

Chemodectomas of the Glomus Intravagale: Vagal Body Tumors, Nonchromaffin Paragangliomas of the Nodose Ganglion of the Vagus Nerve

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CHEMODECTOMAS (nonchromaffin paragangliomas) particularly those tumors of the intravagal paraganglionic tissues, although rare, have lately attracted increased attention. These tumors arise in the sites of distribution of the chemoreceptor system which consists of a group of widely scattered structures morphologically identical with the carotid body. They include: the carotid body, the glomus jugulare body, the vagal body, the aortic bodies, the paraganglion ciliare, and collections of similar tissue along the course of the femoral arteries.^{19, 29}

Structures of the chemoreceptor system have in common the following points: (1) they are histologically similar; (2) embryologically they are associated with the ganglion of the cranial nerves and aortic arches; (3) they have similar innervation by sensory branches, probably sympathetic, of the ninth and tenth cranial nerves; (4) they contain no chromaffin substance; (5) they secrete no pressor substance or any other hormone; (6) they function as chemoreceptors and respond to changes in pH or

CO₂ and oxygen concentration of the peripheral blood.¹⁷

Historical

Von Haller³³ in 1743 first described the carotid body and named it the ganglion minutum. The first carotid body tumor was reported by Marchand in 1871.²⁰ The glomus jugulare was described in 1840 by Valentin³² who called it the ganglion tympanicum. Rosenwasser²⁸ in 1945 reported the first chemodectoma of this organ and Otani described it pathologically. In 1902 Biedl and Wiesel² observed the first chemoreceptors in the mediastinum, the aortic bodies. Lattes¹⁷ in 1950 was credited with describing the first tumors of aortic bodies. An intraorbital tumor of the ciliary body was reported in 1932 by Fisher and Hazard.¹¹ Although three human ciliary body tumors have been reported, the ciliary body itself has been identified only in monkeys, but not yet in humans. Smetana and Scott²⁹ in 1951 reported a series of malignant chemodectomas occurring in close relation to the femoral vessels.

Vagal Body Tumors

Muratori²⁴ observed cells resembling the carotid body in the ganglion nodosum of the vagus nerve of birds in 1932. White³⁵ first described this paraganglion intravagale in humans in 1935. That same year Stout³¹

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published the first report of a carotid-body-like tumor of the nodose ganglion of the vagus nerve. Lattes and Waltner¹⁸ in 1949 named this type of tumor, arising from chemoreceptor tissue, nonchromaffin paraganglioma to distinguish it from true paraganglia or chromaffin tissue which secretes epinephrine and norepinephrine such as the adrenal medulla and the organ of Zuckerkandl. Lattes¹⁷ in 1950 reported two more cases including the first considered malignant (recurrence with intracranial extension). Mulligan²³ in 1950 designated these tumors of chemoreceptor tissue chemodectomas (*chemia*—infusion; *dechethai*—to receive; *oma*—tumor). Birrell³ termed this structure the vagal body and chemodectomas developing within it vagal body tumors. Burman⁵ in 1955 reported the first case of a widely metastasizing vagal body tumor.

At this time over 600 carotid body tumors and more than 300 glomus jugulare tumors have been reported.²⁵ To our knowledge only 37 vagal body tumors are recorded.³⁻³⁴ Of note is the fact that approximately one third of these have been reported from the Mayo Clinic.^{13, 14, 26}

The present study is concerned with seven instances of chemodectomas of the vagal body treated at Memorial Hospital between 1937 and 1969. Since histologically these tumors are identical with carotid body chemodectomas, the distinction is a clinical one based solely on the surgical anatomy. Vagal body tumors in contrast to those of the carotid body lie more cephalad in the neck, extending to the base of the skull at the jugular foramen in most instances; displace the internal and external carotid vessels anteriorly and medially without widening the carotid bifurcation; are more likely to invaginate the posterior pharyngeal wall; may cause paralysis of the hypoglossal nerve with hemiatrophy of the tongue, and may produce unilateral vocal cord palsy or a Horner's syndrome or both.¹⁶ Deafness, tinnitus and vertigo are not associated with

vagal body tumors but are common with glomus jugulare tumors.⁶ The vagus nerve fibers fan out or are "splayed over" the surface of the vagal body tumor so that function is usually preserved until late in the process.

