Postoperative hypofractionated intensity-modulated proton therapy to control recurrent paraganglioma at the jugular foramen: A case report and literature review

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Abstract. Paragangliomas (PGLs) are rare neuroendocrine tumors with malignant potential that may prove challenging to manage. Those arising at the jugular foramen are particularly problematic, especially if recurring after primary surgical treatment. Long-term follow-up is required, and effective treatment options for such recurrences are needed. The present study chronicles a recurring PGL of the jugular foramen that emerged after two surgeries. Alternative therapeutic strategies were accordingly pursued. This account of the related clinical course includes a discussion of the associated literature, focusing on the role of proton beam therapy (PBT) in PGL management and its benefits. The patient under treatment received hypofractionated PBT, utilizing intensity-modulated proton therapy/pencil-beam scanning techniques. The prescribed dose was 40 Gy in 15 fractions [equivalent dose in 2-gy fractions (EQD2), 42.09 Gy, assuming α/β=10) delivered to the gross tumor volume (GTV). Simultaneous integrated boosts to two inner subvolumes [GTV reduced by 2-mm margin, 50 Gy/15 fractions (EQD2, 55.49 Gy); and GTV reduced by 3-mm margin, 60 Gy/15 fractions (EQD2, 70.00 Gy)] took place as well. This process ensured precise radiation dosing, while adhering to strict dose constraints for adjacent critical structures. Hence, a quicker therapeutic response (aligned with that of stereotactic radiotherapy principles) was tenable, aiming for both tumor control and clinical improvement. Long-term follow-up is imperative to assess outcome durability. The aforementioned events illustrate the potential utility of advanced PBT techniques (namely pencil-beam scanning, hypofractionated regimens) in managing PGL recurrences of this type, especially if surgical options are limited or carry substantial risks. PBT offers a precise therapeutic alternative, with tumor control capabilities that promise to preserve critical tissues near key locations at the base of the skull.

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Introduction

Paragangliomas (PGLs) are rare neuroendocrine tumors originating from paraganglionic cells adjacent to blood vessels and nerves. The tumors are classifiable as parasympathetic or sympathetic in type. Parasympathetic PGLs primarily involve the head and neck region, whereas sympathetic variants typically arise in the retroperitoneum, thoracic cavity and pelvis (1,2). Such tumors are seldom encountered, having an estimated annual incidence of 2-8 cases per million individuals (1,3). Overall, 6-19% are known to exhibit malignant behavior, developing distant metastases that often affect the regional lymph nodes, lungs and bones (1,4). According to World Health Organization guidelines, all PGLs should be viewed as potentially malignant and thus require vigilant, long-term follow-up, even after surgery (3,5).

Head and neck paragangliomas (HNPGLs) account for 65-70% of all PGLs (1). Although generally slow-growing, HNPGLs must be regarded as potentially malignant subsets of PGL, warranting long-term follow-up after treatment (4). Common sites of origin include the carotid body, temporal bone, jugular foramen, mastoid foramen and areas surrounding the vagus nerve (2,6).

The estimated incidence of HNPGL ranges from 0.3-1 case per 100,000 individuals every year in the general population,

underscoring its rarity (1). Our limited understanding of their biological attributes and a lack of standardized treatment strategies complicates interventional decisions, whether surgery, radiotherapy or observation, which remain challenging in each instance (1,6). Importantly, those tumors that recur near critical structures (such as the brainstem) are in need of safe and effective therapeutic strategies.

The present study details the course of a patient undergoing two surgical procedures for PGL. The tumor arose and then recurred at the jugular foramen, invading the medulla oblongata. Use of hypofractionated intensity-modulated proton therapy (IMPT) ultimately allowed successful tumor control. A discussion of pertinent resources in the literature is also provided.

Case report

Patient history: The patient was a 52-year-old woman who first experienced tinnitus in the left ear in November 2013 and presented to Yanshan Phoenix Hospital (Beijing, China). No clear cause was determined, but the patient was diagnosed with sensorineural hearing loss at the same hospital several months later. The patient received oral neurotrophic drugs and hyperbaric oxygen therapy. Subsequently, vasodilators, Traditional Chinese Medicine (herbal medicine), and acupuncture were administered at the Departments of Internal Medicine and Otolaryngology of Yanshan Phoenix Hospital, but there was no major improvement. The left-sided hearing loss continued to progress.

In August 2014, the patient also developed hoarseness. Left vocal cord paralysis was observed using a laryngeal fiberscope, so standard oral neurotrophic therapy (drug name and dose unknown) was initiated at Fangshan Chinese Medicine Hospital (Beijing, China), again without improvement. Another month after this, the patient presented with left-sided tongue deviation and dysphagia during liquid intake. According to the patient's medical history records from Zhuozhou Chinese Medicine Hospital (Zhuozhou, China), a space-occupying lesion was visible on magnetic resonance imaging (MRI). This lesion involved the left cerebellopontine angle, which raised suspicion of a primary tumor at the jugular foramen. The patient underwent a left paraganglioma resection via the retroauricular transmastoid and labyrinthine approach, combined with abdominal fat filling for cavity obliteration at the Chinese People's Liberation Army General Hospital (Beijing, China).

