Carotid Body Tumors: Radiotherapy as an Alternative Approach

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Paragangliomas in general are an uncommon group of neoplasms that may originate anywhere glomus bodies are found. In the head and neck region the normal paraganglia are associated with the parasympathetic nervous system and paragangliomas arising from these parasympathetic sites account for up to 70% of extra-adrenal paragangliomas. The most common site is the carotid body (1). These lesions are rare before the age of 20, and there is a female predominance in some series (2). This female predominance has also been demonstrated and discussed in the interesting study by *Nazari et al* on carotid body tumors reported in this issue of *Acta Medica Iranica* (3). The great majority of their 45 patients (82%) were female.

The mechanisms of carotid body tumor formation remain unknown, but since 1930 it has been accepted that the carotid body is a chemoreceptor which monitors the oxygen tension of systemic arterial blood (4). Thus carotid body tumors are associated with conditions producing chronic hypoxia, such as high-altitude habitation, as shown by *Nazari et al*. in this journal. Of their patients, 64% lived at a place with an altitude of higher than 1500 m above the sea level; the relationship of carotid body tumor with chronic exposure to hypoxia has been discussed concisely in their report.

Paragangliomas are histologically benign tumors resembling the parent tissue and consist of nests of epithelioid cells within stroma-containing, thin-walled blood vessels and nonmyelinated nerve fibers. Although the tumor is well circumscribed, a true capsule is not seen. The criterion of malignancy is based on the development of metastases rather than the histologic appearance (2). Although it is estimated that less than 10% of paragangliomas are malignant, it is important to remember that all have malignant potential and it is not always possible to predict malignant behavior based on histologic features alone (1).

Lymphatic metastases occur in about 5% of carotid body tumors (2). Nazari *et al.* found one female from their 42 followed up patients with metastasis to regional lymph nodes six years after resection of the carotid body tumor. Carotid body tumors have a low risk for distant metastases, and no metastatic disease was reported by Nazari *et al.*

Carotid body paragangliomas are vascular lesions, and this is reflected in their imaging appearance. CT and/or MRI scan with contrast provides the diagnosis. In contrast, Doppler sonography was performed for the vast majority (80%) of Nazari *et al.*'s patients, with CT scan for 57% and MRI for just one patient. This may reflect the ease of access to the different imaging procedures at the study center during the time of the study (1999-2009). Octreotide scanning, a nuclear medicine imaging procedure, could also be useful for detecting the presence of multicentric or metastatic paragangliomas, and for distinguishing scar from residual tumor after surgery (1).

The management of head and neck paragangliomas include surgical resection, external beam radiotherapy, and stereotactic radiotherapy (5,6). Small lesions may be successfully removed with little risk to the patient. However, if resection of the carotid vessels is anticipated or if a large lesion is fixed or unresectable because of size, radiotherapy is the preferred initial treatment. The major risks of surgery for these tumors are hemorrhage and injury to the cranial nerves (2). Accordingly Nazari et al found seven patients out of their 42 followed up cases with post-operative cranial nerve injuries, and this was mostly seen in tumors larger than 5cm (table 1 of their report in this issue of Acta Medica Iranica). This too seems to emphasize the use of radiotherapy for large carotid body tumors.

Irradiation is used frequently to treat glomus tumors, particularly those in the tympanicum and jugulare bulb, or carotid body tumors (7). There is a high success rate: For example in a long term study of head and neck paragagliomas by Hinerman et al, the overall local control rate for all 121 lesions treated with radiotherapy was 95%, with a low incidence of treatment-related complications (8). Local control after radiotherapy is defined as stable disease or partial regression with no evidence of growth. Radiotherapy dose is usually around 45-50 Gray in 25 fractions over 5 weeks, which is below the tolerance of the normal tissues included in the treatment volume. The median dose of gamma knife

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radiosurgery is 15 Gray. Acute side effects of radiation in this setting are almost nonexistent and there are few late complications. Patients are treated with CT-based radiation treatment planning, stereotactic radiotherapy or radiosurgery (2,7).

espite this successful treatment mentioned above, no use of radiotherapy has been mentioned in Nazari et al's report, but of course their patients are all from a large referral vascular surgery center. Both the advanced techniques of radiotherapy mentioned above are readily available in radiation oncology centers in Tehran and other major cities in Iran. All the authors of the study report by Nazari *et al.* in this journal are hereby acknowledged for their very interesting and worthwhile work, while it is hoped that a more optimal cooperation could be shaped in future between vascular surgery and radiation oncology academic centers here in Iran for the treatment of the intriguing tumors of carotid body and other paragangliomas.

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