CASE REPORTS

NONCHROMAFFIN PARAGANGLIOMA OF THE JUGULAR FORAMEN

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This paper deals with a carotid-body-like tumor found in the jugular foramen, similar to the tumors recently described by Lattes as nonchromaffin paragangliomas.

Kohn, in 1900, classified the carotid body as a paraganglion, in the belief that it was of sympathetic origin and part of the chromaffin system.

Small masses of similar paraganglionic tissue have since been described in the following locations:

1) At the level of the middle ear. As early as 1840, Valentin described a gangliolum tympanicum, associated with the tympanic branch of the 9th cranial nerve. Later, in 1879, Krause showed that this structure resembles the carotid body and this has been confirmed recently by the studies of Guild and Lattes and Waltner. In addition to the paraganglion tympanicum, Guild described what he called the glomus jugularis “in the adventitia of the dome of the jugular bulb, immediately below the bony floor of the middle ear.”

2) At the aortic-pulmonary region. Paraganglia related to the major vessels at the base of the heart were mentioned in 1902 by Biedl and Wiesel. In the middle thirties, Palme, Seto, Muratori and Nonidez described these structures in detail. From their contributions, well summarized by Boyd, we learn that these “aortic bodies” are similar to the carotid bodies and that they can be found in four different locations: a) above the ductus arteriosus; b) on the trunk of the pulmonary artery, near the origin of the left coronary artery; c) near the root of the innominate artery; d) on the left part of the aortic arch.

3) Within the ganglion nodosum. Muratori described in 1932 a paraganglionic formation inside the vagus nerve, at the level of the ganglion nodosum, and called it paragangli intravagali. He found it in different species of the bird, “Ucelli.” His findings were confirmed by the works of White and Lattes, who described the paraganglion intravagale in man.

4) In the vicinity of the ciliary ganglion. Botár and Pribék and Gosses have described a paraganglionic formation related to the ciliary ganglion of monkeys. This structure has not been described in man.

Although serious doubts have been raised as to the sympathetic origin of the carotid body and related structures, the term paraganglion has continued to appear in the literature. In 1926 and 1928 de Castro produced good evidences questioning the chromaffin reaction in the cells of the carotid body. Hollinshead in

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1940 made a review of the subject, arriving at the conclusion that the carotid bodies and cardio-aortic bodies are nonchromaffin in nature. Watzka\textsuperscript{27} classified these bodies as "nonchromaffin and nonepinephrine producing paraganglia."

Accordingly, tumors related to these structures have been most often described as paragangliomas. Lattes and Waltner\textsuperscript{13} suggested that all these tumors originating from the carotid body or related structures be designated nonchromaffin paragangliomas, stressing that "the modifying adjective 'nonchromaffin' would help to avoid confusing them with the chromaffin paraganglioma or pheochromocytoma."

Nonchromaffin paragangliomas have been described in association with the carotid body, aortic bodies, glomus jugularis and paraganglion intravagale.

Carotid-body-like tumors have been recognized and described in the literature since 1891.\textsuperscript{14} Recently, Monro\textsuperscript{16} surveyed 223 reported cases which he considered acceptable as carotid-body tumors and added 5 more cases to the literature.

Carotid-body-like tumors originating away from the bifurcation of the common carotid artery are a relatively recent discovery. Stout,\textsuperscript{25} in 1935, was the first to report such a tumor, when he described a neoplasm "developed in the course of the vagus nerve, in connection with the ganglion nodosum, ... morphologically a paraganglioma."

Rosenwasser,\textsuperscript{22} in 1945, described a "carotid body tumor of the middle ear and mastoid" and suggested its origin from the glomus jugularis. Further reference to carotid-body-like tumors of the glomus jugularis can be found in the paper of Lattes and Waltner,\textsuperscript{13} in which they reviewed the literature and contributed 8 new cases. Isolated cases have been reported since their paper, giving a total of 28 cases.

Lattes,\textsuperscript{12} in 1950, reported the first two examples of such tumors occurring in the vicinity of the aortic arch and suggested that they originated from the aortic bodies. One more case has since been added by Monro.\textsuperscript{17}

