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Healing Efficacy After Surgery and Intensity-Modulated Radiotherapy for Extremely Rare Maxillary Giant Cell Tumor

Lena Marinova[1]*, Radoslav Georgiev[2] and Nikolay Evgeniev[3]

[1]Complex Oncology Center, Department of Radiotherapy; Russe, Bulgaria

[2]UMHAT"St. Marina", Varna, Department of Imaging, Radiation therapy and Nuclear medicine; Varna, Bulgaria

[3]Complex Oncology Center, Department of Medical oncology; Russe, Bulgaria

ABSTRACT

Giant cell tumors are rare benign borderline tumors, and maxillary localization is extremely rare. Because of the few clinical cases, healing behavior is very different, although the primary is the surgery. We present a 72-year-old man in which, on the occasion of difficulty left nasal breathing with four months of length, in January 2021 an operation was carried out on a left maxillary sinus. Histological diagnosis is a giant cell tumor (GCT) of the maxillary sinus. The patient is targeted for post-operative radiotherapy (RT). After one month of surgery, an intensity-modulated RT (IMRT) by the VMAT metod in the tumor area in the left nasal cavity and the left maxillary sinus up to total dose (TD) 66 Gy, as well as a 5 mm zone in the surrounding healthy tissue (CTVp) up to TD 64 Gy with daily dose (DD) 2 Gy were performed. The main purpose of this article is to emphasize the difficult pathologist diagnosis, as well as presenting the healing capabilities of intensity- modulated radiotherapy (IMRT). In the central cranial and facial GCTs, due to the impossibility of carrying out radical surgery, a postoperative IMRT is imposed, which achieves a homogeneous distribution of the radical dose in the target volumes with simultaneously strict haircuts of surrounding healthy tissues and organs.

***Corresponding author**

Lena Marinova, Complex Oncology Center, Department of Radiotherapy, Russe, Bulgaria, E-mail: rad_marinova@abv.bg

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Introduction

Soft tissue giant cell tumors (GCTs) of low malignant potential are rare benign borderline tumors located in superficial and deep soft tissue [1,2]. They make up 3,9%-5% of all primary bone neoplasms and 20% of all benign bone tumors [3-5]. Although it is composed of mature tumor cells, distant metastases, most commonly lung (1% -5%), are found in 2% of clinical cases [6-8]. Nasal cavity represents a very unusual location for this type of tumors [2]. A review of the literature showed that GCT of the maxilla has been seldom encountered [9]. In the area of the tumor there is local pain with soft tissue edema, combined with reduced motor activity, and in large inoperable tumors - severe neurological pathology [10]. Due to the rare diagnosis of sino-nasal GCTs and the relatively small number of clinical cases treated with different methods, the treatment of these tumors is considerable controversy [11]. This article discusses a complex treatment approach for giant cell sino-nasal tumors, focusing on the indications for radiotherapy combined with surgery.

Clinical Case

We present a 72-year-old man in which, on the occasion of difficulty left nasal breathing with four months of length, in January 2021 an operation was carried out on a left maxillary sinus.

Preoperative local status after the front rhinoscopy

Formation clogs the lower left of the nasal cavity. Unable to visualize tumor in depth. There is a deformation with a protrusion of the left maxillary sinus wall as well as a slight soft edema. On the left, there are no increased submandibular lymph nodes palpated.

Preoperative contrast-enhanced cranial CT

Mixed osteolytic and osteosclerotic lesion of the left maxilary sinus and left nasal cavity with a heterogeneous structure. Presence of a soft tissue component, associated with bone expansion and erosion (Figure: 1).

Intraoperative

Tumor with solid consistency engaging all left maxillary sinus with exteriorization to the front wall and the lateral bone wall of the nasal cavity. A tumor curettage with clean resection edges was performed.

Histological result

Giant cell tumor of the the left maxilary sinus and left nasal cavity with destructive biological behavior of borderline malignancy. There is proliferation of osteoclast-like multinuclear giant cells and polygonal, oval and drained mononuclear stromal cells.