At operation when the bulk of the tumor is grossly demonstrated below the jugular foramen and arising from the vagus nerve a designation of vagal body tumor is justified.¹³ All seven of our cases unequivocally arose in the nodose ganglion.

Case Reports

Case 1. A. T., a 25-year-old woman, came to Memorial Hospital in June 1943 complaining of a lump in the right side of the neck present for 2 years and hoarseness of 1½ years' duration. One month prior to examination here, a tonsillectomy was performed at another hospital.

Examination revealed a right retropharyngeal mass contiguous with a mass in the right upper neck. The right vocal cord was paralyzed in the mid-line. Blood pressure was 100/68. The clinical impression was lymphosarcoma.

An open biopsy was performed on July 28, 1943. Because the tumor was pulsatile, a mere wedge biopsy was done which was non-diagnostic. Due to continued enlargement of the tumor, surgical exploration of the neck was undertaken on March 19, 1944. A large mass was found extending from the carotid bulb through the jugular foramen. It was adherent to the transverse processes of the second and third cervical vertebrae. The origin of the tumor from the vagus nerve was clearly demonstrated. The hypoglossal nerve entered the mass. The tumor was excised, sacrificing the common carotid artery, the vagus and hypoglossal nerves, and the cervical sympathetic trunk. The tumor was very vascular; operative blood loss was in excess of 2,000 cc. Residual tumor was left *in situ* at the jugular foramen.

The specimen measured 5 cm. in diameter and gave rise to a string-like projection representing the vagus nerve. Microscopically it was a chemodectoma.

Postoperatively the patient experienced great trouble swallowing and required a tracheostomy and a feeding tube for over 1 year. Two years after operation frontal headaches appeared and she developed gradual onset of right facial weakness, right sided deafness, and right lateral rectus palsy. She died 4 years after operation with recurrence



FIG. 1. Patient J. K. (Case 2). Right-sided neck mass contiguous with a 4 cm. retropharyngeal lesion.

in the neck and intracranial extension causing destruction of the right cranial nerves 6 through 12.

Case 2. J. K., a 20-year-old woman, entered Memorial Hospital because of a painless lump in her right neck of 1½ years' duration. A tonsillectomy 3 months before admission failed to relieve the symptoms (Fig. 1).

Examination revealed a 4 cm. retropharyngeal mass contiguous with a right sided neck mass. She exhibited a right Horner's syndrome. Blood pressure was 120/60.

On September 25, 1944, she underwent surgical exploration with a preoperative diagnosis of the tumor of the deep lobe of the parotid gland. The tumor lay anterior to the transverse processes of the cervical vertebrae and pushed the carotid vessels anteriorly. The vagus nerve ran into the posterior surface of the tumor and its fibers fanned out over the surface of it (Fig. 2). The vagus and hypoglossal nerves were sacrificed; the carotid artery was preserved.

The tumor measured 6 × 4 × 2.5 cm.; microscopically it was a chemodectoma, and an adjacent lymph node contained similar tissue representing either metastases or direct extension.

Postoperatively she had no complications despite the loss of the vagus nerve and 16 years later showed no evidence of recurrence.

Case 3. R. B., a 48-year-old woman, entered Memorial Hospital on February 14, 1955, because of a painless lump below the right ear that had been present for 5 years. Three years before she had undergone tonsillectomy elsewhere. Pain in the right ear 2 weeks before admission prompted her to seek medical attention. She was treated with antibiotic agents and the pain disappeared.

Examination revealed a 5 cm. compressible, pulsatile mass at the anterior margin of the right sternocleidomastoid muscle extending from the mastoid process to the superior cornu of the thyroid cartilage. The blood pressure was 125/85.