After the original case of a paraganglioma of the ganglion nodosum reported by Stout, there appeared in the literature only one paper reporting such tumors. Lattes,\textsuperscript{12} in addition to contributing the first 2 cases of nonchromaffin paragangliomas of the aortic bodies, presented a follow-up study on Stout's case together with 2 new cases of nonchromaffin paragangliomas of the ganglion nodosum. It is interesting to observe that in his 2 new cases the paragangliomas were multicentric in origin: one involved the ganglion nodosum on one side and the carotid body on the opposite side; the other "exhibited three independent but histologically identical growths originating respectively in the vagus nerve at its exit from the base of the skull, at the bifurcation of the common carotid artery and in the adventitia of the aortic arch near the obliterated ductus arteriosus." There is another case that should be mentioned. Dr. R. E. Semmes, discussing a paper by Alexander, Beamer and Williams\textsuperscript{4} on tumors of the glomus jugularis, stated that he had found a similar tumor blocking the jugular foramen and incorporating the 9th, 10th, 11th and 12th cranial nerves in a 32-year-old woman. Dr. W. H. Mathews\textsuperscript{15} told us of his experience with a similar tumor "in the region of the internal and external jugular veins, involving the vagus nerve and whose true extent was not determined though it apparently extended upwards to the base of the skull." This tumor was only partially removed and was diagnosed as a nonchromaffin paraganglioma of the vagus nerve.

\textbf{REPORT OF OUR CASE}

Mrs. R.G., 42-year-old white female, was admitted to The Chicago Memorial Hospital on Jan. 15, 1951, with the chief complaint of continuous vomiting during the previous 5 days.
She had had dull frontal headaches off and on most of her life, easily relieved by aspirin. Otherwise she had always enjoyed good health until 2 months prior to admission, when, for the first time, she began to notice some pains in the head. These pains were of a different character and consisted of an almost continuous feeling of pressure in the back of the head and a sharp pain behind the right ear. More or less at the same time she began to notice strange noises in the right ear, such as roaring and ringing, followed by slight impairment of hearing on that side. Some difficulty with her throat, described as a feeling that the “throat has swollen up” also made its appearance about 2 months prior to admission. These symptoms were followed by occasional vomiting and a change of her voice. Speech at first acquired a nasal quality and this grew progressively worse. During the last 5 days prior to admission she was barely able to whisper. She had three very severe episodes of vomiting, during which she also vomited through the nose. The vomiting lasted several hours on one occasion, all day on another, and had been continuous for 5 days at the time of her admission. She stated that she had noticed during the previous 2 months that her right arm was slightly awkward and that she felt slightly lightheaded every morning.

Examination. She was an acutely ill patient, very dehydrated, vomiting clear or bile-like fluids or else retching continuously. She was very restless and apprehensive. B.P. was 130/80, pulse 90, and respiratory rate 22. Her abdominal muscles were somewhat tender, particularly close to the ribs. This was interpreted as being caused by her continuous vomiting.

The positive neurological findings were: (1) Slight loss of hearing on the right, with air conduction better than bone conduction, indicating a nerve type of deafness. When the tuning fork was applied to the vertex the sound was referred to the left ear. (2) The palate deviated

Fig. 1. Section through jugular foramen, with internal auditory meatus in the background. Jugular foramen is filled with paraganglioma which enmeshes the normal structures.
to the left, with a typical curtain phenomenon. The gag reflex and the sensibility of the palate were decreased on the right side. (3) The right vocal cord was bowed and paralyzed, indicating involvement of the vagus. Phonation was very impaired, the patient only being able to whisper. (4) The right sternocleidomastoid muscle was very weak and atrophic. (5) There were slight dysmetria and dysynergia and slight impairment of rapidly alternating movements of the right arm. There was weakness of the right trapezius muscle which affected the movements of that arm.

Caloric tests were normal. All tendon and superficial reflexes, including corneal reflexes, were normal, except for the gag reflex on the right. Except for the palate and pharynx, as noted above, sensation was normal throughout. There was no nystagmus, no facial weakness, no weakness of any extremity. No lymph nodes or other masses could be palpated in the neck or elsewhere. There was no evidence of any pathology in the nasopharynx.

Laboratory findings, including the Wassermann and Kahn tests, were within normal limits. Roentgenograms of the chest and skull were normal except for a very slight haziness of the periantral cells of the right mastoid and a lack of pneumatization of the right mastoid tip.

A diagnosis of a tumor in the right jugular foramen was made.

Operation. On Jan. 18, 1951 a right cerebellar craniotomy was performed under intratracheal ether anesthesia. The right 7th, 8th, 9th, 10th, and 11th cranial nerves were exposed. The 7th and 8th appeared normal both in size and color. The 9th, 10th, and 11th nerves, on the other hand, were grayish in color and did not appear at all healthy. However, no tumor could be seen about them or about the jugular foramen. The brain stem and the space anterior to it were visualized and no tumor mass was seen. Just as we were preparing to close the incision, the anesthetist announced that the systolic blood pressure, which had been running from 160 to 180 throughout the procedure, had dropped to 110 mm. of Hg. The glucose solution, which had been running intravenously during the operation, was replaced with blood. Suddenly respiratory and cardiac activities ceased and the blood pressure could not be obtained. In spite of accelerating the administration of blood, giving artificial respiration and stimulants, and forcing oxygen through the intratracheal tube, respiratory and cardiac activities were not resumed.