The pathology report issued by the Chinese People's Liberation Army General Hospital documented that postoperative tissue analysis confirmed the diagnosis of paraganglioma. Immunohistochemical staining was performed, demonstrating focal positivity for chromogranin A (CgA), as well as synaptophysin (Syn), CD56, S-100 protein and vimentin positivity. The Ki-67 index was low (3%) (data not shown).

Approximately 6 and one-half years after the initial resection, diplopia became an issue. Preoperative MRI at that time confirmed a recurrent lesion (data not shown). A second tumor resection took place 3 months later, at Beijing Tiantan Hospital (Beijing, China). Following analysis using standard procedures (fixation in 10% neutral buffered formalin, paraffin embedding and sectioning to 4 μm thickness, followed by hematoxylin and eosin staining), histological findings confirmed recurrent PGL. As shown in Fig. S1A, the tumor cells exhibited a nested arrangement (Zellballen pattern). Immunohistochemical staining performed using standard procedures (fixation in 10% neutral buffered formalin, paraffin embedding and sectioning to 4 μm thickness, followed by staining using DAB as the chromogen) showed strong positivity for CD56 (Fig. S1B) and CgA (Fig. S1C). The Ki-67 proliferation index was low (3-7%) (Fig. S1D). S-100 protein staining was positive in the sustentacular cells surrounding the tumor nests (Fig. S1E). Furthermore, the pathology report recorded positive results for other markers, including Syn, somatostatin receptor type 2 and CD34 (in vascular endothelium) (data not shown). There was partial positivity for transcription factor SOX10, and staining for STAT6, cytokeratin, thyroid transcription factor-1 and progesterone receptor was negative. Postoperatively, left facial nerve paralysis was apparent.

At 18 months after the second surgery, tumor progression was evident on MRI performed at Beijing Tiantan Hospital, and had extended into the medulla oblongata.

Current presentation. The patient underwent concurrent IMPT at Hebei Yizhou Cancer Hospital (Zhuozhou, China) in May 2023.

Planning and delivery of hypofractionated proton beam therapy (PBT). PBT was performed as a standalone procedure, using intensity-modulated proton therapy (IMPT) with pencil-beam scanning (PBS) and limiting treatment to local irradiation. The gross tumor volume (GTV) was configured by fusing contrast-enhanced MRI and planning computed tomography (CT) views, adding a 5-mm margin to GTV to ascertain clinical target volume (CTV). The enhancing lesion on MRI signified the GTV. For treatment planning, the patient's head was immobilized in a custom-made thermoplastic mask, and daily cone-beam CT (CBCT) imaging input offered guidance. Planning CT was performed in the treatment position at a 1-mm slice thickness, with CTV representing a 3-mm expansion of GTV. A further 3- to 5-mm margin was added to the CTV to arrive at planning target volume (PTV). IMPT served for dose delivery, adjusting prescribed doses based on tumor location. The treatment plan was designed to ensure that ≥95% of the PTV received prescribed dosing at the isocenter. A summary of the doses prescribed and constraints for organs at risk (OARs) is provided as Fig. 1. The equivalent dose in 2 Gy fractions (EQD2) was calculated to evaluate dosing, setting α/β ratios of 2 for the brainstem, optic nerves and optic chiasm, and 10 for the tumor itself. The presumed relative biological effectiveness of protons was 1.1, and the prescribed dose for the GTV was 40 Gy in 15 fractions (EQD2, 42.09 Gy, assuming α/β=10).

Two interior subvolumes of GTV were specified as GTV reduced by 2-mm margin and GTV reduced by 3-mm margin. Prescribed doses were 50 Gy/15 fractions (EQD2, 55.49 Gy) and 60 Gy/15 fractions (EQD2, 70.00 Gy), respectively.

The CTV determined as the contrast-enhancing lesion on MRI plus a 3-mm margin, received 30 Gy in 15 fractions (EQD2, 30.00 Gy).

As OARs, the cochlea received 44.61 Gy in 15 fractions (EQD2, 55.48 Gy, assuming α/β=2) and the brainstem received 34.1 Gy in 15 fractions (EQD2, 36.42 Gy, assuming α/β=2) (Fig. 2).