Aspiration of the mass yielded only blood. Preoperative diagnosis was schwannoma. At operation on July 6, 1955, a markedly vascular fusiform enlargement of the right vagus nerve was found which extended to the base of the skull. An attempt was made to preserve the vagus nerve by separating the tumor from it by sharp dissection. Adjacent structures were separated from the tumor with the greatest of difficulty attended by considerable oozing of blood requiring packing at the end of the operation.

The tumor measured 4 × 2.3 × 1.5 cm. Microscopically it was a chemodectoma. An adjacent lymph node was negative.

Postoperatively the patient required a feeding tube for 2 days and thereafter had no dysphagia. Paralysis of the right vocal cord was permanent. Examination 8 years after operation indicated no evidence of recurrence.

Case 4. A. S., a 70-year-old diabetic woman, entered Memorial Hospital on August 1, 1956, because of a mass below her right ear of 8 weeks' duration. A 4 cm. moveable mass was found in the right neck adjacent to the angle of the mandible. Blood pressure was 155/90. The larynx functioned normally. A needle aspiration biopsy was interpreted as a carotid body tumor or metastatic adenocarcinoma.

At operation a vascular spongy tumor was found not attached to the carotid vessels. The fibers of the vagus nerve were "splayed over" the surface of the tumor, and an attempt was made to preserve the nerve by dissecting the tumor off its fibers. The nerve was left anatomically intact. A right radical neck dissection was performed.

The tumor measured 4.5 × 3 × 2 cm., microscopically it was a chemodectoma, and all the lymph nodes were negative.

Postoperatively she had temporary dysphagia. Permanent right cord palsy resulted in spite of

anatomic preservation of the vagus nerve. No evidence of disease was found 4 years after operation.

Case 5. R. P., a 58-year-old woman physician, found a large left retropharyngeal mass on self examination prompted by a 2-month history of snoring. Sinus x-rays had shown a cloudy left maxillary antrum, for which she underwent a Caldwell-Luc operation at which a Schneiderian papilloma was excised.

Examination revealed a large rubbery left retropharyngeal mass contiguous with a left upper neck mass felt externally at the angle of the mandible. The preoperative diagnosis was a salivary gland tumor.

At operation on January 29, 1959, a 6 cm. vascular tumor was found to which the vagus nerve was intimately adherent. The hypoglossal nerve entered the mass but was dissected free. The external and internal carotid vessels ran anterior and medial to the tumor. The tumor was stripped from the vagus nerve by blunt dissection and was amputated at the jugular foramen.

The gross specimen measured 6.5×3 cm.; microscopically it was a chemodectoma.

Postoperative course was marked by dysphagia, aspiration, and phlebitis. Laryngoscopy disclosed a partial left vocal cord paralysis. In 3 weeks she was swallowing adequately and was discharged. She was without recurrence when last seen.

Case 6. J. R., a 70-year-old man, first entered Memorial Hospital on June 17, 1963, because of a progressively enlarging mass in the left neck of 14 years' duration, more recently accompanied by dysphagia, hoarseness and pain in the left ear. Fourteen years previously operative exploration of the neck, performed elsewhere, revealed a vascular, bleeding mass concluded to be an aneurysm and a ligation of the left external carotid artery was performed. One month before admission an arteriogram done elsewhere revealed a vascular tumor displacing the left internal carotid artery anteriorly and medially. A tracheostomy was performed at the time of the arteriogram for an episode of hypotension and apnea.

Examination at Memorial Hospital revealed a bulky mass in the left upper neck contiguous with a left retropharyngeal mass extending to the midline. There was deviation of the palate to the right, hemiatrophy of the left side of the tongue and the voice suggested a vocal cord palsy. The larynx, however, could not be seen due to the size of the retropharyngeal mass. Blood pressure was 130/80.

