Post-operative Radiotherapy for the Treatment of Malignant Solitary Fibrous Tumor of the Nasal and Paranasal Area

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Objective: Solitary fibrous tumor is a rare tumor occurring in almost every anatomic location of human body; however, reports of malignant solitary fibrous tumor in the nasal and paranasal area are especially rare. In this report, we describe a case of non-recurrent malignant solitary fibrous tumor of the nasal and paranasal area.

Methods: The patient was initially treated with nasal and paranasal tumor cytoreductive surgery, followed by post-operative three-dimensional conformal intensity modulated radiation therapy (dynamic MLC Varian 600CD Linac, inversely optimized by the Eclipse system) and stereotactic body radiation therapy to provide a radical cure for residual tumor.

Results: The tumor of the nasal and paranasal area was effectively treated and the integrity of the right eye kept. There were no signs of recurrence after four and a half years of further follow-up.

Conclusions: This is the first attempt to successfully combine cytoreductive surgery with intensity modulated radiation therapy and stereotactic body radiation therapy together to treat solitary fibrous tumor of the nasal and paranasal area, which may provide a potential strategy for the treatment of similar cases.

Key words: solitary fibrous tumor – radiotherapy

INTRODUCTION

Solitary fibrous tumor (SFT) is an uncommon spindle cell tumor that was first recognized and fully characterized in 1994 by Westra et al. (1). SFT often originates from the pleura, and occasionally from other parts of the body, including the extremities, mediastinum, peritoneum, parotid gland and orbit (1–6). Radical surgical resection is the preferred treatment for SFT. Here, we present a case of malignant SFT of the nasal and paranasal area that was treated by cytoreductive surgery combined with intensity modulated radiation therapy (IMRT) and solitary fibrous tumor (SBRT). No recurrence was seen in long-term follow-up.

CASE REPORT

An 18-year-old female was admitted to the Xijing Hospital of Shaanxi Province, China in April due to painless proptosis, decreased visual acuity and epiphora in the right eye. Prior to the onset of symptoms, the uncorrected visual acuity was 4.3 and 4.8 in the right and left eyes, respectively. The patient had no family history of similar symptoms.

An orbital computed tomography (CT) scan showed that a large mass fully occupied the right nasal cavity, sinuses and frontal sinuses (Fig. 1A and B). The mass impinged on the right eye and the right maxillary sinus, and caused nasal septum perforation with oppressing on the left ethmoidal cellules (Fig. 1A and B). In order to keep the integrity of the right eye, nasal and paranasal tumor cytoreductive surgery was performed to partially resect the paranasal sinus tumor inside the right nasal cavity with image navigation. During the operation, a wider range of tumor invasion was observed, showing invasion of the ethmoid bone roof, the sphenoid sinus anterior wall, nostrils and the laminapapyrus.
The tumor tissue was grayish-white, like fish with brittle textures, covered with a fibrous bone shell. The post-operative specimen was a dark brown nodular mass (9 × 6.5 × 5 cm) with incomplete envelope. On the cut section, the tumor was grayish-white, lobulated, firm and well-demarcated, with a whorled and fasciculated surface. Light microscopic examination of the resected tumor showed large numbers of tumor cells that are oval and fusiform, distributed in patches with significant atypia by Hematoxylin and eosin staining. The branched blood vessels, abnormal cells, mitotic figures and nuclear polymorphisms were frequently noted (Fig. 2A and B).

Due to the low incidence and histologic similarity to other spindle cell tumors, early diagnosis of nasal and paranasal SFT is difficult. The main clinical manifestation is painless proptosis. The diagnosis is mainly dependent on immunohistochemical studies. It has been documented that SFT exhibits strong positivity with CD99 (70%), vimentin (95%) and Bcl-2 (35%) antibodies, and is negative for S-100 (7). In addition, Ki-67 proteins are excellent markers for determining the so-called growth fraction of a given cell population. In the present case, immunohistochemical staining revealed that cells were positive for CD99 (Fig. 3A), Vim (Fig. 3B) and Bcl-2 (Fig. 3C), and contained scattered CD34-positive cells (Fig. 3D). Ki67-positive cells accounted for almost 28% of all cells (Fig. 3E). All cells were negative for S-100 (Fig. 3F). On the basis of the aforementioned results, pathological evaluation ascertained the presence of a malignant SFT with bone invasion.

