MALIGNANT CAROTID BODY TUMOR

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CASE PRESENTATION

A 38-year-old woman initially presented with a 3-week history of decreased hearing in the left ear. Evaluation revealed left serous otitis media, with no evidence of a nasopharyngeal mass. She was treated for allergic rhinitis, with subsequent resolution of her serous effusion. During the third trimester of her subsequent pregnancy, she noted a progressive globus sensation and left-sided intermittent pain. A CT scan after her pregnancy showed a 2 × 2-cm enhancing mass at the left carotid bifurcation. In addition, prominent soft tissue was noted in the nasopharynx and tongue base, with bilateral 1-cm level II nodes. She was subsequently referred for further evaluation and management. She had had an upper respiratory infection 2 weeks before the CT scan but no fevers, chills, or night sweats. She smoked one pack of cigarettes per day for 20 years but otherwise was in good health.

Physical examination at the time of referral revealed an obese, anxious woman, with a slightly hyponasal voice. There was a left-sided serous middle ear effusion. No trismus was present, but prominent Waldeyer’s ring lymphoid tissue was. Fiberoptic nasolaryngoscopy revealed prominent nasopharyngeal lymphoid tissue abutting the left eustachian tube orifice with purulent exudate. A laryngeal and hypopharyngeal examination was unremarkable. A mildly tender, 2-cm mass was detected at the left carotid bulb, and rubbery, mobile small lymph nodes were found at level II bilaterally. There were no cranial nerve deficits.

Question 1: What is your differential diagnosis at this time?

Dr. Carroll: The salient features of the history and physical examination of this patient include: unilateral serous otitis in a smoker, neck mass, fullness in Waldeyer’s ring, and progression of symptoms with pregnancy. Initial diagnostic considerations include nasopharyngeal or oropharyngeal neoplasm (epithelial or lymphoid). Progression of symptoms with pregnancy could be due to benign lymphoid hyperplasia, but an estrogen receptor (+) malignancy such as metastatic breast carcinoma could also be responsible, particularly in a 38-year-old woman.

Dr. Stenson: Nasopharyngeal carcinoma with metastatic lymphadenopathy should be the diagnosis of exclusion. Other diagnoses to consider would be lymphoma as well as infection of the adenoid tissue secondary to her recent upper respiratory infection. The finding of an enhanced
mass at the carotid bifurcation raises the diagnosis of carotid body tumor.

Dr. Stringer: At this point, my differential diagnosis includes lymphoma, a carotid body tumor, a nasopharyngeal carcinoma, oropharyngeal carcinoma, eustachian tube dysfunction, adenoiditis, and chronic rhinosinusitis. However, my level of concern for anything other than adenoiditis, eustachian tube dysfunction, and a carotid body tumor is very low given the lack of any other findings on the CT scan. I would continue to consider lymphoma as a possibility, however.

Question 2: She was treated with a 10-day course of Augmentin (GlaxoSmithKline, U.K.), and re-evaluation at 2 weeks revealed resolution of the purulent exudate and about 50% regression of the nasopharyngeal soft tissue. Results of her neck examination remained unchanged. What would be your next step in evaluation?

Dr. Stenson: In terms of the nasopharyngeal abnormality and lymphadenopathy, one should consider performing a biopsy of the nasopharyngeal tissue (after evaluation for vascular anomaly), performing fine-needle aspiration (FNA) of the cervical lymphadenopathy, or both. These low-risk procedures can be done in the clinic setting. Significant information about the diagnosis of the nasopharyngeal abnormality and ultimate further testing (if and when) for the carotid body tumor can be acquired. If the index of suspicion for malignancy were low or if biopsy and FNA as outlined above were negative for malignancy, the surgeon could counsel the patient about treatment for her carotid body tumor. The surgeon would then order a four-vessel angiogram to assess patency of circle of Willis and cross-filling of the cerebral hemispheres. The carotid body tumor should then be embolized, and surgery planned 1–3 days thereafter.