Diagnosis-Giant cell tumor of bone/ osteoblastoclastoma

The patient is targeted for post-operative radiotherapy (RT). After

one month of surgery, an intensity-modulated RT (IMRT) by the VMAT metod in the tumor area in the left nasal cavity and the left maxillary sinus up to total dose (TD) 66 Gy, as well as a 5 mm zone in the surrounding healthy tissue (CTVp) up to TD 64 Gy with daily dose (DD) 2 Gy were performed (Figure: 2,3). Three months after RT was held postoperative contrast-enhanced cranial CT with significant reduction of the tumor volume and the mass effect, and osteosclerotic transformation of the lesion (Figure: 4).

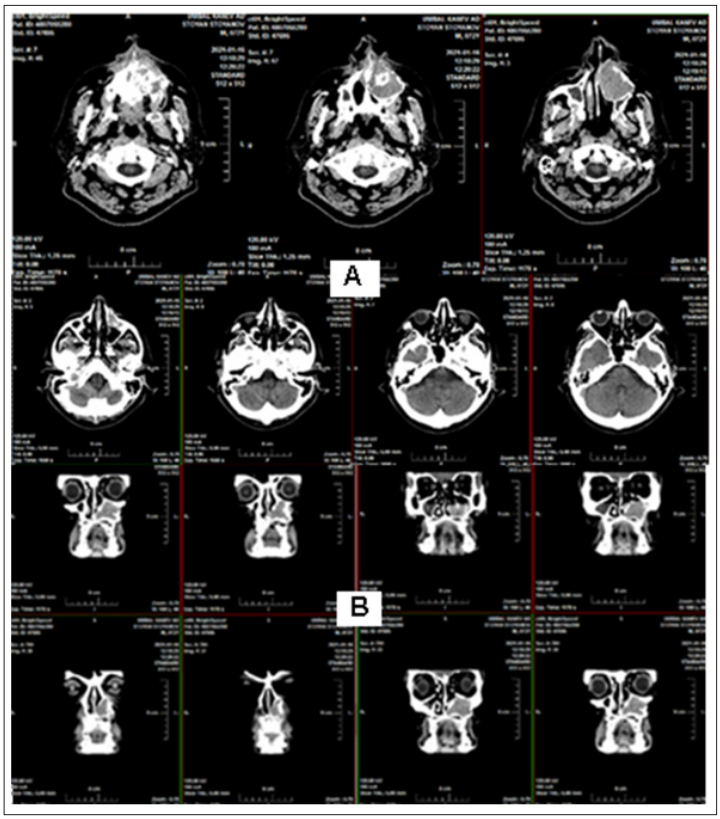
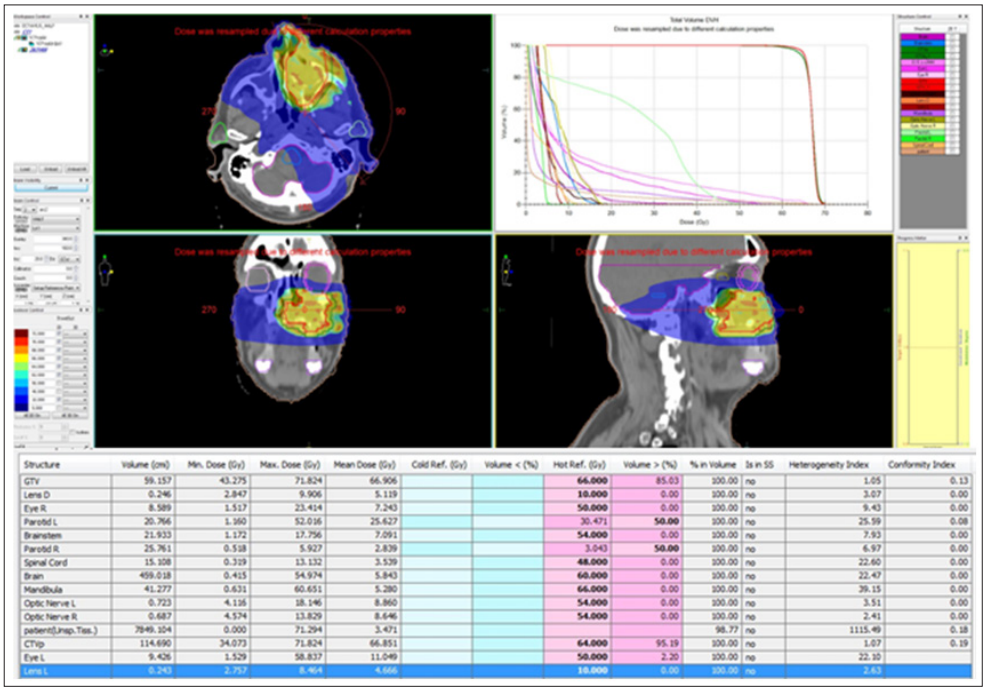