Needle aspiration confirmed histologically the preoperative diagnosis of carotid body tumor. At operation a 9 cm. mushy vascular tumor was found surrounded by a network of tortuous venules. It

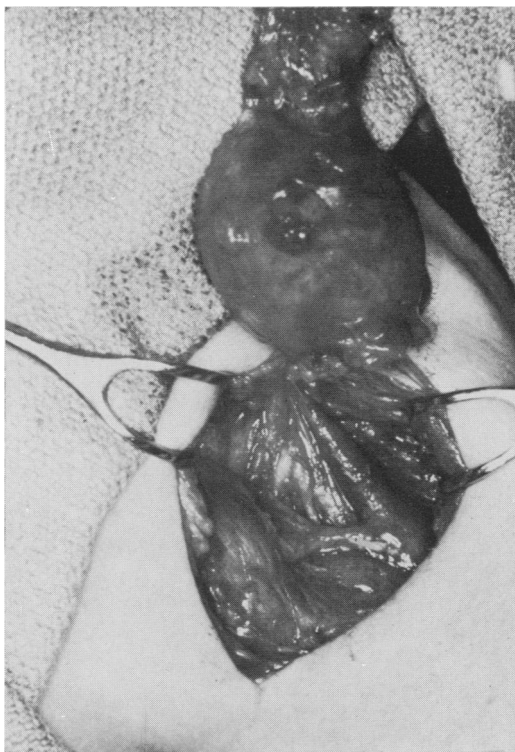


FIG. 2. Patient J. D. (Case 2). Onion-shaped mass with the carotid vessels below.

extended from the 4th cervical vertebra to the base of the skull. A rather atrophic vagus nerve exited from the caudal end of the mass. The hypoglossal nerve and sympathetic chain entered the tumor. A left radical neck dissection with sacrifice of the vagus nerve, the hypoglossal nerve and the sympathetic chain was performed with preservation of the carotid artery. The tumor was amputated at the jugular foramen and residual tumor was left at the base of the skull. Packing was required to control bleeding at this point. Transfusion of three units of blood were required during operation.

The excised tumor measured $9 \times 6 \times 5$ cm. Microscopically it was a chemodectoma interpreted to be malignant. The lymph nodes were negative for tumor.

Postoperatively the patient had palsy of the left cranial nerves 10, 11 and 12 and a Horner's syndrome. Aspiration of food upon eating was a problem requiring the use of a feeding tube, but this resolved spontaneously after several weeks. Five years after operation the patient showed no evidence of recurrence.

Case 7. C. S., a 50-year-old woman, noted a mass at the angle of the right mandible 6 months