Dr. Stringer: Assuming that there was no evidence of deep infiltration in the nasopharynx or oropharynx on the CT scan, I would proceed with planning excision of the carotid body tumor. My suspicion for lymphoma or a nasopharyngeal carcinoma has become even lower given the response to antibiotics. However, I have occasionally observed an apparent response of malignant tumors to antibiotics due to a decrease in associated infection. Therefore, I would consider a nasopharyngeal examination under anesthesia, with a possible biopsy, depending on the status of the serous effusion at this point. It will also be possible to access the lymphadenopathy directly at the time of excision of the carotid body tumor.

Were it not for the lymphoid hypertrophy in Waldeyer's ring, I would not be overly concerned about bilateral, stable, 1-cm level II lymph nodes in this patient.

Dr. Carroll: Most carotid body tumors are strongly suspected on the basis of examination and CT. The physical findings of carotid body tumor are distinctive and alone raise suspicion. A 2-cm carotid body tumor is typically much more fixed to the bifurcation and is firmer and more pulsatile than is a metastatic node of the same size. When coupled with typical CT findings of a mass splaying the carotid bifurcation, the surgeon is alerted that the case is more than a neck mass of unknown primary. The usual workup for persistent neck mass of unknown primary is staging endoscopy followed by excision node biopsy. If carotid body tumor is not suspected before this stage, the results can be disastrous. The persistence of multiple small nodes and fullness in Waldeyer's ring following antibiotics in this case does warrant examination under anesthesia and biopsy to exclude concurrent lymphoma or carcinoma.

Question 3: A bilateral carotid angiogram was obtained (Figure 1) because the patient refused MRI. No other vascular lesions are noted in the head and neck, and the circle of Willis is patent. Are any other diagnostic studies indicated?

Dr. Stringer: If the patient has a positive family history for paragangliomas, I would counsel her in regard to genetic testing. If possible, I would also obtain MR images to be sure there are no other undetected paragangliomas that would alter my treatment planning. Without a positive family history, I believe that the CT alone is an adequate examination. Isolated carotid body tumors are rarely catecholamine-secreting, so, absent any other symptoms, I would not order a urine catecholamine analysis. I do not routinely order angiograms for diagnosis of carotid body tumors. I obtain an angiogram only if I plan to embolize the tumor preoperatively, and the benefit of embolization is controversial.

Dr. Carroll: Once the diagnosis of carotid body tumor, or any mass in the parapharyngeal space, is entertained, we recommend MRI/MRA. The classic splaying of the internal and external carotid arteries is usually seen clearly on MRI. Flow voids within the tumor raise the suspicion of a paraganglioma. With MRA, the course or the great vessels, the feeding vessels to the mass, and any significant tortuosity or luminal narrowing of the great vessels are often evident.
Once the diagnosis of carotid body tumor is strongly suspected, multicentric tumors need to be excluded. MRI is an excellent screening tool for this purpose. Carotid body tumors can be associated concurrently with paraganglioma in any of the head and neck sites. With this patient’s history of middle ear disease and ear pain, the possibility of a co-existent glomus jugulare or glomus tympanicum should not be ignored. Most carotid body tumors are not vasoactive (1–5%). We typically screen, however, for elevated urine catecholamines. Blood pressures should also be checked, and symptoms of flushing and tachycardia discussed.

The final diagnostic study that we typically obtain for a carotid body tumor is a cerebral angiogram. This is scheduled the day before surgery so that the tumor can be embolized if indicated. Most tumors at our institution are embolized preoperatively. Small tumors with limited vascularity are an exception.

Dr. Stenson: The treating physician should order either a serum or 24-h urine studies for vanillylmandelic acid (VMA) and metanephrines to determine if the tumor is catecholamine-secreting.

Question 4: What are your indications for preoperative test occlusion of the carotid artery?