Figure 1: Preoperative contrast-enhanced cranial CT with axial slices (A) and coronal slices (B) revealed mixed osteolytic and osteosclerotic lesion of the left maxilary sinus and left nasal cavity with a heterogeneous structure. Presence of a soft tissue component, associated with bone expansion and erosion.



Structure	Volume (cm)	Min. Dose (Gy)	Max. Dose (Gy)	Mean Dose (Gy)	Cold Ref. (Gy)	Volume < (%)	Hot Ref. (Gy)	Volume > (%)	% in Volume	Is in SS	Heterogeneity Index	Conformity Index
GTV	59.157	43.275	71.824	66.906			66.000	85.03	100.00	no	1.05	0.13
Lens D	0.246	2.847	9.906	5.119			10.000	0.00	100.00	no	3.07	0.00
Eye R	8.589	1.517	23.414	7.243			50.000	0.00	100.00	no	9.43	0.00
Parotid L	20.766	1.160	52.016	25.627			30.471	50.00	100.00	no	25.59	0.08
Brainstem	21.933	1.172	17.756	7.091			54.000	0.00	100.00	no	7.93	0.00
Parotid R	25.761	0.518	5.927	2.839			3.043	50.00	100.00	no	6.97	0.00
Spinal Cord	15.108	0.319	13.132	3.539			48.000	0.00	100.00	no	22.60	0.00
Brain	459.018	0.415	54.974	5.843			60.000	0.00	100.00	no	22.47	0.00
Mandibula	41.277	0.631	60.651	5.280			66.000	0.00	100.00	no	39.15	0.00
Optic Nerve L	0.723	4.116	18.146	8.860			54.000	0.00	100.00	no	3.51	0.00
Optic Nerve R	0.687	4.574	13.829	8.646			54.000	0.00	100.00	no	2.41	0.00
patient(Unsp.Tiss.)	7849.104	0.000	71.294	3.471					98.77	no	1115.49	0.18
CTVp	114.690	34.073	71.824	66.851			64.000	95.19	100.00	no	1.07	0.19
Eye L	9.426	1.529	58.837	11.049			50.000	2.20	100.00	no	22.10	
Lens L	0.240	2.757	8.464	4.666			10.000	0.00	100.00	no	2.63	

Figure 2: Intensity-modulated RT by the VMAT metod for left sino-nasal giant cell tumor / left nasal cavity and maxillar sinus/ up to TD 66 Gy, as well as a 5 mm zone in the surrounding healthy tissue (CTVp) up to TD 64 Gy with daily dose (DD) 2 Gy. The maximum and minimum doses in different target volumes (GTV, CTVp), and various realized doses in the critical normal surrounding tissues and organs such as left eye lens, left parotid gland and left mandibulla are presented. The heterogeneity index in the gross tumor volume (GTV) is 1.05 and in CTVp- 1,07.