ROI statistics POI statistics

Dose	ROI	ROI vol. [cm³]	Dose [cGy] D99	D98	D95	Average	D50	D2	D1	% outside
Plan dose: 1st05 (CT 1)	BrainStem	27.74	3	7	25	1634	1691	3315	3410	0 %
Plan dose: 1st05 (CT 1)	CTV	21.98	2900	3000	3105	4606	4595	6664	6777	0 %
Plan dose: 1st05 (CT 1)	SpinalCord	12.21	0	0	0	240	0	2577	2839	0 %
Plan dose: 1st05 (CT 1)	GTV	11.93	3146	3235	3391	5058	5165	6768	6853	0 %
Plan dose: 1st05 (CT 1)	Eye_R	11.65	0	0	0	0	0	0	0	0 %
Plan dose: 1st05 (CT 1)	GTV-p	11.61	3211	3311	3460	5105	5203	6768	6854	0 %
Plan dose: 1st05 (CT 1)	Eye_L	10.77	0	0	0	0	0	3	6	0 %
Plan dose: 1st05 (CT 1)	GTV_in1	7.28	3434	3538	3776	5420	5572	6829	6880	0 %
Plan dose: 1st05 (CT 1)	GTV_in2	3.72	3957	4020	4246	5836	6089	6879	6890	0 %
Plan dose: 1st05 (CT 1)	InnerEar_L	1.9	2212	2314	2411	3388	3197	5310	5458	0 %
Plan dose: 1st05 (CT 1)	InnerEar_R	1.86	0	0	0	3	1	20	21	0 %
Plan dose: 1st05 (CT 1)	OpticChiasm	1.51	0	0	2	76	30	536	617	0 %
Plan dose: 1st05 (CT 1)	Pituitary	0.57	127	147	211	894	725	2214	2364	0 %
Plan dose: 1st05 (CT 1)	OpticNerve_R	0.54	0	0	0	1	0	8	9	0 %
Plan dose: 1st05 (CT 1)	Lens_L	0.3	0	0	0	0	0	0	0	0 %
Plan dose: 1st05 (CT 1)	Lens_R	0.26	0	0	0	0	0	0	0	0 %
Plan dose: 1st05 (CT 1)	OpticNerve_L	0.26	0	0	0	8	6	23	24	0 %
Plan dose: 1st05 (CT 1)	Cochlea_R	0.18	0	0	0	2	1	8	9	0 %
Plan dose: 1st05 (CT 1)	Cochlea_L	0.17	2627	2736	2941	3520	3551	4455	4461	0 %

Figure 1. Summary of prescribed doses and constraints for organs at risk. CTV, clinical target volume; GTV, gross target volume; R, right; L, left; GTV_in1, GTV reduced by 2-mm margin; GTV_in2, GTV reduced by 3-mm margin; ROI, region of interest; GTV-p, gross tumor volume-primary; CT, computed tomography (planning image); D99, dose received by 99% of the target volume.

Pretreatment physical examination. At the start of PBT, the patient presented with left facial nerve paralysis and oral commissure deviation to the right. Both pupils were equal in size (~3 mm) and reactive to light. Right-eye esotropia and left-eye diplopia were both noted, without visual field defects. Complete hearing loss was also documented on the left, whereas the right ear retained normal function. The patient reported intermittent dysphagia, with choking during fluid intake and difficulty consuming solid foods.

Imaging findings at baseline. Pretreatment MRI revealed a mass lesion of the left anterior medulla (jugular bulb region), showing somewhat increased signal intensity on both T1- and T2-weighted images. This lesion was heterogeneous but proved strongly enhanced by contrast, displaying an irregular shape and measuring ~2.5x2.1x1.7 cm. The medulla was compressed, deformed and displaced to the right (Fig. 3).

Follow-up imaging evaluation at 11 months post-surgery. MRI showed no evidence of significant tumor growth or recurrence 11 months after treatment, indicating stable post-treatment changes. Follow-up imaging conducted 18 months after treatment also demonstrated stable conditions, supporting the long-term efficacy of PBT in suppressing tumor progression and preventing recurrence (Fig. 4).

Clinical course 1 year after PBT. The patient's neurological function had markedly improved at the 1-year follow-up, showing substantial recovery of the facial nerve palsy. The strabismus and diplopia had largely resolved, and there were major strides in the abatement of choking frequency and swallowing difficulty. The patient's hearing had also partially returned on the left, although vertigo persisted.

Overall, the patient had experienced acute adverse effects, such as vertigo, headache, nausea, vomiting and reflux, during the first year after treatment. These were effectively addressed through symptomatic management. By the 1-year mark, most symptoms had considerably lessened, indicating good overall tolerability of PBT. Late adverse effects further improved over time, gradually diminishing between 6- and 18-months post-treatment. This aided the recovery process and enhanced the patient's quality of life. The patient is currently followed up with clinical assessments and MRI scans every 3 months. Given the high local control rates typically associated with high-dose PBT for paragangliomas, the likelihood of local recurrence is considered low, and the long-term prognosis for tumor control is expected to be favorable. The patient has remained recurrence-free for 24 months since PBT, showing marked symptom improvement

Discussion

As seen in the present patient, PGL recurrence in close proximity to vital neurovascular structures has serious clinical ramifications. Both anatomical considerations and difficulties entailed in separating tumor from nerves and vessels create inordinate opportunities for surgically related damage and