Dr. Carroll: Balloon occlusion of the internal carotid artery and cerebral perfusion using radio-nuclide-enhanced SPECT are used on all patients. One of our neuroradiologists, Dr. Joe Horton, was part of the team at Pittsburgh in the late 1980s that demonstrated the value of this technique for establishing safety of sacrifice of the internal carotid artery. About 5% of patients develop neurological symptoms in the radiology suite with balloon occlusion alone. These patients do not have nuclear medicine imaging and are very high risk if the carotid artery is sacrificed or clamped for an extended period. Of the remaining patients, approximately 14% show a significant focal decrease in the cerebral blood flow on SPECT imaging. The risk of cerebrovascular accident (CVA) is greater than 90% if carotid sacrifice or extended clamping of the carotid is necessary for these patients. For those patients with minimal or no impairment of cerebral perfusion, the risk of CVA is 2–3% with carotid occlusion. Symptomatic complication rates for these studies are less than 1%. We believe this clinical information is valuable. Given the difficulty of surgical resection of these tumors and the possibility of having to apply clamps to the carotid arteries to gain control or replace the segment of the artery with a graft, we believe that these studies are justified.

Dr. Stenson: Shamblin1 describes three different types or stages of carotid body tumors. Type I consists of a small tumor that is easily dissected from the adjacent vessels in a periadventitial plane. Type II tumors are larger and more adherent and partially surround the vessel. Type III tumors are large and completely surround the carotid bifurcation. As described, types II and III tumors are most likely to require carotid resection.

One should determine via CT scanning if the tumor encases the common and/or internal carotid artery. If there appears to be a type II or III tumor, preparation for carotid replacement, including test balloon occlusion with electroencephalogram monitoring (during the test occlusion as well as during resection) should be arranged. The subsequent intraoperative expertise of our vascular colleagues is critical for the carotid shunting and replacement aspects of this operation.

Dr. Stringer: I no longer use any preoperative carotid artery blood flow analysis, including pre-
operative test occlusion. The relationship between this test and patient outcome in terms of stroke is not reliable enough for planning purposes. The size of the tumor would not affect my decision in this regard.

Question 5: What are your treatment recommendations?

Dr. Stenson: If the patient has not already had a biopsy of the nasopharyngeal tissue, this step should be completed. If nasopharyngeal malignancy is ruled out, the patient should be prepared for resection of her carotid body tumor. Preoperative four-vessel angiogram with embolization of the tumor should be completed at this time. Schedules permitting, surgery should occur 1–3 days thereafter to minimize post-embolic neovascularization and inflammation. As a routine part of the surgical approach, the level II and III lymph nodes are removed via a selective neck dissection. This not only enhances exposure but also allows for pathologic analysis of the lymph nodes for metastatic paraganglioma. Surgical technique involves early identification of cranial nerves, ligation of the external carotid artery, and meticulous peri-adventitial dissection of the tumor from the carotid bifurcation and internal carotid artery with liberal use of the bipolar cautery.

Dr. Stringer: I recommend excision of the carotid body tumor and nasopharyngeal and oropharyngeal examination with possible biopsy, depending on the findings. If after upper endoscopy I noted abnormal lymph nodes upon entering the neck, I would excise them and send one or more for frozen section analysis in this particular case, primarily because of the nasopharyngeal abnormalities described. If it returned as squamous cell carcinoma, I would proceed with a full, modified neck dissection. Otherwise, I would proceed with excision of the carotid body tumor. If I were informed intraoperatively of paraganglioma cells being present in the nodes, I would complete a selective neck dissection encompassing levels II–IV. However, it is not my normal practice in the course of carotid body tumor surgery to send lymph nodes for frozen section analysis unless they are clearly abnormal. As described in the answer to Question 6, I send the immediate pericarotid bulb lymph nodes, if present, for permanent section analysis.

The likelihood of having to sacrifice the internal carotid artery in this case would be very low given the small size of the lesion. However, it is my practice to have a vascular surgeon on standby in some fashion for all carotid body tumors for medicolegal purposes and in case of the unanticipated need for vascular bypass and saphenous vein grafting. I do not routinely have the vascular surgeon present in the room during the case.

