. The tumor with radiological features of a malignancy, measuring 30 x 22 mm, was well-circumscribed and deformed the posteromedial aspect of the orbit with optic nerve displacement and without signs of orbital wall destruction. Fig. 1. On December 2 2011, subtotal tumor resection was performed.

Histology and immunohistochemistry

Surgical specimens were preserved in 10% buffered formalin (pH 7.4) and routinely processed into paraffin blocks. Four mm thick

fragments were stained with hematoxylin and eosin (H+E) while fragments for immunohistochemical testing were placed on silanized slides (DAKO, Code No S3003) in order to prevent their detachment during the procedure. Immunohistochemical reactions were performed with the following reagents: CD99 (DAKO; Cat. No

M3601; dilution 1:50), CD34 (DAKO; Cat. No M7165; dilution 1:25), EMA (DAKO; Cat. No N1504), S-100 (DAKO; Cat. No Z0311; dilution 1:400), AE1/AE3 (DAKO; Cat. No M3515; dilution 1:50) and MIB-1 (DAKO; Cat. No M7240; dilution 1:150), using the EnVision system (Dako Real™ EnVision™ Detection

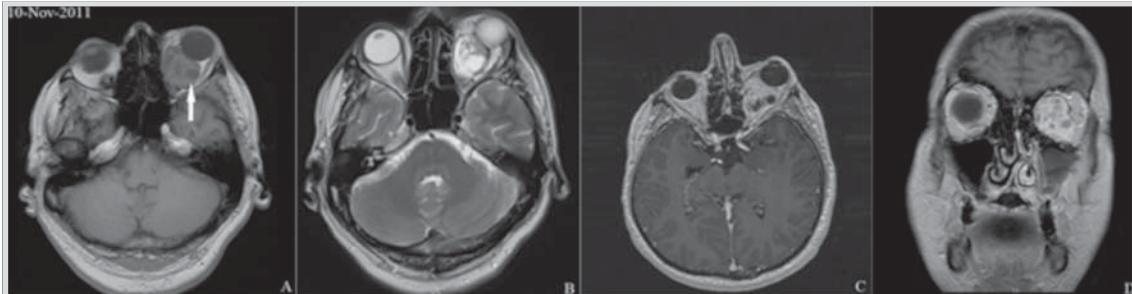


Fig. 1. MRI of left orbital tumor (before surgery), **A:** T1-weighted image, **B:** T2-weighted image, **C:** contrast-enhanced T1-weighted image (axial plane), **D:** contrast-enhanced T1-weighted image (coronal plane)