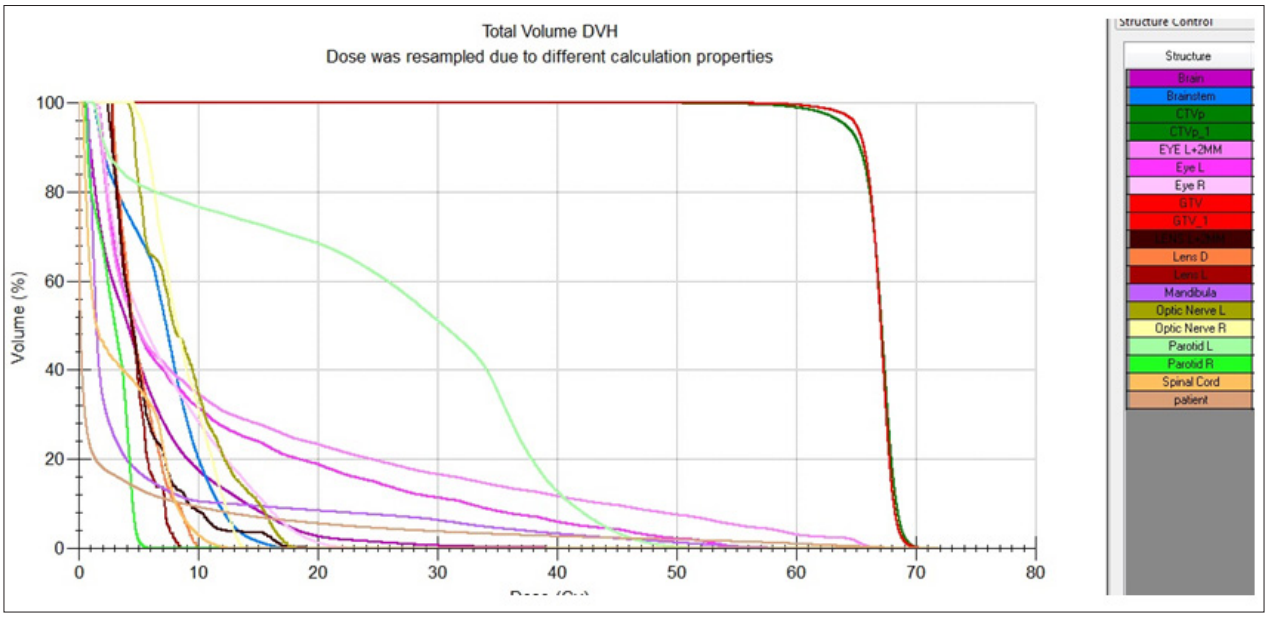


Figure 3: A cumulative dose-volume histogram (DVH) with the steep drop of doses after GTV and CTVp, resulting from good homogeneity of the realized dose and presents the various realized doses in the critical normal surrounding tissues and organs