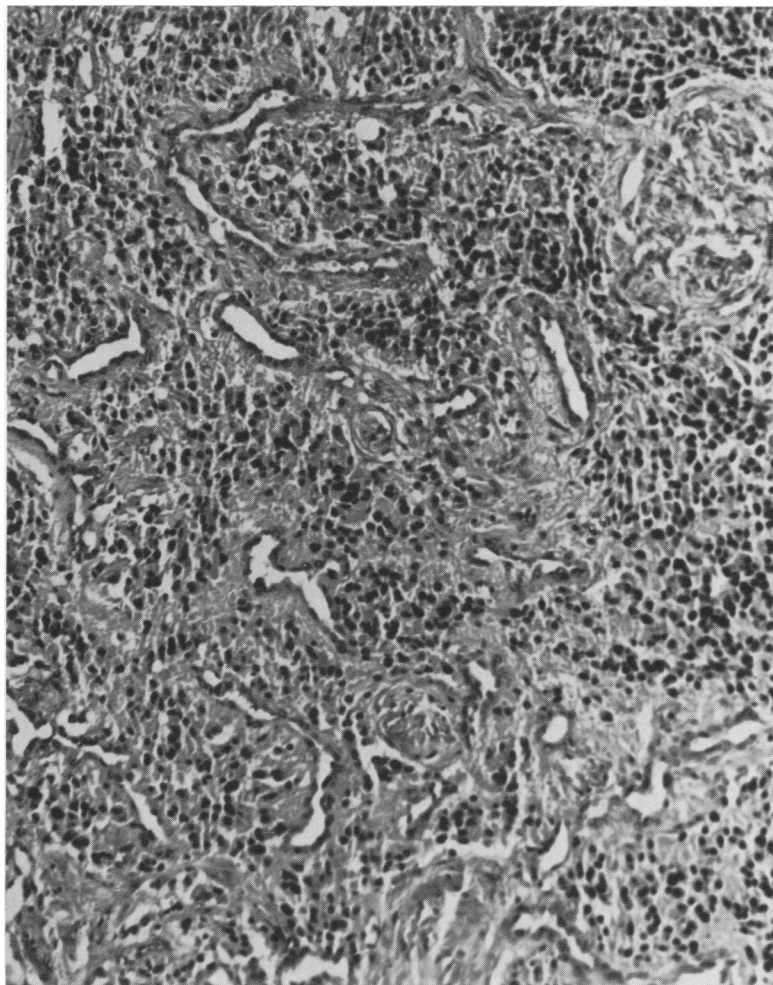


FIG. 3. Characteristic pattern of complex inter-anastomosing blood vessels surrounded by small ill-defined cells with pyknotic nuclei. (H & E \times 100.)

before entering Memorial Hospital. One month before admission a node in the right neck was biopsied at another hospital. She was told this was metastatic carcinoma. Review of the slides here showed metastatic carcinoma in a lymph node; the primary was thought to be probably an epidermoid carcinoma. She had had a cholecystectomy 8 years before admission and a thyroid operation 2 years prior to admission. Review of the thyroid slide here showed only a benign colloid goiter.

Examination revealed a healed scar near the angle of the right mandible with induration surrounding this area. Thorough inspection of the oral cavity, pharynx, nasopharynx, hypopharynx and larynx failed to reveal the source of the primary tumor. A chest x-ray was normal.

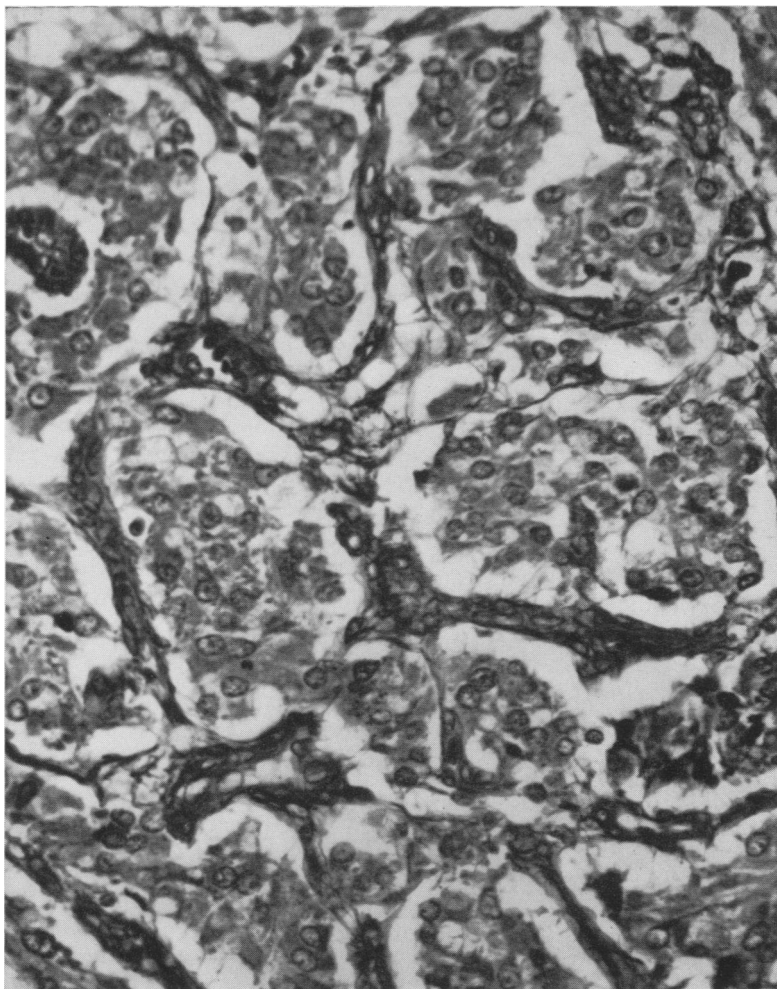
Faced with a diagnosis of metastatic carcinoma in cervical lymph nodes with an undiagnosed pri-

mary a right radical neck dissection was performed on March 9, 1969. The hypoglossal nerve entered the tumor mass and was sacrificed. There was a mass of lymph nodes of the upper jugular chain matted together. Separate from this mass was a fusiform enlargement of the nodose ganglion of the vagus nerve. The vagus nerve was divided both at the base of the skull superior to the tumor and 2 cm. below the tumor, thus resecting both the tumor and the nodose ganglion.