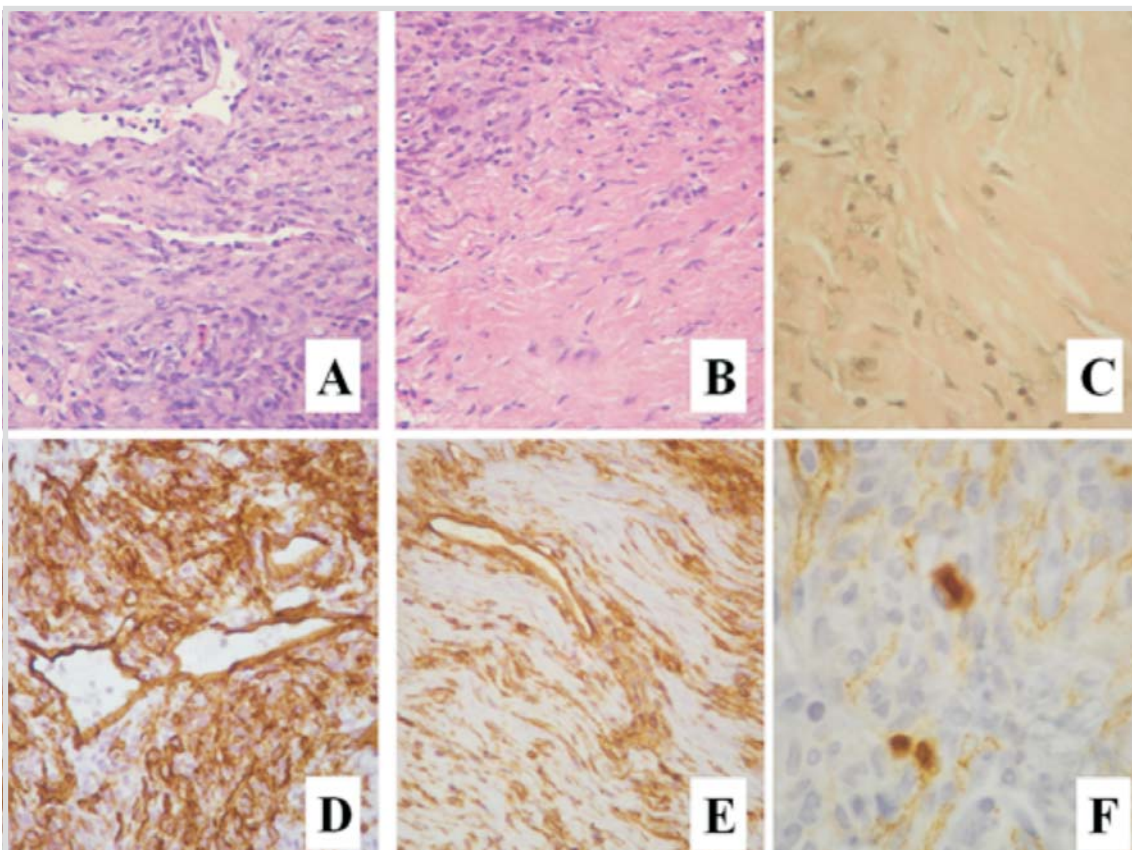


Fig. 2. Histology and immunohistochemistry. **A:** (H+E, 200x) – Areas of increased and decreased cellularity with oval and elongated nuclei as well as slit-like blood vessels. **B:** (H+E, 200x) – Area of decreased cellularity with dense collagen fiber bundles. **C:** (Van Gieson, 400x) – Dense collagen fiber bundles in areas of decreased cellularity, positive upon staining according to the Van Gieson protocol (pink-red). **D:** (CD34, 200x) – Strongly positive immunohistochemical reaction of tumor and vascular endothelial cells in a reaction with CD34 antibody. **E:** (CD99, 200x) – Strongly positive immunohistochemical reaction of tumor cells in areas of decreased cellularity in a reaction with CD99 antibody. **F:** (MIB-1, 600x) – Immunohistochemical reaction with MIB-1 antibody (proliferative index 2%).

System, Peroxidase/DAB+, Rabbit/Mouse, Cat. No K5007).

On histology, within the neoplastic lesion, there were areas of increased and decreased cellular density. Fig. 2A and 2B. Cancer cells had oval or elongated nuclei and formed bundles separated from one another by thick bundles of collagen fibers that were strongly positive in immunohistochemical staining according to the Van Gieson protocol. Fig. 2B and 2C. Moreover, round cells and branching “antler horn” vessels were also seen.

Immunohistochemistry revealed neoplastic cells with a strongly positive reaction to CD34 (Fig. 2D) and CD99 antibodies (Fig. 2E), and

a negative reaction to S-100, EMA and AE1/AE3 antibodies. MIB-1 proliferative index was 2%. Fig. 2F.

Based on the microscopic image and immunohistochemical testing, the following histological diagnosis was established: “Solitary fibrous tumor (SFT) of a lower grade of malignancy. Long-term observation is indicated.”

Postoperative radiotherapy

Postoperative MRI revealed an oval 17 x 19 mm area of heterogeneous signal in the left orbit. In its solid fragment, it was hypointense in T2 sequence and normointense in T1 sequence. It also underwent slight contrast enhance-