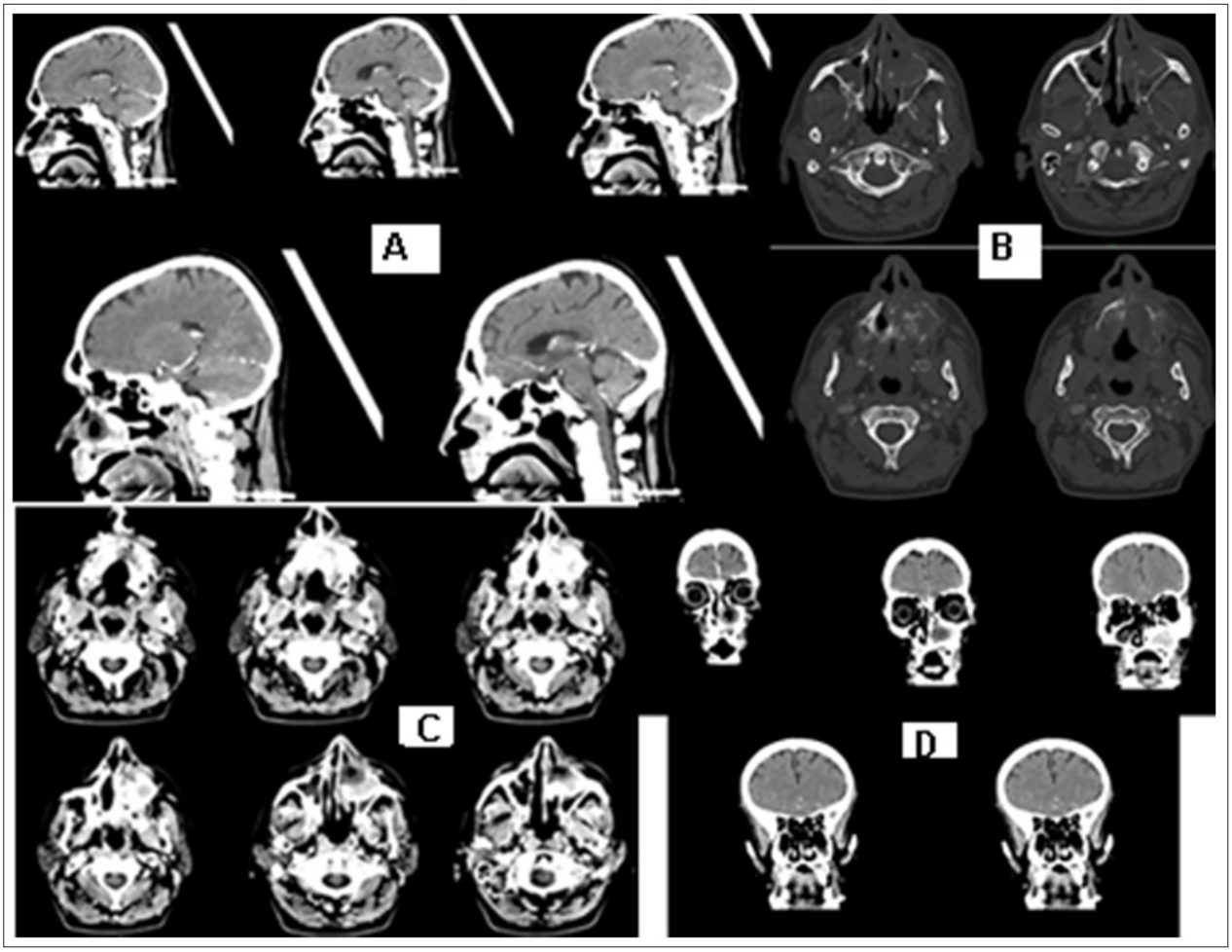


Figure 4: Postoperative contrast-enhanced cranial CT – A/ in sagittal plane; C/ in axial plane and D/ in coronal plane, including bone window in axial plane (B), done 6 months from the surgery and 3 months from the radiotherapy revealed significant reduction of the tumor volume and the mass effect, and osteosclerotic transformation of the lesion

Discussion

The GCT's had been described under a variety of names viz: haemorrhagic osteomyelitis, ossifying haematoma, osteitis fibrosa cystica, atypical subperiosteal giant cell tumor, aneurysmal giant cell tumor, hemangiomatous bone cyst, subperiosteal bone aneurysm, expansile haemangioma and pulsating giant cell tumor [12]. Giant cell lesions of the maxilla and paranasal sinuses represent a rare, locally aggressive disorder which present as a soft tissue mass with distinct histologic and clinical features [11]. Occurrence of such tumors in the cephalic segment is rarely observed, and most frequently they are located in the mandible, maxilla, temporal bone and calvarium [3]. Because of the low frequency of giant cell tumors (GCTs) in the skull and face, Lichtenstein L./1965, affirmed that, before accepting a diagnosis in such sites, a careful histological investigation is required [13]. GCTs are composed of evenly spaced multinucleated giant cells in a background of mononuclear component composed of round, oval or spindled cells [2-14]. They are characterized by a profuse multinucleate giant cell scattered throughout the stroma of mononuclear cells. These giant cells have some similarity with osteoclasts, and so are called osteoclastoma [15,16]. GCTs were formerly considered benign, but in the last years, the clinical experience has demonstrated, that such tumors are aggressive and present malignancy potential in about 20% of cases [17]. As criteria to establish the malignancy degree, one should consider the number of giant cells and respective nuclei, the mitotic index, osteoid development, and the presence of cell atypias or metaplasias [18]. GCT are non neoplastic but locally aggressive tumors with occasional rapid growth, that may be differentiated from other multilocular lesions like ameloblastoma, giant cell granuloma and sarcomas [19]. GCTs require a strict differential diagnosis with giant cell reparative granuloma (GCRG), which is an uncommon and benign reactive tumor [20,21]. Although histologically GCRG's are very similar to GCTs, GCRG are distinguished from giant cell tumors on the basis that GCRGs exhibit low mitotic activity, while GCTs exhibit a high rate of mitotic activity which explains GCT's malignant potential [22]. The most differential radiological GCT characteristics are multiple anomalous branches in angiogram, multilocular cystic structure in the Computed Tomography (CT) with bone window, presence of liquid both in the CT or Magnetic Resonance Imaging (MRI) [23].