The vagal tumor measured $2 \times 1.5 \times 0.3$ cm. Microscopically both the ganglion nodosum and the lymph nodes showed nonchromaffin paraganglioma.

Postoperatively despite the loss of the vagus nerve she had no problems with aspiration and only slight dysphagia which subsided by the time of discharge 1 week after operation.

FIG. 4. The pattern of Zellballen in which groups of tumor cells are surrounded by a definite reticulum framework. (Silver reticulin stain $\times 250$.)



Pathology

Histologic material was available in all cases, and hematoxylin and eosin and silver reticulin stains were employed. The fundamental presentation of these neoplasms was distinctive and constant. The neoplastic growth pattern was that of an elaborately complex framework of blood vessels about which there were small irregularly outlined, ill-defined cells with deeply staining nuclei. The tumor cells appeared in small nests and aggregates, a pattern designated as Zellballen. These cell clusters were surrounded by a delicate reticulum network. In three cases, a clear histologic association of the neoplasm could be demonstrated

with peripheral nerve fibers and the ganglion cells of the vagal body (Fig. 3). In two, in whom regional lymph node metastases were clearly demonstrated, the primary tumors showed a lack of clear-cut encapsulation. The histologic appearance of these tumors in no way differed from those of their benign counterparts, and even the metastases appeared deceptively benign.

Discussion

Age and Sex

The average age of patients at the onset of symptoms was 48.4 years with a range between 18 years and 70 years. This compares with an average age of 44.4 years in