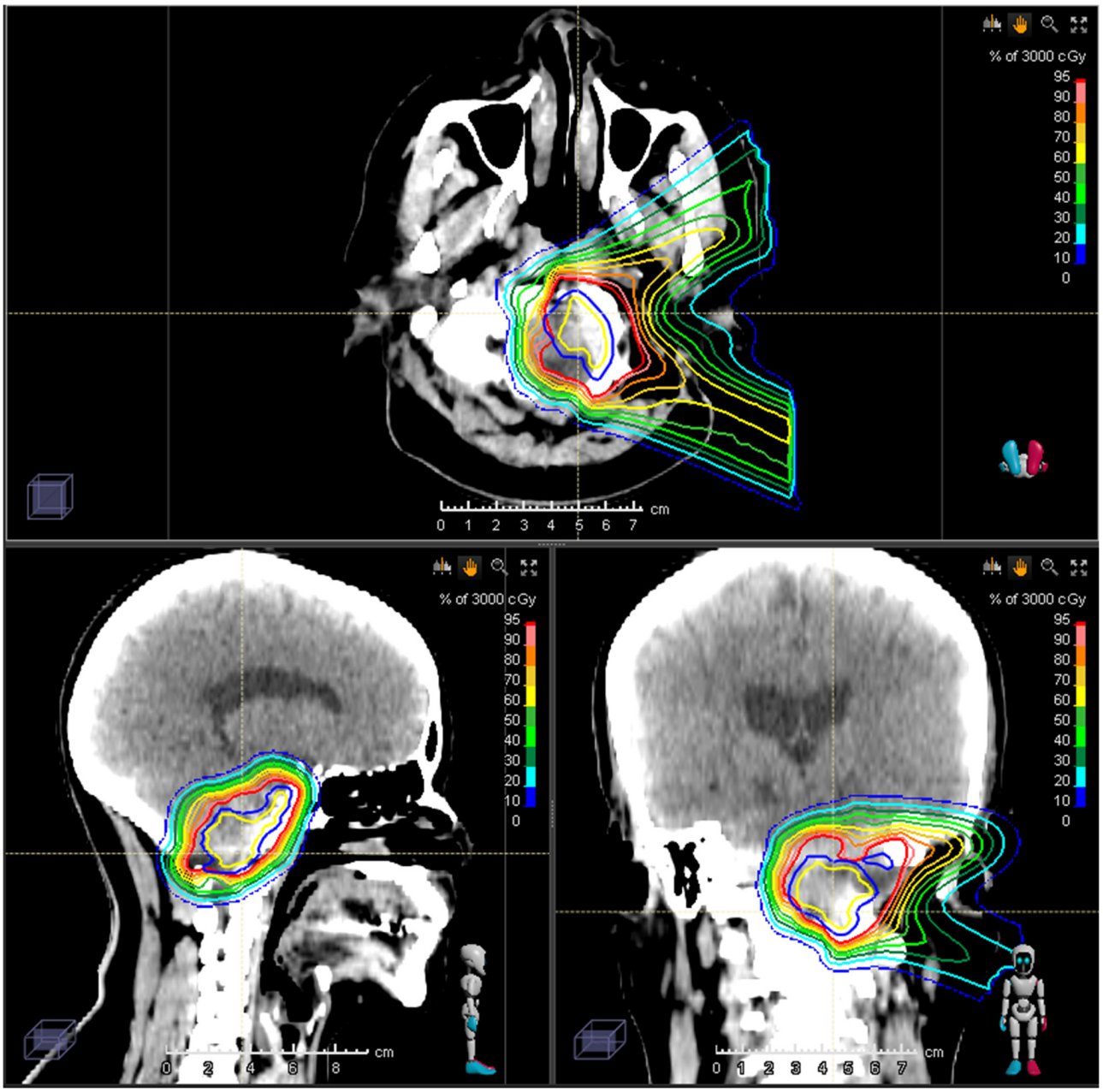

Figure 2. Planning and delivery constructs for hypofractionated proton beam therapy.

complications. The majority of PGLs arise within the head and neck regions, and commonly originate from paraganglionic tissue near the carotid body, vagus nerve, middle ear and jugular foramen (2,6). Those abutting the jugular foramen are spawned by adventitial paraganglionic cells of the jugular bulb, set within the temporal bone; they are slow-growing and yet intensely vascular. Although typically benign, such tumors may enlarge, infiltrate or destroy surrounding bony structures and inflict complications due to mass effects (1,2,7). Traditionally, their clinical management (especially those at the jugular foramen) has centered on complete surgical resection (8,9). However, advances in neuroimaging and radiotherapy technologies, along with mounting demand for less invasive strategies in this rather benign setting, have prompted a shift toward more conservative efforts fostering retention of cranial nerve function (10,11).