Dr. Carroll: The natural history of these tumors is often slow, steady growth. A recent publication from The Netherlands estimated the tumor-doubling time at 4.2 years. This slow growth rate certainly allows time to weigh options. A rushed decision for surgical resection is rarely needed. In the index case, the patient is 38 years old with a small tumor and no documented cranial nerve deficit. There are no multifocal lesions. We would usually recommend surgical therapy—particularly in the case when the neck will be violated for a node biopsy. A wait-and-watch approach with repeat scanning on a yearly basis is not unreasonable, and we give patients this option. We are careful to explain that these tumors typically grow slowly over time and gradually become more difficult to remove without accompanying cranial nerve damage. Collateral cerebral profusion may diminish with age as well, making risk of carotid occlusion for significant. The option of primary radiation is discussed as well. Our preference is to reserve radiation for very large lesions and for those who are elderly or infirm.

We approach carotid body tumors in a multidisciplinary fashion. The neuroradiologist is involved, as discussed above. The Vascular Surgery service is also involved in all cases. For small tumors, the vascular surgeons may simply be on stand-by status and are called if needed. For large tumors with a high likelihood of carotid resection, the vascular surgeons arrange their surgery schedules to be immediately available. This team approach allows aggressive and complete resection of large tumors with a reasonable margin of safety for the patients.

The patient underwent nasal endoscopy with biopsy of the nasopharyngeal soft tissue revealing acute and chronic inflammation of lymphoid tissue. She then underwent neck exploration with excision of left level IIa and IIIa nodes, which showed no evidence of lymphoma or other malignancy. Her carotid body tumor was then removed uneventfully, with the plane of dissection readily established just deep to the loose carotid adventitia. Her postoperative course was uncomplicated. One week after surgery, the final pathologic analysis revealed that the neck mass was consistent with paraganglioma, but there was a microscopic focus of paraganglioma cells in an excised lymph node.
Question 6: Would you recommend any other additional treatment for her malignant carotid body tumor?

Dr. Stenson: The principles of carotid body tumor resection include early operative management, adequate lymph node sampling, and complete tumor resection. These techniques apply to both benign and malignant carotid body tumors. Carotid body tumors are known to be slow growing and generally thought of as radioresistant. One might consider postoperative radiotherapy for a large malignant tumor with positive margins and several positive lymph nodes. If, however, as in this young patient’s case, there is only one positive node, the surgeon should consider complete neck dissection and/or close observation without adjuvant postoperative therapy. In either situation, routine follow-up CT may help detect subclinical recurrences that will facilitate timely operative management.

Dr. Stringer: Absent an extremely aggressive appearance of the tumor or abnormally enlarged nodes, the role of routine intraoperative nodal sampling is not established. It is difficult to obtain necessary data owing to the rarity of carotid body tumors and the even more rare incidence of malignancy. Therefore, we do not know the true incidence of paraganglioma cells being incidentally present in lymph nodes with a relatively normal appearance. It is my usual practice to excise all lymph nodes encountered in the immediate region of the carotid body tumor for permanent histopathologic analysis. As in the present case, frozen section analysis is not always diagnostic of the presence of paraganglioma cells in the lymph nodes.

I would recommend moderate-dose radiation therapy postoperatively and reserve neck dissection for a treatment failure. As discussed above, I would perform a selective neck dissection only if I knew of the diagnosis of a malignant lesion intraoperatively, but I do not think the morbidity of a secondary neck dissection 1 week later is justified given our limited knowledge of the benefit of neck dissection for these tumors and given the success of moderate-dose radiation in stopping the growth of paragangliomas.

Dr. Carroll: Malignancy in carotid body tumors is rare. There are no distinguishing histologic features of malignancy, and the diagnosis is confirmed only by finding the tumor in adjacent lymph nodes or distant sites. For documented metastases in regional nodes with no evidence of systemic spread, node dissection with postoperative radiation is reasonable. I am aware of no definitive studies supporting this position.