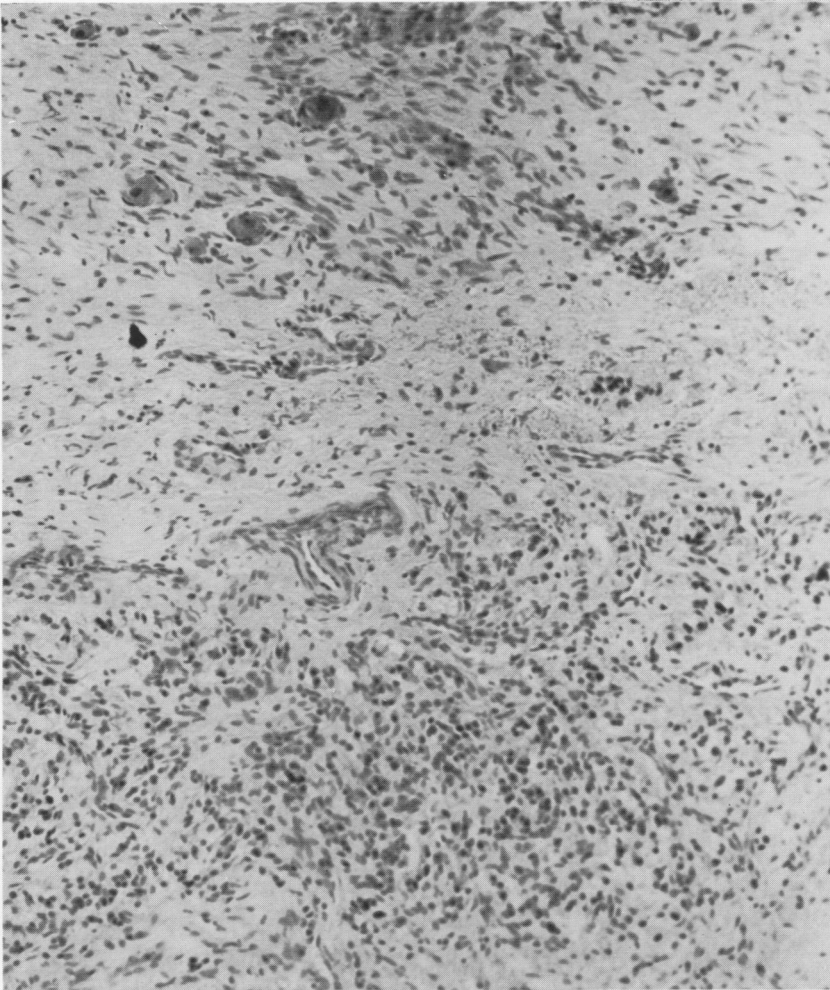


FIG. 5. Peripheral nerve fibers entering tumor tissue in the presence of ganglion cells of vagal body. (H & E $\times 100$.)

a previous report.¹⁴ The average age at the time of treatment was 51.7 years. Six of our patients were women and one was a man. This corresponds to the preponderance of females in reported cases.¹⁴

Symptoms

The average duration of symptoms was 3.3 years; the longest duration being 14 years and the briefest 8 weeks. The most common complaint was a lump in the lateral portion of the neck. Six patients presented with this symptom. Three gave histories of recent tonsillectomies for enlarged tonsils. Two complained of hoarseness, one

complained of snoring, and one had dysphagia.

Findings

All seven patients had masses palpable in the neck behind and deep to the angle of the mandible. Only three had bulging retropharyngeal masses. Approximately two thirds of reported cases have retropharyngeal masses.¹⁴ In three of our patients the masses were pulsatile. Ipsilateral vocal cords were paralyzed in both those patients who complained of hoarseness. In addition, one patient had paralysis of the twelfth nerve on the side of the mass with hemiatrophy

of the tongue. One patient had a Horner's syndrome on initial examination. No patient had hypertension. The masses were right-sided in five cases and left in two. The tendency for right-sided location has been noted in the literature.²⁶

Differential Diagnosis

Table 1 depicts the initial impression of the first examining physician, the range of preoperative diagnoses and finally the less frequently entertained diagnostic possibilities.

Previous Procedures

Three patients had operations on the neck performed elsewhere before coming here (Table 2). In two cases lymph node biopsies were performed and in the third operation was abandoned because of excessive bleeding and the diagnosis was aneurysm of the carotid artery. Lymph node bi-

TABLE 1. *Differential Diagnosis*

Initial diagnosis:	
Schwannoma	1
Aneurysm	1
Metastatic ca.	3
Salivary gland tumor	2
Preoperative diagnosis:	
Carotid body tumor	2
Branch. cleft cyst	1
Metastatic ca.	1
Salivary gland tumor	2
Schwannoma	1
Other diagnoses:	
TB adenitis	
Vagus tumor	
Lymphosarcoma	
Peritonsillar abscess	
Neck tumor	

TABLE 2. *Diagnostic Procedures*

Neck exploration	1
Neck node Bx.	2
Tonsillectomy for pharyngeal mass	3
Needle aspiration	5
Arteriogram	1

TABLE 3. *Results of Needle Aspiration Biopsies in 5 Patients*

Non specific tumor	1
Carotid body tumor	1
Adenocarcinoma or CBT	1
Schwannoma	1
No conclusion	1

TABLE 4. *Surgical Procedures*

Radical neck dissection	3
Excision of tumor (enucleation)	2
Carotid sacrifice	2
Vagal nerve sacrifice	4
XII nerve sacrifice	4
Cervical sympathetic trunk sacrifice	3
Vagal preservation attempted unsuccessfully	3

opsy was interpreted as lymph node hyperplasia in one case and metastatic carcinoma in a lymph node in the other. Three patients had retropharyngeal masses misdiagnosed as enlarged tonsils and had tonsillectomies. One patient had a preoperative arteriogram which identified the pulsating mass as a well vascularized tumor but not an aneurysm. Arteriogram showed the mass located more cephalad than the usual carotid body tumor, displacing the internal carotid artery anteriorly, and not separating the bifurcation of the carotid vessels as pointed out initially by King in 1955.¹⁶ Percutaneous needle aspiration biopsies were performed on five patients preoperatively and the various diagnoses made are shown in Table 3: carotid body tumor in one, schwannoma in one, either carotid body tumor or adenocarcinoma in one, non-specific tumor in one, and no conclusion in the fifth. No patient was treated with preoperative irradiation. There are mixed reports in the literature regarding its efficacy.^{25, 30, 34}