For PGLs at the jugular foramen, the reported rates of total resection vary (83-90%), depending on published sources (7-9,12,13). Conventional surgical procedures are more disruptive in general, calling for external auditory canal closure and facial nerve manipulation. Risks of cranial nerve palsy, dysphagia and cerebrospinal fluid leakage are thereby increased. To minimize such hazards (especially in large tumors) and preserve cranial nerve function, a subtotal resection is often preferred (10,14-16). A number of studies have confirmed that a subtotal resection not only provides tumor stability or volume reduction, but also helps safeguard critical neurovascular structures (10,14-18). Huy *et al* (18) analyzed patients after treatment with a combined subtotal resection and adjuvant radiotherapy. Although some (27%) experienced regrowth, which was curtailed through additional therapy, the majority (73%) showed residual tumor stability (18). This

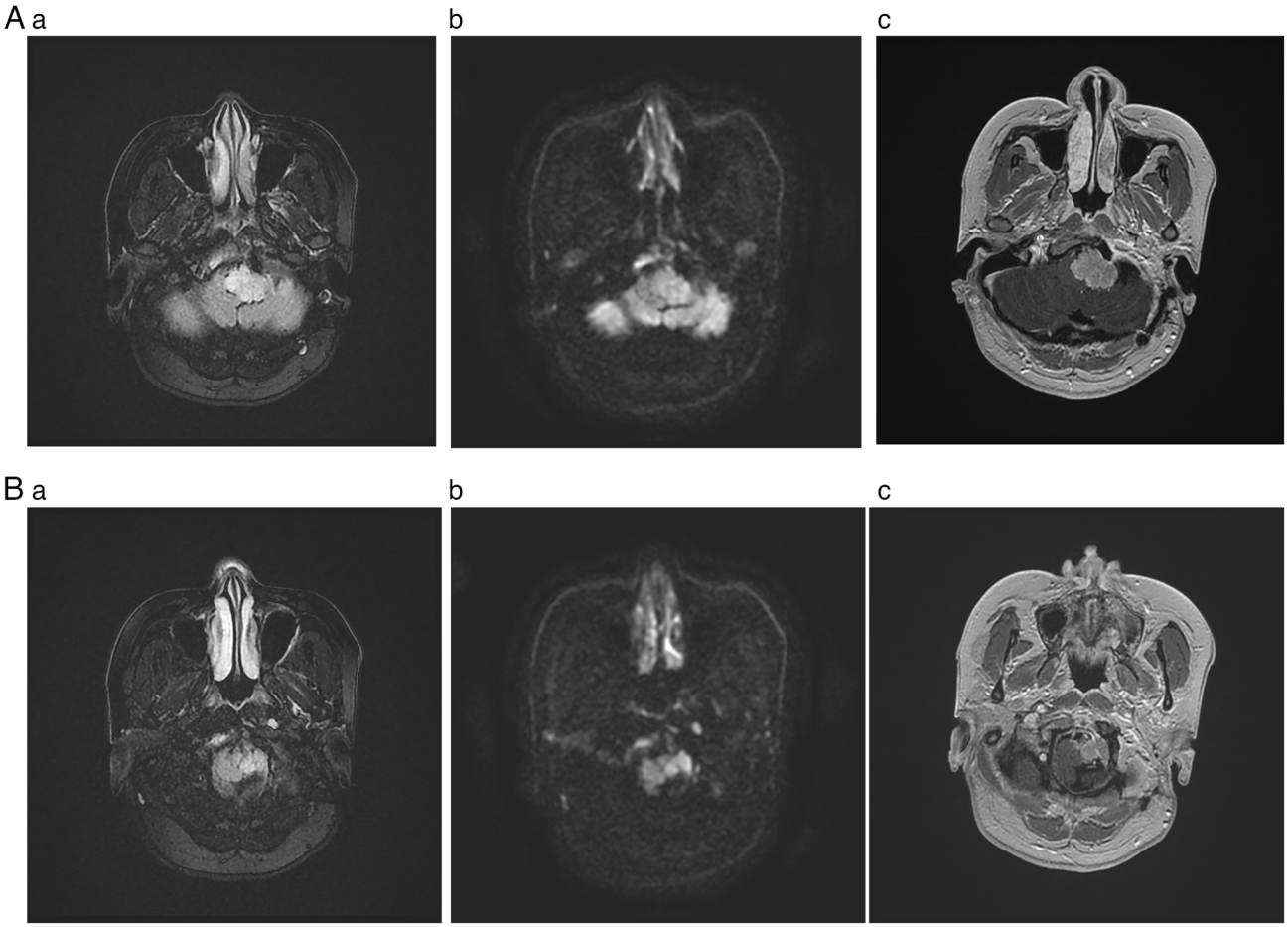

Figure 3. MRI study before treatment. (A-a and B-a) T2-weighted fluid-attenuated inversion recovery sequences showing a mass-like, marginally hyperintense signal involving the left jugular bulb region and the left lateral medulla oblongata. (A-b and B-b) Diffusion-weighted imaging revealing isointense or somewhat hyperintense signaling of the lesion in the same areas. (A-c and B-c) T1-weighted imaging displaying heterogeneous, mild-to-moderate contrast enhancement of the lesion at same sites. (A) and (B) represent different axial section levels of the same MRI sequence. MRI, magnetic resonance imaging.

combination approach maintains a balance between tumor removal and functional preservation.