Three weeks after surgery, magnetic resonance imaging (MRI) imaging of the nasopharynx revealed an irregular, inhomogeneous mass in the right nasal cavity and ethmoid sinus (4.1 × 2.8 cm) (Fig. 4). A radiation treatment plan, three-dimensional conformal IMRT was developed for the patient after CT-guided tumor localization. VRIN 600CD was used as the treatment machine. The Eclipse planning system was LUNA TM 260. The gross tumor volume (GTV), including residual tumor, was visualized on CT and MRI. The clinical tumor volume (CTV) was calculated including the right nasal cavity, part of the left nasal cavity, right maxillary sinus, anterior and posterior ethmoid sinus, sphenoid sinus and part of the nasopharyngeal mucosa. The planning target volume (PTV) was 0.3 cm outside of the CTV. The total GTV irradiation received was 60 Gy/24F, 2.5 Gy/F, one session/day and five sessions/week. The total PTV irradiation was 55.2 Gy/24F, 2.3 Gy/F, one session/day, and five sessions/week. During the second treatment course, SBRT therapy was delivered targeting the GTV, with a total irradiation dose of 12 Gy/3F, 4 Gy/F, one session/every other day. A 50% isodose line surrounded the targeted region. Dose constraint for each organ

Figure 1. Orbital computed topographies scan of right orbit solitary fibrous tumor (SFT). (A) The image shows a 5 cm-sized, well-demarcated nodule with an eccentric nodular enhancement. (B) A coronal image shows a mass lying in the orbit.

Figure 2. Hematoxylin and eosin-stained slide. (A) Microscopic examination of the orbit lesion shows proliferation of relatively uniform spindle cells that are either patternless or have a focally storiform pattern. (B) Focal vascular dilatation with collagenized stroma, dense collagen nodules and perivascular hyalinization is also observed.
at risk were as follows: brainstem, $D_{\text{max}} \leq 54 \text{ Gy} \ D_1 \leq 60 \text{ Gy}$; optic chiasma, $D_{\text{max}} \leq 54 \text{ Gy} \ D_1 \leq 60 \text{ Gy}$; bilateral crystal, $D_{\text{max}} \leq 5 \text{ Gy} \ D_{33} \leq 8 \text{ Gy}$; bilateral eye, $D_{\text{max}} \leq 50 \text{ Gy}$; and the left optic nerve, $D_{\text{max}} \leq 54 \text{ Gy} \ D_1 \leq 60 \text{ Gy}$. Besides, the DVH for each organ were as follows: brainstem ($D_{\text{max}} 44.1 \text{ Gy} \ D_1 45.6 \text{ Gy}$), optic chiasma ($D_{\text{max}} 43.2 \text{ Gy} \ D_1 44.1 \text{ Gy}$), bilateral crystal ($D_{\text{max}} 5.1 \text{ Gy} \ D_{33} 5.4 \text{ Gy}$), bilateral eye ($D_{\text{max}} 41.2 \text{ Gy}$) and the left optic nerve ($D_{\text{max}} 45.4 \text{ Gy} \ D_1 46.5 \text{ Gy}$).

After radiation therapy, the patient complained of xerostomia, ageusia and anosmia. Furthermore, there was no significant relief of right nasal cavity obstruction and binocular visual acuity after treatment.

With reexamination for primary tumor 5 months after radiotherapy, nasal congestion symptoms were abated in the right nasal cavity, but still accompanied with the xerostomia, ageusia and anosmia. The visual acuity of the right eye was $4.3$, indicating no change compared with levels before radiation therapy. MRI analysis showed an absence of the right turbinate and the medial wall of the right maxillary sinus. The lesions on the right nasal cavity and ethmoid sinus showed hyper signals ($2.9 \times 3.4 \times 2.1 \text{ cm}$) with defined border using enhanced MRI (Fig. 5A1 and A2).

Eighteen months after radiation therapy, reexamination showed that the xerostomia was significantly ameliorated. Symptoms of stuffy nose and headache had disappeared. The

Figure 3. Immunohistochemical test of the SFT. Immunohistochemical tests showed that the tumor was positive for CD99 (A), Vim (B) and Bcl-2 (C), and contains scattered CD34-positive cells (D). Ki67-positive cells accounted for $\approx 28\%$ of all cells (E). All cells are negative for S-100 (F).

Figure 4. Tumor image of MRI at 3 weeks after surgery.
Figure 5. Follow-up reviews. The follow-up reviews after 5 months (A1, A2) and eighteen months (B1, B2) showed a reduction in the size of the mass, and four and a half years after therapy, no change was seen in the size of the mass in the right nasal cavity (C1, C2).
sense of taste and smell had almost returned to normal levels. Visual acuity of the right eye was 4.3. MRI showed a reduction in size of the mass (2.5 × 3.1 × 1.6 cm) in the right nasal cavity and ethmoid sinus (Fig. 5B1 and B2).

Four and a half years after radiation therapy, the symptoms of xerostomia had completely disappeared. The left eye visual acuity was stable (4.6) and the right eye visual acuity decreased slightly (4.1). The senses of taste and smell were normal. MRI showed no change in the size of the mass in the right nasal cavity and ethmoid sinus (2.0 × 3.1 × 1.5 cm). No local recurrences were observed (Fig. 5C1 and C2).