No patient had multicentric chemodectoma, although this is well-known.^{4, 17, 21} Likewise, no patient had familial chemodectoma; however, carotid body tumors have occurred in siblings who were patients at this institution.¹⁰ The only inci-

TABLE 5. *Post-operative Complications*

Aspiration	2
Dysphagia - mild: 3 } severe: 2 }	5
Pneumonitis	2
Horner's syndrome	3
Thrombophlebitis	1

dentally occurring tumor was a Schneiderian papilloma of the antral mucosa.

Surgical Procedures

Of seven patients undergoing resections of tumors three had radical neck dissections (Table 4). In each, preoperative studies such as needle biopsy or open node biopsy gave the impression that the tumor was malignant. The vagus nerves were sacrificed deliberately in four cases. An attempt at preservation of vagi was made in three instances stripping the tumor from the nerve fibers; however, no anatomically preserved nerve ever functioned again. The hypoglossal nerves were sacrificed in four patients in whom the nerve entered the tumor. In two the carotid arteries were resected with the tumors. In each one the internal carotid artery was entered near the base of the skull as the cephaladmost part of the tumor was being resected, and ligation of the internal carotid artery was required to control hemorrhage. There were no neurological sequelae in either case. A mortality of 50% was reported by Farr,¹⁰ however, in carotid body tumors resected with sacrifice of carotid vessels. This high complication rate from carotid ligation associated with resection of carotid body tumor in contrast to the low incidence with elective carotid ligation is due to associated operative blood loss and shock, as pointed out by Moore and Baker.²² We now recommend that these tumors be resected, with great care to preserve carotid vessels even at the expense of leaving small amounts of tumor *in situ*.

In three patients cervical sympathetic

trunks were adherent to the tumors and were therefore sacrificed. All three had Horner's syndrome postoperatively, only one preoperatively.

Complications

Five had dysphagia postoperatively (Table 5). In three it was mild and swallowing without the aid of a feeding tube was possible at the time of discharge. In two patients dysphagia was marked, one required a feeding tube for a year, the other required tube feedings for several weeks. Both patients aspirated food and both had one or more episodes of pneumonitis in the postoperative period. Phlebitis occurred in one patient after operation. Bleeding at operation was moderately severe in four instances. One patient required transfusion of four units of blood, another three units, a third two units and one had oozing at the base of the skull in the operative field which required packing to tamponade the hemorrhage.

Clinical Course

A malignant histologic appearance of these tumors is not necessarily a grave prognostic sign. Stout³¹ interpreted the first reported case as malignant because of vascular invasion; however, the patient was alive and well 16 years postoperatively. One of our cases was interpreted originally as malignant histologically but was living and well 5 years after operation. Two patients had nonchromaffin tissue in cervical lymph nodes indicative of either direct extension or metastases. Both are alive and well, one 3 months after operation and one 16 years. One patient died of local recurrence with intracranial extension and progressive dysfunction of the cranial nerves 6 through 12 on the ipsilateral side 3 years after operation. No patient had distant metastases, but widely metastasizing chemodectomas have been reported.^{5, 29} Of seven patients, six survived an average of 6.6

years, ranging from 3 months to 16 years after operation.

Summary and Conclusions

To our knowledge 37 cases of chemodectomas of the nodose ganglion of the vagus nerve have been reported in the literature. Seven new cases are reported in this paper. Recommended treatment is resection of the tumor with sacrifice of the vagus nerve and any other attached nerves, but with great care to preserve the carotid artery. A brief review of the reported cases is included.

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