The decision to combine a subtotal resection with radiotherapy should be based on the size and location of the tumor, and the presence or absence of neurological symptoms. In a study of 47 patients with tumors classified as Fisch C or D (19), a subtotal resection was the more frequent choice in patients who were elderly or had no preoperative neurological deficits (20). Another study involving 56 patients found that a subtotal resection was often performed in the context of advanced tumors classified as Fisch C3 or D (21).

Radiotherapy is particularly suitable for elderly patients or for those with comorbidities, as it is less invasive and carries fewer complications (11,22-25). The patient in the present study showed complete tumor-related brainstem compression, so postoperative complications seemed unavoidable. Radiotherapy alone was therefore chosen as the primary treatment method.

The principal dosimetric advantage of PBT lies in the physical properties of the Bragg peak. This allows for the delivery of high-dose, conformal radiation to the tumor while largely sparing adjacent OARs from the broader low-dose 'bath' associated with intensity-modulated radiation therapy (IMRT), which may intensify long-term toxicity risk (26,27). This capability is vital for sensitive structures such as the brainstem, cochlea and salivary glands. Several dosimetric studies have confirmed that PBT can significantly lower radiation doses to these critical structures, thereby reducing risks of hearing impairment, xerostomia and hypothyroidism, with some evidence suggesting improved long-term survival (26,27).

Furthermore, the IMPT with PBS utilized in the present case represents the most advanced form of PBT. Unlike older passive scattering techniques, PBS employs a fine proton pencil beam that is magnetically scanned across the tumor layer-by-layer (11). This technology creates exceptionally steep dose gradients, providing superior dose conformality and the ability to pre-set tolerable doses for OARs, ensuring an optimal dose distribution that further minimizes exposure compared with traditional broad-beam PBT. This level of precision is particularly advantageous when treating tumors in complex anatomical regions, such as the skull base (27,28).

However, these dosimetric advantages must be weighed against practical limitations. The primary disadvantages of PBT are its substantially higher cost and limited availability. Moreover, its precision makes it highly sensitive to positional uncertainties arising from patient setup or physiological motion. Such shifts can alter the position of the Bragg peak,