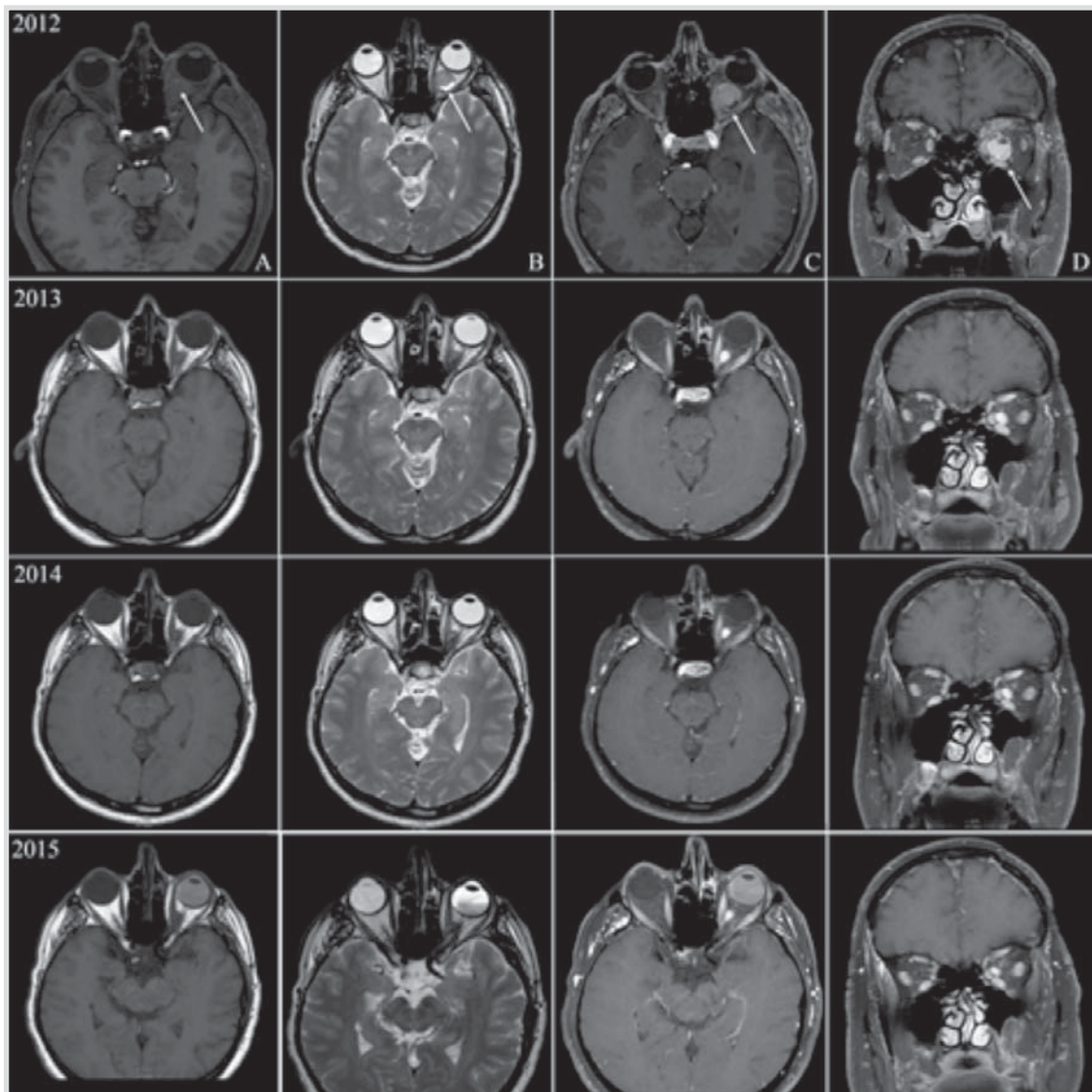


Fig. 3. Left orbital tumor during treatment. A: T1-weighted images, B: T2-weighted images, C: contrast-enhanced T1-weighted images (axial plane), D: contrast-enhanced T1-weighted images (coronal plane)

cement and showed the presence of two smaller crescent-shaped fluid areas. The lesion located medially in the posterior part of the left orbit compressed and deformed the medial rectus muscle and the optic nerve. Fig. 3.

Due to subtotal tumor resection, postoperative stereotactic radiosurgery (SRS) was conducted. The treatment plan was prepared in the iPlan system of BrainLab; 6 MV photon beams were applied. On May 18 2012, a dose of 20 Gy with a 100% isodose was delivered to the infiltration found on MRI. The tumor volume was 4.92 cm³. Fig. 4.

Observation

Within 36-month follow-up, slight proptosis of the left eyeball persisted and radiological stabilization of the lesion was observed. Control MRI scans performed in 2013 and 2014 revealed a solid-cystic pathological retrobulbar mass measuring 16 x 9 mm within the left orbit, located at medial and inferior rectus muscle and displacing the optic nerve. The lesion underwent intense enhancement upon contrast medium injection. Fig. 3. In 2015, 36 months after treatment, control MRI showed a stable image of the lesion in the left orbit, but a polycyclic metastatic lesion measuring 39 x 28 mm was found in the left frontal lobe. Fig. 5. The pa-

tient did not express consent to sampling of the new focus for histological examination.

DISCUSSION

This paper presents the application of SRS after non-radical orbital SFT resection. Moreover, 119 cases of orbital SFT found in the literature up to 2015 were analyzed.

Clinical course of SFT

SFT of the orbit was reported in patients from 9 to 76 years of age, but only 4 cases were noted in children below 10 years of age. SFT occurs equally frequently in both sexes [1, 2, 4-48, 50-57, 59-64, 66].