DISCUSSION

SFT is a rare soft tissue spindle cell tumor. It can occur in every site of the body, including the mediastinum, lung, pleura, liver, kidney, orbit and meninges (3, 8, 9). The age of onset is mainly between 40 and 70 years. There was no significant difference between males and females (9, 10). Most SFT cases are benign neoplasms; however, ~10–15% are malignant neoplasms, especially those in mediastinal, abdominal, pelvic and retroperitoneal locations (6, 11). Metastases may occur in the lungs, bones and liver. Malignancy is defined as a significantly increased tumor cell density, clear cell atypia, more than four mitotic figures in every 10 HPF, and the presence of necrosis (6, 11–13).

SFT of the nasal and paranasal area was first reported in 1994 (14) and most SFT are benign (15, 16). Infiltrating growth is not a common feature of pathology, and only a few cases reveal malignant transformation. SFT displays high CD34 reactivity in 79–100% of cases (14). On the contrary, malignant SFT may show high mitotic counts and loss of CD34 immunoreactivity (17, 18). Therefore, CD34 is used to distinguish benign and malignant SFT. Most samples in this case report showed immunohistochemistry results that were negative for CD34, resulting in the diagnosis of a possible malignant entity according to the benign–malignant system. Combined with the appearance of branched blood vessels, abnormality cells, mitotic figures and nuclear polymorphisms under the light microscope, it is reasonable to judge this case to be a malignant lesion.

SFT of the nasal and paranasal area is a rare neoplasm, and there are no standard clinical treatment guidelines. Complete surgical removal is the main treatment strategy, but some drawbacks still exist in the clinical application in SFT of the nasal and paranasal area. Complete resection is often restricted due to the small volume of the nasal and paranasal tissue, the presence of vital organs, large tumor volumes, a lack of complete encapsulation and invasive growth. Recently, tumor cytoreduction combined with post-operative adjuvant therapy has been considered more advantageous in SFT from nasal and paranasal area. Stereotactic radiation therapy is often used as post-operative therapy, and has been reported to effectively control residual tumors (19, 20). However, radiation therapy can damage the optic nerve, optic chiasm, cornea and lens, resulting in decreased visual acuity or visual field defects. Consequently, post-operative radiation therapy may need to be improved for the treatment of SFT in the head.

IMRT is known to enable the delivery of lower doses of radiation to normal tissue, while increasing or maintaining the tumor dose, which exhibits more advantages than two-dimensional radiotherapy (2DRT) or three-dimensional conformal radiotherapy (3D CRT). The potential of IMRT for sparing organs has been demonstrated in patients with mixed head and neck tumors (21) and nasopharyngeal cancers (22). In this study, the patient had a large localized nasal and paranasal tumor with diffuse local extension. To preserve the right eye, as required by the patient, the tumor was partially resected. In order to better control the primary tumor and avoid recurrence and metastases, a post-operative IMRT was used to eliminate residual tumors. In this patient, IMRT was well used and the healthy tissues of the left side received non-toxic doses of radiation, which preserved the visual acuity and visual field of the patient’s left eye. In the subsequent follow-up, the vision of the patient was maintained at a stable level after treatment, confirming that our strategy was effective and can be referenced. However, the eye, lens and optic nerve of the right eye were closely related to the tumor, so IMRT could not be strictly targeted.

SBRT is a relatively new type of radiosurgery that is capable of the precise delivery of converging beams of radiation on a small target in almost any location in the body (23, 24). Studies have shown that SBRT after external irradiation improves the local control and survival rates in nasopharyngeal cancer. SBRT could effectively enhance the protection of healthy tissues, which is important in the treatment of head and neck cancers (25, 26). In this case, SBRT was used in combination with IMRT in the residual tumor to remedy the deficiency of IMRT and protect contralateral healthy organs and reduce the acute and late-stage side effects of radiation. In the subsequent follow-up, the right nasal cavity and paranasal sinus tumors progressively decreased in size. The patient experienced no obvious decline in visual acuity or visual field defects, even though the maximum dose delivered to the right optic nerve and right eye were up to 64 and 62 Gy, respectively. The symptoms of nasal obstruction, xerostomia, ageusia and anosmia disappeared gradually during follow-up.

CONCLUSION

In this report, we described a case of malignant SFT originating from the nasal and paranasal area. Following cytoreductive surgery, two post-operative radiation therapies of IMRT and SBRT were performed; no recurrences or metastases occurred during long-term follow-up. Therefore, this report indicates an effective strategy for the treatment of malignant SFT of the nasal and paranasal area. More research and longer follow-up should be explored in the future based on the recommended strategy.
Conflict of interest statement

None declared.

References