Natural History of Cervical Paragangliomas

Outcomes of Observation of 43 Patients

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Objective: To evaluate the outcomes, growth rate, and symptoms of nonoperated cervical paragangliomas.

Design: Retrospective review of clinical and radiologic records and images.

Setting: Tertiary academic medical center.

Patients: We studied all patients presenting with cervical paragangliomas between 1993 and 2010 who were observed rather than operated on.

Main Outcome Measures: Growth of tumors and need for surgical removal.

Results: Forty-three patients with 47 tumors were identified. Mean patient age was 56 years (age range, 17-86 years). Thirty patients were asymptomatic (70%) (22 diagnosed by imaging for other reasons and 8 for workup of a neck mass), and only 5 presented with cranial nerve abnormalities (12%). No patients presented with lymphadenopathy, rapid growth, or pain. Reasons for observation were patient preference (n=15; 35%), advanced age of patient (n=12; 28%), and preexisting contralateral cranial nerve deficits (n=11; 26%). Twenty-eight of the 47 tumors were suspected carotid body tumors based on imaging (60%), and 19 were suspected vagal tumors (40%). The mean greatest dimension at presentation was 2.6 cm (range, 1-7.2 cm). During a mean follow-up of 5 years (range, 1-17 years), 19 tumors remained stable in size (42%); 17 grew (38%); and 9 regressed (20%). Of the 17 tumors that grew, the mean growth was 0.2 cm/y.

Conclusions: Observation of cervical paragangliomas is an option in selected patients who do not present with worrisome symptoms. The natural history of paragangliomas in these patients is typically little to no growth over time. Regular follow-up is important to ensure minimal change and stable symptoms.


THERE IS A CHANGING PARADIGM in treatment of cervical paragangliomas. While these lesions historically have been considered highly aggressive tumors in need of equally aggressive surgery, greater experience and a recognition of the low incidence of malignancy have allowed individualization of treatment. For some patients, comorbidities or personal preference have resulted in a strategy of observation. In addition, for patients with small tumors thought to arise from the vagus nerve with no preoperative deficits, a strategy of observation is often followed in recognition of the significant morbidity of postoperative vagal paralysis. Radiation is also considered in some centers but is controversial. The purpose of this study was to analyze the indications for and outcomes of observation in our patients with paragangliomas who were managed nonsurgically. We hypothesized that paragangliomas are slow-growing tumors and that most patients would not experience significant changes in tumor size during observation.

METHODS

Billing records for the senior authors (R.J.S. and J.L.N) at Vanderbilt University were searched for encounters from 1997 to 2010 with diagnosis codes typically used at our institution for paragangliomas, schwannomas, and neurofibromas of the parapharyngeal space (International Classification of Diseases, Ninth Revision codes 237.3, 194.5, and 194.6). After verification of each record using electronic hospital records dating as early as 1993, a database of 209 patients was created for this and other projects. All Otolaryngology Clinic notes for each
patient were reviewed to identify patients who underwent a trial of observation for a presumed paraganglioma of the carotid body (carotid body tumor), vagus nerve (cranial nerve [CN] X), or other CN or sympathetic chain.

Initial and subsequent radiology data were then reviewed for all observed patients. Full image sets were used when available as well as single-image snapshots and radiology reports. When possible, radiology reports were cross-checked with repeated measurements on original images to produce the most accurate possible estimation of size and growth data for the tumors. These measurements were taken using an IMPAX workstation (Agfa Healthcare). We also included data from patients whose records had radiology reports with size information but no images, as long as subsequent reports included serial measurements and references to earlier studies. While including these patients may have limited our precision regarding tumor size calculation, this strategy was consistent with the primary goal of this study, which was tumor behavior and not precise volumetric calculation.

Data were entered in an Excel (Microsoft Corp) spreadsheet for analysis. We performed both 1-dimensional (single greatest) and 2-dimensional (axial area) calculations of size and growth. Too few patients had 3-dimensional (volumetric) data to allow this calculation.

RESULTS

Forty-three patients with 47 tumors were identified. Thirteen patients were male (30%), and 30 were female (70%). Mean age was 56 years (age range, 17-86 years).

Most of the patients presented with a personal history of multiple paragangliomas (58%; n = 25), and 19% (n = 8) had a family history. Thirty were asymptomatic (70%) (22 diagnosed by imaging for other reasons and 8 for workup of a neck mass); 5 presented with CN abnormalities (12%) (3 with CN X, 1 with CN XII, and 1 with CN X and XII); 4 had dysphagia (9%); 2 had pulsatile tinnitus (5%); and 2 had isolated Horner syndrome (5%). Two of the patients with CN abnormalities also had Horner syndrome, for an overall total of 4 patients with Horner syndrome (9%) (3 patients with suspected carotid body tumor and 1 with concurrent vagal and carotid body tumors). No patients presented with lymphadenopathy, rapid growth, or pain.

Reasons for observation were patient preference in 15 (35%), advanced patient age in 12 (28%), and preexisting contralateral CN deficits in 11 (26%). The mean age of those observed owing to age and comorbidities was 73 years (age range, 61-86 years). Twenty-eight of the 47 tumors were suspected carotid body tumors based on imaging (60%), and 19 were suspected vagal tumors (40%). No paragangliomas of other CNs or sympathetic chain were managed with observation.