Orbital SFT is a slow-growing tumor, developing for months or even years (from 1 month to 20 years, average 26 months) in the orbit, usually causing no pain and leading to eyeball protrusion in 81% of cases [2, 4, 5, 7, 8, 10-16, 18, 22, 23, 27-42, 44-47, 50-53, 55, 56, 59, 62, 64, 66]. Other reported symptoms were: vision disorders (19%) including double vision (58%), eyeball mobility disorders (21%), edema and tumor mass (19%) or ptosis (14.5%) [2, 8, 12, 15, 16, 18, 27-38, 40, 41, 45-47, 50-53, 56]. Orbital SFT is usually (71%) located in the superior orbit. Its inferior orbital and

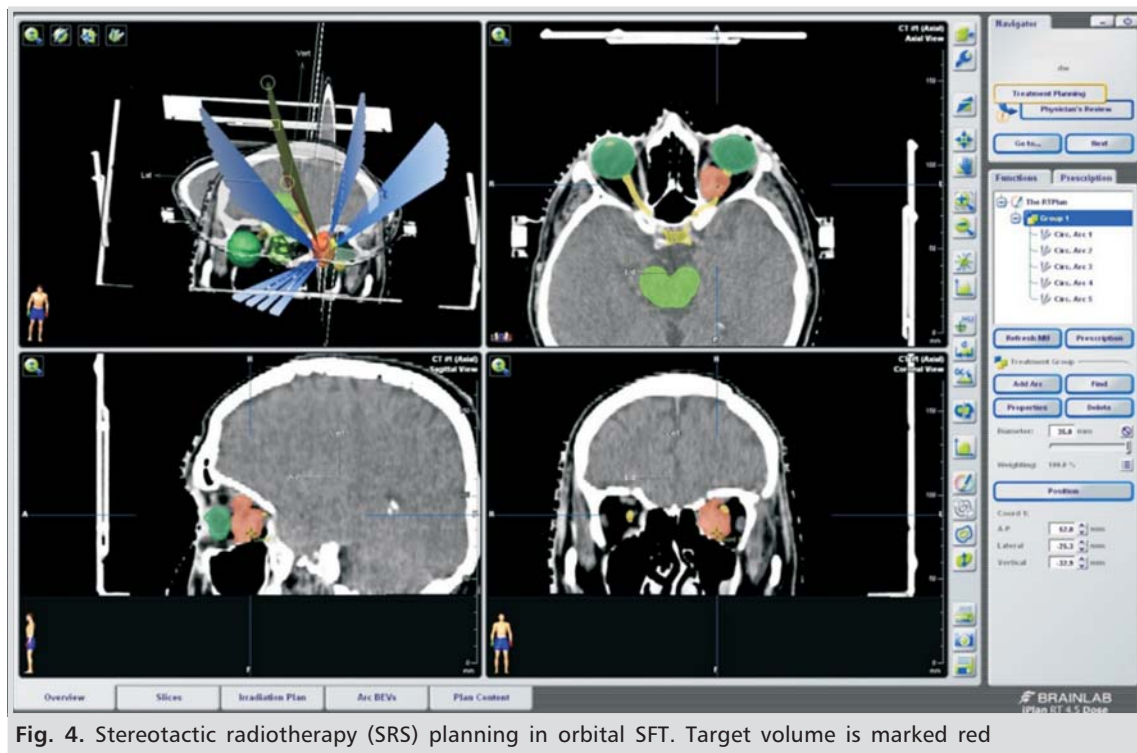


Fig. 4. Stereotactic radiotherapy (SRS) planning in orbital SFT. Target volume is marked red

retrobulbar location constitute 19% and 10%, respectively [2, 4, 6, 8, 9, 11–13, 17–23, 25, 27–32, 34–40, 42–48, 51–55, 60, 63, 66].

The clinical course of SFT of the orbit is usually slow, and symptoms develop in a period from 1 month to 20 years, on average 26 months. By contrast with SFT in other sites, which tends to recur and produce distant metastases, SFT of the orbit is rarely aggressive, and recurrences after surgery are observed in approximately 20% of cases [29, 32, 67, 68].

Moreover, certain recurring tumors present features of malignant transformation in the form of enhanced cellular atypia and increased mitotic activity. Complete tumor resection is the most significant prognostic factor in preventing a relapse [54, 4, 37, 28]. Distant metastases from orbital SFT were reported in only 2 cases. They were located in the foramen magnum, clivus, paraspinal muscles and peritoneum and occurred 3 years after surgery [41, 42]. In one patient, as in our case, intracranial spread was observed [43].