COMMENTARY

The clinical presentation of this patient is similar to many patients seen in a general otolaryngology practice, but the salient features of this history and physical examination that warrant formulation of a careful differential diagnosis and evaluation are outlined by Dr. Carroll in Question 1. All of the consultants outline the important diagnostic considerations, which highlights a key pitfall to avoid: the CT finding of a carotid body tumor should not distract one from considering other pathologic processes in cases in which the clinical picture does not “fit” the typical presentation of a carotid body tumor, because more than 90% of carotid body tumors are benign and slow growing and its treatment may be deferred. As stated by Dr. Stringer, the most likely etiology of the nasopharyngeal mass and serous otitis in this patient was adenoiditis, and a trial of antibiotics can be safely given. When there was incomplete resolution of the nasopharyngeal abnormality and lymphadenopathy, all of the consultants recommended nasopharyngeal biopsy either in the clinic or under general anesthesia. The importance of sampling lymph nodes to exclude lymphoma is noted by Drs. Carroll and Stringer. Once the possibility of a concurrent malignancy is ruled out, the carotid body tumor can be addressed.

Appropriate preoperative evaluation of a carotid body tumor centers around three issues: (1) screening for multiple paragangliomas, (2) imaging of the cerebral circulation, and (3) use of preoperative embolization. The 24-h urine screening for VMA and metanephrine is recommended by Drs. Carroll and Stenson but not by Dr. Stringer. Because the incidence of vasoactive carotid body tumors is low, this may not be necessary in the absence of hypertension, tachycardia, and flushing. MRI is the diagnostic study of choice, both for establishing the diagnosis of carotid body tumor and for screening for multiple paragangliomas. Screening MRI is performed routinely by Dr. Carroll, but Dr. Stringer recommends this only in case of a positive family history of paragangliomas. The consultants’ approaches to imaging the cerebral circulation and test occlusion of the carotid artery are widely divergent. Preoperative carotid blood flow analysis is no longer used by Dr. Stringer, regardless of size of the tumor, because he believes test occlusion is not a reliable predictor of
stroke. Dr. Stenson uses test balloon occlusion with EEG monitoring if the carotid body tumor is large and partially or completely surrounds the carotid artery. Dr. Carroll uses balloon occlusion and SPECT imaging of the cerebral perfusion in all patients and outlines his rationale for obtaining this information, which he believes is valuable. While this area remains controversial, preoperative cerebral perfusion testing is warranted in the unusual patient with large tumors, in which case obtaining distal control of, or sewing a graft to, the internal carotid artery near the skull base may be difficult.

Preoperative embolization is performed by Dr. Stenson 1–3 days before surgery in all patients and by Dr. Carroll the day before surgery in all patients except those with small tumors. This again is controversial, since preoperative embolization can cause inflammation, which may obscure the surgical plane of dissection. It is possible to resect these tumors with minimal blood loss without embolization by first circumferentially ligating and dividing all feeding vessels to the tumor prior to dissection off the carotid artery. The only vessel that is difficult to control because it is usually not accessible until the end of the dissection is a small artery that routinely arises from the posterior aspect of the carotid bulb and enters the base of the tumor near its attachment to the carotid bifurcation.

All of the consultants agree that this tumor should be surgically treated because of the patient’s young age, small tumor, and natural history of slow, progressive growth (doubling time of 4.2 years, as noted by Dr. Carroll). There is unanimity in the need for having vascular surgery colleagues available and/or present if there is a high likelihood of carotid sacrifice. In this patient, excisional biopsy of level II and III lymph nodes to rule out lymphoma is also planned by the consultants.

The finding of paraganglioma cells with surrounding lymph nodes is one of the hallmarks for malignant carotid body tumor. Unfortunately, this was seen only on permanent, not frozen, sections; this leaves a dilemma as to appropriate additional treatment. The consultants all recognize that there is very little information in the medical literature to strongly support a particular approach. Dr. Stenson suggests completion neck dissection or close observation with serial CT scans, Dr. Stringer recommends postoperative radiation therapy, whereas Dr. Carroll suggests neck dissection with postoperative radiation.

This patient illustrates many of the nuances and unanswered questions that arise in the management of carotid body tumors. Careful review of the clinical experience by institutions with large cohorts of patients with this entity may help address some of these questions.

REFERENCES