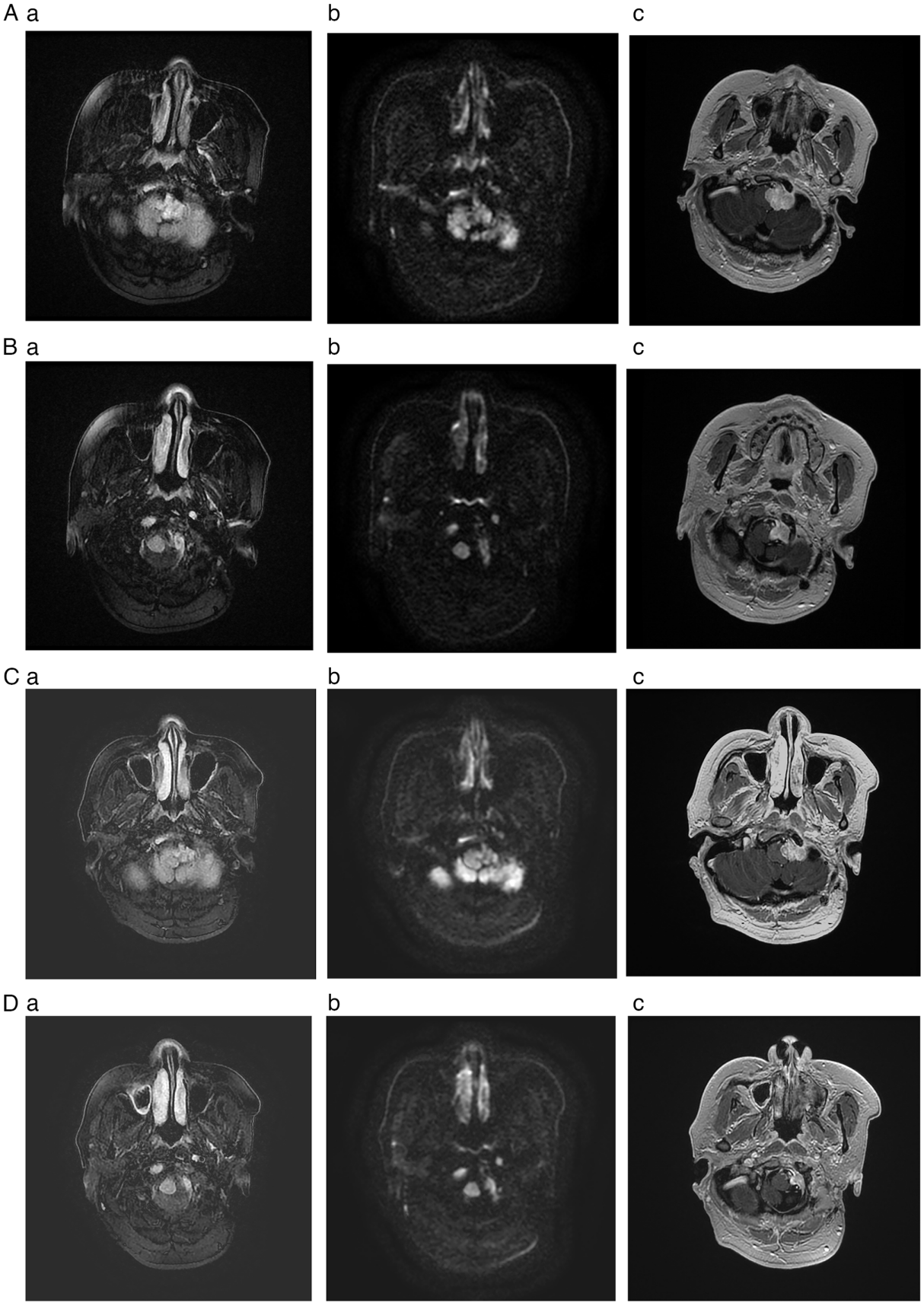

Figure 4. Magnetic resonance imaging study during follow-up. (A and B) Images obtained at 11 months post-treatment (April 2024). Images (A) and (B) represent different axial section levels. (C and D) Images obtained at 18 months post-treatment (December 2024). Images (C) and (D) represent different axial section levels. (A-a, B-a, C-a and D-a) T2-weighted fluid-attenuated inversion recovery sequences marked by a nodular, somewhat hyperintense signal involving the left jugular bulb region and the left lateral medulla oblongata. (A-b, B-b, C-b and D-b) DWI demonstrating isointense or now vaguely hypointense signaling in these areas. (A-c, B-c, C-c and D-c) T1-weighted imaging, again disclosing moderate contrast enhancement in a heterogeneous pattern at the aforementioned sites. Relative to pretreatment status in Fig. 3 (May 2023), follow-up views (A and B) at 11 months and (C and D) 18 months confirm significant tumor volume reduction and diminished DWI signal intensity, suggesting pronounced decline in tumor activity. DWI, diffusion-weighted imaging.

potentially undermining target coverage and the OAR-sparing benefit (26). Therefore, rigorous quality assurance, such as the daily CBCT used in this case, is essential to mitigate these risks (27,28). In contrast to PBT, while IMRT is dosimetrically inferior in terms of OAR sparing, it is more widely accessible, less costly and offers greater robustness against tumor motion, making it a more tolerant option for such uncertainties.

Stereotactic radiosurgery (SRS) and IMRT my offer high local control rates but often confer more risk in terms of acute and late toxicities, owing to limited dose modulation in surrounding tissues (22,29,30). Despite the reported efficacy of SRS in controlling PGLs, acute side effects, such as headache and fatigue, and late toxicities, including dysphagia and otalgia, have resulted (30,31).

PBT is broadly categorized as broad-beam methodology and IMPT. Various studies have reported the efficacy of PBT treatment in patients with PGLs (27,28). During one single-center trial, a median dose of 50.4 GyE over 25-34 fractions reduced tumor volumes by ≥20% in 40% of patients with HNPGLs (28). A second study similarly documented 100% local control in 10 patients receiving 45-67 Gy [median, 50.4 gray equivalents (GyE)] who were followed up for a median of 24.6 months (26). Yet another study (median follow-up time, 50.1 months) showed 100% local disease control after irradiation at 50.4 GyE (32). The aforementioned findings imply that local tumor control is attainable at doses of ~50 GyE. However, in treating malignant PGLs of high grade or with recurrent features, doses of 54-60 Gy may be warranted (22,33-35).

For greater precision in dose delivery, IMPT by PBS was used in the present case, rather than engaging conventional broad-beam techniques. Earlier efforts at PBT use in patients with PGL have deployed broad-beam methods alone, without this advanced PBS technology. As in IMRT, PBS allows for pre-defined dose constraints on nearby normal tissues and augmented dose conformity to the CTV, minimizing adjacent critical organ exposure (26-28).

Moreno *et al* (36) reported respective differences in dose distribution characteristics of broad-beam and PBS methods, emphasizing that PBS allows for more flexible adjustment of the spread-out Bragg peak (SOBP) along the beam axis (36). By contrast, broad-beam techniques utilize ridge filters to generate a uniform SOBP, which may result in excessive radiation to surrounding tissues if the shape of the CTV is suboptimal (37,38). PBS instead may deliver individually modulated spots tailored to tumor shape, forming an SOBP that follows tumor contours more precisely. The combination of IMPT and PBS permits focal dose escalation to the tumor center and spares normal tissues at the perimeter (39,40).