Treatment

Due to rare occurrence of orbital SFT, an optimal treatment scheme has not been established thus far. According to the WHO classifica-

tion, the risk of recurrence or distant metastases in SFT is approximately 10–15%, and it is believed that surgery is the treatment of choice in this type of cancer.

Surgical treatment

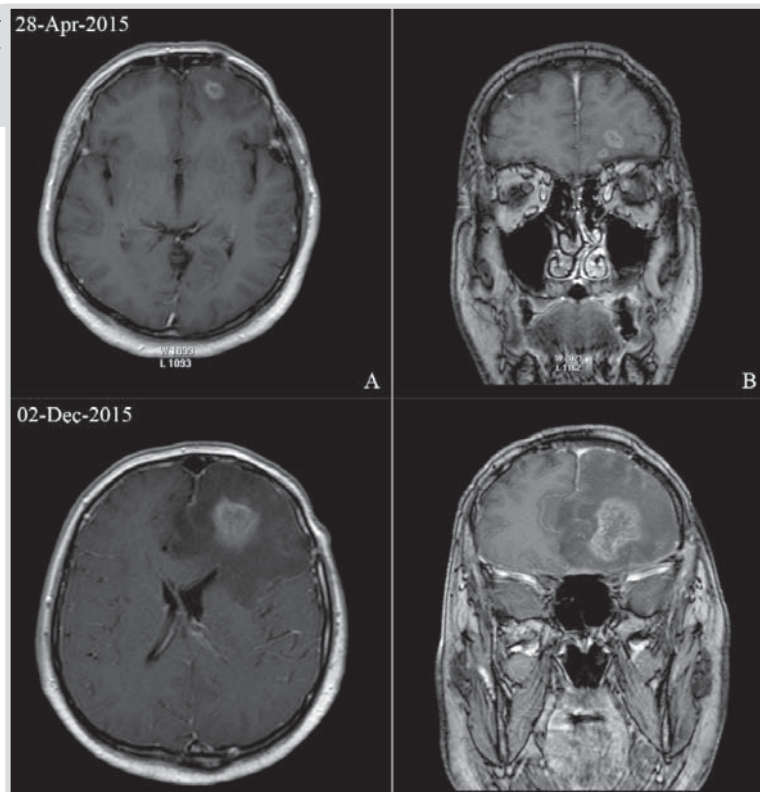
All patients with orbital SFT described in the literature underwent a surgery: in 75 cases (63%) it was radical, in 10 (8.4%) it was non-radical and in 30 (25.2%) the type of surgery was not specified. In 3 (2.5%) cases, no treatment method was specified. One patient (0.8%) with non-operative SFT underwent palliative radiotherapy. Tumors recurred in 13 patients (11%). Average time to relapse was 38.4 months after radical procedure and 28 months after subtotal resection [4, 28, 32, 36, 43, 54, 63].

Radiotherapy

Non-radical character of surgery and presence of so-called positive margins correlate with a higher risk of recurrence in patients with SFT. It therefore seems justified to apply postoperative radiotherapy in such cases [69]. To date, there have been no publications on the efficacy of radiotherapy in SFT of the orbit.

Among cases of orbital SFT described in the literature, postoperative radiotherapy was ap-

Fig. 5. Metastases in the left hemisphere, frontal lobe, contrast-enhanced T1-weighted images. **A:** axial plane, **B:** coronal plane



plied only in 2 patients after radical surgery and in 2 patients after subtotal tumor resection. Tab. 1. Only one patient, after non-radical surgery and delivery of 2 Gy to the total dose of 40 Gy, developed local relapse and distant metastases. In the remaining patients, stable disease was obtained with SRS. In our case, there was no local recurrence 36 months after SRS and the lobe.

Radiation doses and techniques were described in only in 2 of 4 patients with orbital SFT reported by other authors. One patient received a single dose of 15 Gy using radiosurgery, and the other patient received conventional fractionated doses of 2 Gy to the total dose of 40 Gy [41, 52]. In our case, a single dose of 20 Gy was delivered in SRS conditions.

Radiotherapy was also used for treatment of relapse as the only treatment in one patient or as adjuvant treatment after surgery in two patients. In the former case, the patient received a dose of 59.4 Gy (33 fractions), and in the other case – 50.4 Gy (28 fractions) [58, 64].

