



## Letter to the editor

## Regression and long-term control after radiotherapy of carotid body paraganglioma – Are these still issues?



The carotid body, a highly specialized organ located in the adventitia at the common carotid artery bifurcation, is composed of two cell types – the chief/paraganglionic type I cell and the sustentacular/supporting type II cell. Its ascribed function is the promotion of homeostasis through sensing fluctuations in blood pH and oxygen tension. The paraganglia are collections of neuroectodermal-derived cells which help the autonomic nervous system respond to physiologic stress.

Carotid body paragangliomas (CBPGs) or chemoreceptor tumors, mostly belonging to the non-chromaffin category, represent approximately 8–39% of people with head and neck paragangliomas (PGs) [1,2]. Only clinical investigations with five years or longer follow-up can be considered relevant in the evaluation of the effectiveness of therapy for CBPG given the fact that their median tumor doubling time is 4.2 years to 10.1 years [1]. Herein a case is described as it depicts one of the accepted indications for treatment with radiotherapy (RT). Moreover, the literature is reviewed because, although there is clear acceptance that tumor growth can be arrested with the application of RT, the long-term consequences of irradiation are unclear [3,4].

In March 2017, a 76-year-old woman presented with left-sided throat and neck pain which were experienced for about a year and a history of hypertension. Clinical examination revealed a mass in the left parapharyngeal space extending from the level of the soft palate down to the epiglottis. The neck was free of lymphadenopathy, and cranial nerve deficits were not observed. The urinary catecholamines profile test was normal. Comparison of serial computed tomographic imaging including an angiographic study showed an enlarging contrast-enhancing, well-circumscribed mass at the left carotid artery bifurcation extending up to the base of skull; the tumor measured 6 cm × 4 cm. RT was recommended for the unresectable CBPG at the head and neck

multidisciplinary oncology conference. Fractionated ipsilateral conformal external beam megavoltage irradiation encompassing the neoplasm administered 45 Gy in 25 fractions; treatment was completed in May 2017. Radiological examination in August 2018 indicated stable disease. The patient remained symptom-free at follow-up a month later.

Regarding the effect of RT on CBPGs, these tumors have been labeled as radioresistant neoplasms because cessation of neoplastic growth has often been considered the basis for treatment efficacy rather than disappearance. Moreover, histologic examination after radiotherapy of the PG has shown that the chief cells are minimally affected by the irradiation [5]. Conventional wisdom suggests that RT ought to be reserved for large tumors (large defined as Shamblin class III cases [6–8]) or for lesions which are unresectable (such as when the neoplasm is within the foramen lacerum [9]). CBPG regression and long-term (over 10 years) tumor control following irradiation have been documented (Table 1) even for neoplasms as large as 10 cm [10–15]; subjective and objective responses to radiation therapy have also been occasionally observed [4,14]. In general, a dose-fractionation scheme of 45 Gy given in 25 fractions is advocated because a higher dose is not associated with improved results [16]. Survival is not a meaningful endpoint in the treatment of these patients because mortality due to the tumor is usually rare [1,16].

Notwithstanding the very limited number of pooled cases extracted from the literature to support the assertion made about the favorable effects of irradiation, in our view, contemporary RT can safely achieve extended tumor regression and prevent progression of these generally held benign neoplasms. More evidence will have to corroborate this expressed belief.

**Table 1**

Long-term outcomes and toxicity<sup>a</sup> after contemporary radiotherapy for carotid body paragangliomas.

Author [Ref.]	(No. of patients)	Dose	Tumor response (No. of patients)	Long-term follow-up in months
Chino et al. [10]	(1)	NS	CR (1)	168
Guedea et al. [11]	(5)	40.8 Gy to 48 Gy	CR (1) <sup>a</sup> PR (2) Stable (1) <sup>a</sup> TP (1)	60, 84 & 102
Schild et al. [14]	(2)	16 Gy; 40 Gy	CR (1) Stable (1) <sup>a</sup>	60 & 84
Valdagni et al. [15]	(3)	50 Gy to 60 Gy	PR (2) <sup>a</sup> Stable (1) <sup>a</sup>	72, 108 & 228

Contemporary radiotherapy meant million-voltage external beam radiotherapy (except some patients may have received 0.662 MeV Cesium-137 teletherapy<sup>15</sup>). NS (Not stated); CR (Complete resolution); PR (Partial regression); TP (Tumor progression).

<sup>a</sup> (Bilateral paragangliomas).

\* Toxicity was minimal or not observed.

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**Conflict of interest**

None declared.

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