Surgery

As it is a borderline benign locally aggressive tumor, the treatment of choice is surgical excision and curettage of the cavity [24,25]. The volume of surgical resection depends on the tumor location. It is desirable to perform a radical volume operation - "en-bloc" resection with clean cells resection lines / without the presence of tumor cells or resection sufficiently tight [7,26]. In smaller lesions in the cervical spine, spondylectomy is possible, followed by a bone graft [27]. After radical surgery, 85-90% local tumor control (LTC) is achieved [5,28]. J P Stolovitzky, et al./1994 hypothesize that giant cell "granuloma" of the maxilla and paranasal sinuses and GCTof other bones represent a continuum of a single disease process, which may have an aggressive clinical behavior and they advocate surgical resection for all giant cell lesions [11]. Regardless of the site of presentation, partial resection or curretage results in a recurrence rate of up to 70%, whereas recurrence after wide resection is about 7% [29]. More than 50% of local recurrences are diagnosed after non-radical surgery, despite improved surgical techniques and the pursuit of complete tumor removal [30,31]. In the clinical case presented, the tumor shall be manifested by the mixed osteolytic and osteosclerotic lesion of the left maxilary sinus and left nasal cavity (Fig.1), which is a sign, that the surgery can not achieve LTC. The risk of relapse is high, which imposes post-operative RT.

Radiotherapy (RT)

RT is imposed as adjuvant therapy after nonradical surgery or as alternative treatment for inoperible tumors, as well as in tumors with certain local disadvantages of functional deficiency after surgery [32,33]. Local recurrences after a single RT reached 49%, after surgery with positive resection lines -47%, after a positive resection lines surgery followed by RT-46% and 0% after a radical operation [28]. GCTs offers a very large range of realized doses up to 35-54-64Gy through conventionally fractionated RT [32,34]. After RT up to TD 40-60 Gy realized with 15-30 fractions for a period of 3-6 weeks, 90% LTC was achieved [33,35]. RT up to TD 35-55 Gy at average TD 43 Gy with DD 1.67-2.33 Gy achieves 65% -77% -80% LTC [35,36]. In GCTs less than 4 cm in diameter after single RT up to TD 40-45Gy 90% LTC is reported, and in larger ones recommended a combination of the surgery and RT [37]. 3D conformal RT and IMRT are possible to realize high radiation doses to increase LTC without significant late radiation changes in the adjacent healthy tissues. In the presented clinical case, we performed IMRT up to OOD 66 Gy (Fig. 2, Fig. 3). Maximum and mean doses in different planning target volumes (GTV, CTVp), as well as in critical adjacent tissues and organs such as left eye lens, left parotid gland and left mandibulla are presented. The heterogeneity index (HI) is a tool for evaluating dose gradients within a planning target volume (PTV). In the clinical case presented, the heterogeneity index in the gross tumor volume GTV is 1.05 and in CTVp- 1,07 (Fig. 2).

A dose-volume histogram (DVH) is a histogram, relating radiation dose to tissue volume in RT planning [38]. Fig.3 shows cumulative dose-volume histogram (DVH) with the steep drop of doses after GTV and CTVp, resulting from good homogeneity of the realized dose and presents the various realized doses in the critical normal surrounding tissues and organs. Three months after RT was held postoperative contrast-enhanced cranial CT with significant reduction of the tumor volume and the mass effect, and osteosclerotic transformation of the lesion (Fig.4).

Bisphosphonate (BPh)

has recently attracted attention also as an adjunct therapy for patients with GCT [39]. The treatment with bisphosphonate significantly reduced the recurrence rate of the disease in patients with GCT who received operative therapy [40].

Targeted therapy (TT)

In the inoperable recurrences of sino-nasal GCTs successfully targeted therapy after which the lesion maintained stable dimensions and became sclerotic and heavily ossified [31].

Conclusion

Giant cell bone tumors are rare benign, locally aggressive neoplasms. The main treatment method is surgery. The main purpose of this article is to emphasize the difficult pathologist diagnosis, as well as presenting the healing capabilities of intensity-modulated radiotherapy (IMRT). In the central cranial and facial GCTs, due to the impossibility of carrying out radical surgery, a postoperative IMRT is imposed, which achieves a homogeneous distribution of the radical doses in the target volumes with simultaneously strict haircuts of surrounding healthy tissues and organs. Three months after RT was held postoperative contrast-enhanced cranial CT with significant reduction of the tumor volume and the mass effect, and osteosclerotic transformation of the lesion. After 6 months of RT, the patient is without symptoms and with good quality of life.

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