In the present patient, tumor shrinkage was observed relatively early after PBS irradiation, coupled with symptomatic improvement. Given the tumor's proximity to the brainstem and the overt prognostic devastation dealt by cranial nerve dysfunction, these extraordinary results may underscore the utility of PBS-based proton therapeutics in treating similar cases.

Beyond dosimetric considerations, practical factors, such as treatment cost and duration, also influence modality selection. Within China, PBT (vs. IMRT) is associated with substantially higher costs (US $40,000 vs. US $4,000-14,000) and prolonged treatment sessions (30-45 min vs. 15-20 min) (41). Patient selection is therefore paramount. PBT is preferentially recommended for specific patient populations, including children and young adults in whom long-term growth, development and radiation-induced secondary malignancy risks are major concerns. PBT is also an ideal option in instances where tumors border critical OARs or where cost is not an issue. Conversely, IMRT may be more appropriate for patients with limited life expectancies, certain tumor profiles (large, superficial or highly mobile), or dire economic prospects (42).

To minimize the risk of radiation-induced toxicity, strict dose constraints were applied during PBT in the present study. The fractionation scheme was designed to achieve tumor shrinkage and impart clinical improvement, both deemed essential to therapeutic optimization. Fig. 1 delineates the patient's treatment regimen, including the prescribed doses and aforementioned constraints.

In reviewing the current literature, a trend towards less invasive, function-preserving strategies for recurrent jugular foramen PGLs is clear, especially when surgical options are exhausted (20-24). The present report contributes to the limited but growing body of evidence supporting the use of advanced radiation therapies for this rare and complex condition.

However, the limitations of the present study must be acknowledged. As a single case report, strong conclusions cannot be drawn, and the favorable outcomes observed in the patient cannot be generalized to the entire population of patients with this disease. This highlights a significant potential research gap: there is a lack of large-scale, prospective studies to define the optimal radiation dose, fractionation and long-term outcomes for anaplastic PGLs treated with PBT.

Additionally, it should be noted that the specific immunohistochemical findings for the recurrent tumor described within the present case were extracted from the official clinical pathology reports, as the original slide image files from the external institution were no longer retrievable due to the passage of time.

Therefore, our future recommendations include the establishment of multi-center registries to collect more data on these rare tumors. Further studies with extended follow-up are essential to fully assess the long-term efficacy and safety of PBT, to confirm its benefits in preserving neurocognitive function and to evaluate the risk of late-onset toxicities or secondary malignancies. Such research will be crucial to solidifying the role of PBT in the treatment algorithm for similar cases.

In conclusion, the present case highlights the clinical challenges imposed by the recurrence of PGL at the jugular foramen. Surgery remains a cornerstone of treatment but is clearly quite limited under these circumstances. Proton therapy, particularly if delivered via PBS and hypofractionated regimens, offers an effective and precise alternative modality that may protect critical structures while ensuring meaningful tumor control. Long-term follow-up is essential to monitor disease progression and evaluate the durability of outcomes post-treatment. However, the merit of advanced proton therapy techniques in such complex scenarios stems from compelling evidence and is hard to deny.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

SS was responsible for conceptualization, supervision, methodology, validation, project administration and manuscript writing (reviewing/editing). WW was responsible for conceptualization, data curation, investigation and manuscript writing (original draft). SS and WW confirm the authenticity of all the raw data. YY performed the formal data analysis, investigation and manuscript writing (review/editing). JB was responsible for methodology and data analysis. YZ assisted with resources and data collection. DZ assisted in investigation and data curation. JZ assisted with resources and follow-up data collection. SZ performed data integration and visualization. ZW and JW were responsible for radiotherapy dose data acquisition and software use. JK performed data organization and visualization. LY was responsible for formal analysis and manuscript writing (reviewing/editing). MM assisted in investigation and data validation. HS was responsible for the methodology and conceptualization. All authors took part in the direct clinical care of the patient, and each author contributed significantly to the data collection, dose acquisition or formal analysis processes. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

All procedures involving human participants complied with ethical standards of applicable institutional and national research committees, and with the principles of the 1964 Declaration of Helsinki, its later amendments or comparable ethical standards. This case report was approved by the Institutional Review Board of Hebei Yizhou Cancer Hospital (Zhuozhou, China). Written informed consent was obtained from the patient. Although some journals may not require formal ethics approval for a single case report, it is the policy of Hebei Yizhou Cancer Hospital to obtain such approval for any publication involving patient data to ensure the highest standards of patient privacy protection and ethical conduct.

Patient consent for publication

The patient depicted herein granted written informed consent for publication of this case report and its accompanying images.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, AI tools were used to improve the readability and language of the manuscript or to generate images, and subsequently, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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