Magnetic resonance imaging (MRI) was used for serial examination in 28 of the 43 patients (65%), and computed tomography (CT) was used in 15 (35%). The initial imaging was performed at an outside institution in 72% of patients (n = 31) and was therefore the choice of the referring physician. Repeated imaging was chosen as the same modality to allow comparison. In some cases was instead performed at the outside institution, and the images were loaded into our system at the time of the patient visit. In our experience, we have found both imaging modalities to be useful for following up on these lesions.

Forty-five of the 47 tumors had sufficient data to allow size calculations. Of these, 3 dimensions were available for 8 (18%), 2 dimensions for 32 (71%), and 1 dimension for 5 (11%). Some form of original images was available for 37 (82%), and for the remainder the data were abstracted only from the radiology report.

The mean greatest dimension at presentation was 2.6 cm (range, 1.7-2 cm), and the mean axial area calculated for the 40 patients with these data was 5.4 cm² (range, 0.7-33.8 cm²). Tumors were followed up for a mean of 5 years (follow-up range, 1-17 years) with either CT or MRI. Nineteen tumors remained stable in size (42%); 17 grew (38%); and 9 reduced in size (20%). Forty-one did not change more than 0.5 cm/y over the period of observation (91%) (Figure 2). Of the 17 tumors that grew, the mean growth was 0.2 cm/y, and the mean change in axial area for the 16 patients with these data was 0.38 cm²/y.

There was no trend toward growth or regression based on initial size (Figure 2) or years observed (Figure 2). Three patients who presented with vocal cord paralysis underwent medialization laryngoplasty. The remaining patients did not undergo any operative interventions related to their observed tumors.

COMMENT

A better understanding of the natural history of a disease aids in treatment planning and patient counseling. In patients with paragangliomas, our data suggest that for those who do not present with worrisome symptoms of lymphadenopathy, rapid growth, or pain, a trial of observation is an acceptable alternative to surgery. This is a particularly attractive option for patients who are a poor surgical risk or patients with asymptomatic vagal tumors, in whom surgical resection guarantees vagal paralysis and the attendant morbidity. However, at this time we still consider surgery appropriate for most patients.

To our knowledge, only 1 other study has examined the natural history of paragangliomas. Jansen and colleagues presented volumetric growth data on 20 carotid body tumors, 17 vagal paragangliomas, and 11 jugular paragangliomas with a mean follow-up of 4.2 years. In their series, the median increase in dimension was 0.83 mm/y and 29 of the tumors had a volume increase of more than 20% during the period of observation (60%). It may be that the present article underestimates overall growth because of a reliance on 1- and 2-dimensional calculations. However, we did not find any patient to have a clinically meaningful growth of their tumor, regardless of size calculation.

Moreover, while 1- and 2-dimensional analysis certainly does not encompass the properties of a 3-dimensional tumor, describing tumors in terms of single greatest dimension is simple and particularly useful when discussing size concepts with patients. We wish to restate that our goal was not to precisely calculate the volumetric change in cubic millimeters of these tumors, given the recognized limitations of our data, but rather to get
an overall sense of the behavior of paragangliomas. Do they change much over time? According to our calculations in both single greatest dimension and axial area for patients observed as long as 17 years, most do not. In addition, millimeter changes in a highly vascular tumors may be due to measurement variability or the result of changes in blood flow or pressure at the time of the imaging study and may not reflect true growth or regression.

The results of this study call into question the reported success of radiotherapy for carotid and vagal paragangliomas, which uses cessation of growth as a marker of therapeutic effectiveness ("... absence of tumor progression is equivalent to cure." [p1432]). Future studies examining radiotherapy should include estimations of growth prior to therapy or control arms of observed patients to substantiate claims that therapy alters the natural course of these tumors.

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We wish to stress that none of the patients observed in this series presented with these signs or symptoms.

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Figure 2. Greatest dimension and 1-dimensional growth data from 45 observed paragangliomas. A, The average growth rate for each tumor shows that few grew or regressed more than 0.5 cm/y (shaded area). B, Total change in greatest dimension arranged in order of increasing initial greatest dimension shows no trend toward greater or lesser growth based on initial size. C, Total change in greatest dimension arranged in order of increasing number of years observed shows no trend toward greater growth with more years observed.

Author Contributions: Drs Langerman and Netterville had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Langerman, Rangarajan, and Netterville. Acquisition of data: Langerman, Athavale, Rangarajan, Sinard, and Netterville. Analysis and interpretation of data: Langerman, Netterville, Rangarajan, and Smith.

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Athavale, Sinard, and Netterville. Drafting of the manuscript: Langerman, Athavale, and Netterville. Critical revision of the manuscript for important intellectual content: Rangarajan, Sinard, and Netterville. Statistical analysis: Netterville. Administrative, technical, and material support: Athavale, Sinard, and Netterville. Study supervision: Sinard and Netterville. Financial Disclosure: None reported. Previous Presentation: Presented at the American Head and Neck Society Meeting during the Combined Otolaryngology Section Meetings, 28 April 2011, Chicago, Illinois. Additional Contributions: Thank you to Jeffrey M. Bumpous, MD, for his thoughtful commentary on this study.

REFERENCES