Due to tumor location and the presence of critical structures, the method of choice in orbital SFT is intensity-modulated radiotherapy (IMRT) or SRS. In our case, there were no acute radiation reactions or late symptoms of critical organ injury 36 months post-treatment.

Literature data evaluating the efficacy of radiotherapy in SFT in other locations than the orbit are contradictory. Sonabend et al. [70] assessed 227 patients with SFT in various locations and observed significantly longer survival in patients treated with postoperative radiotherapy. Wushou et al. [71], in turn, demonstrated that postoperative radiotherapy in patients with SFT within the head and neck region improved local control but did not affect survival. Moreover, the authors found no benefits of postoperative radiotherapy with respect to 5-year survival in patients with SFT in the chest [72]. On the other hand, Bisceglia et al. [73], having analyzed 220 cases of SFT of the central nervous system, noticed benefits of post-

Tab. 1. Disease-free survival in patients with orbital SFT treated with surgery combined with radiotherapy

| Applied treatment | Number of patients | Follow-up period in months (average) | Relapse or distant metastases | Radiotherapy | Authors |
|--|--------------------|--------------------------------------|---|-------------------------|--|
| Radical surgery | 5 | 48 48 48 36 12 (38,4) | Relapse Relapse Relapse Relapse Relapse | — | Dorfman [4] Polito [36] Polito [36] Manousardis [54] Blandamura [64] |
| Subtotal resection | 3 | 6 42 36 (28) | Relapse Relapse Relapse | — | Hayashi [28] Tam [32] Young [43] |
| Surgery – no data on the extent | 4 | 3 4 36 3 (11,5) | Relapse Relapse Relapse Relapse | — | de Saint Aubain [16] Aleksandrakis [20] Carrera [23] Kirshnakumra [2] |
| Radical surgery + radiotherapy | 2 | 48 18 (33) | No data No data | No data No data | Polito [36] Wang [55] |
| Subtotal resection + radiotherapy | 2 | 42 12 (27) | Relapse/M No data | 40 Gy/20fr SRS 15 Gy | Parrozzani [41] Cerdeja Nicolas [52] |
| Surgical treatment of relapse with adjuvant radiotherapy | 2 | 36 36 (36) | No data No data | No data 59,4 Gy/33fr | Polito [36] Monosourdis [54] |
| Treatment of relapse with radiotherapy | 1 | 84 | Relapse | 50,4 Gy/28fr | Blandamura [64] |
| Palliative radiotherapy | 1 | No data | PD | 50,4 Gy/28fr | Suzuki [31] |

SRS – stereotactic radiosurgery; PD – progressive disease; M – distant metastases

perative stereotactic radiotherapy or teloradiotherapy only in patients after non-radical surgery [73]. Other authors claim, however, that the usage of radiotherapy has no effects on survival [74].

Since postoperative radiotherapy was applied in only 4 patients with orbital SFT, as reported in the literature, its efficacy cannot be assessed in a reliable way. Based on our case of a patient with orbital SFT who underwent a non-radical procedure and case reports found in the literature, it can be claimed that postoperative irradiation can be a safe and effective treatment method. Administration of a single dose of 15–20 Gy enables local control. Our case shows that even large tumors (4.92 cm³) can be effectively treated with a dose of 20 Gy. Administration of such a dose using SRS does not injure critical structures.

Chemotherapy

The development of a new cerebral lesion 36 months after irradiation with complete local control means that systemic treatment must be considered. To date, there have been no clinical trials assessing the efficacy of chemotherapy in this group of patients. One of drugs that exhibits certain efficacy in SFT treatment is

dacarbazine [75]. Moreover, promising results have been obtained after using Interferon alfa and a combination of bevacizumab and temozolomide in patients with recurring SFT [76, 77]. Another drug used in these patients is toremifene, with good response even in patients with STF presenting no estrogen receptor expression [78]. For malignant and aggressive SFT, tyrosine kinase inhibitors might prove useful. Animal tests have also shown effects after administration of Sunitinib, Pazopanib and Regorafenib [79, 80].

CONCLUSION

SFT of the orbit is a rare cancer. Surgery remains the treatment of choice. Nonetheless, adjuvant radiotherapy should be considered due to frequent application of non-radical procedures and the risk of local recurrence. Based on our patient and literature reports, it can be stated that adjuvant radiotherapy, with a dose of 20 Gy, following a non-radical surgical procedure, is a safe and effective treatment method. However, due to a low number of cases of orbital SFT presented in the literature, clinical trials are needed to reliably assess the role of radiotherapy.

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