Autopsy. The brain was entirely normal. A part of the base of the skull, incorporating the right jugular foramen and related structures, was removed. This specimen consisted of the petrous pyramid and the floor of the posterior fossa on the right side. The petrous pyramid itself, the opening over the tip of the petrous pyramid into Meckel’s cave, the internal auditory meatus and the foramen for the 6th cranial nerve appeared perfectly normal. The dura mater lining the posterior fossa was entirely normal. However, within the jugular foramen was a granular pinkish-gray mass which did not extend quite above the level of the foramen into the posterior fossa (Fig. 1). With a saw the bone was divided just through the posterior margin of the jugular foramen. Thus laid open, we found a mass of pinkish-gray tissue involving all of the nerves of the jugular foramen, that is, the 9th, 10th, and 11th, in one mass, and attached to the posterior wall of the internal jugular vein. When this mass was removed and the jugular vein incised, it was found that a nodule of the tumor, measuring approximately 3 or 4 mm. in diameter, protruded into the vein (Fig. 2). The mass of tumor measured 2 X 1 X 1 cm. The tumor did not have a sharp capsule and seemed
to involve all of the structures of the jugular foramen equally. The entire mass, including the wall of the jugular vein and the three nerves, was removed en bloc. The petrous pyramid was sectioned anteroposteriorly and longitudinally through the internal auditory meatus without disclosing any additional abnormality. On opening the mastoid process there was no evidence of tumor or infection.

No abnormalities were noted in the region of the carotid or aortic bodies. There were a severe fatty infiltration of the walls of the right cardiac ventricle and an acute interstitial pneumonia. The immediate cause of death was believed to be vagal inhibition secondary to the trauma of the operation acting on a heart already the seat of severe fatty degeneration, with a clinically unrecognized interstitial pneumonia being a contributing factor.

Microscopic Examination (Dr. Otto Saphir). Sections revealed a conglomerate mass of tumor imbedding large nerves and filaments, which contained many nerve cells, ganglia, venous sinusoids and the wall of the jugular vein (Fig. 3). The tumor was poorly circumscribed and was composed of loosely packed polygonal cells loosely arranged in small islands, nests and cords of varying sizes (Fig. 4). The cytoplasm was eosinophilic and contained numerous fine amphophilic granules (Fig. 5). The nuclei were moderately pleomorphic and varied considerably in size. They were round to oval and appeared to be of two types, one finely stippled with chromatin and the other containing coarse chromatin clumps. The stroma was composed of richly vascularized fibrous tissue which formed septa which surrounded the islands of tumor but failed to penetrate between the cells. In some areas, the septa became quite thick and col-
Fig. 4. Typical appearance of paraganglioma, with tumor cells arranged in cords.
(Hematoxylin and eosin ×150)

lagenous. The ganglia and nerves were compressed and their epineurium was invaded by the tumor, but the structures themselves were free of tumor. Silver stains showed fragmentation and disappearance of axons. The tumor infiltrated the adventitia and media of the jugular vein, penetrating the intima in one area to form a pedunculated intraluminal tumor mass which appeared to be covered by endothelium. A similar pedunculated tumor was seen inside a vein within the tumor mass. There were also several cavernous spaces within the tumor which were lined by little more than a layer of endothelium (Fig. 6). Iron stains failed to reveal the presence of iron within the tumor and did not stain the cytoplasmic granules.

DISCUSSION

Having the typical appearance of a carotid-body tumor and not being metastatic, it seemed likely that this tumor arose from a structure similar to the carotid body, in this case the paraganglion intravagale of the ganglion nodosum.

There are only 4 other similar tumors in such a location mentioned in the literature. A comparative study of these cases shows that most of the signs and symptoms were indicative of involvement of the structures of the jugular foramen; this is particularly clear in the case of Dr. Semmes and in our case. In Stout’s case (Lattes’ Case 1) the neurological symptoms were mentioned only postoperatively, and they referred particularly to the 9th, 10th, 11th and 12th cranial nerves. In Lattes’ Case 2, with a palpable mass in the neck, there was evidence of involvement
Fig. 5. Clusters of large polygonal cells, containing numerous fine amphophilic granules.
(Hematoxylin and eosin ×570)

of the 11th and 12th cranial nerves. In his Case 4 no neurological findings are recorded. (His Case 3 was a tumor of the aortic body.)

In addition, pain in the back of the head and/or behind the ear on the affected side was present in at least 2 of the 5 cases. A palpable mass in the pharynx or in the side of the neck was recorded in 3 of the 5 cases.

Roentgenograms of the skull were negative in all but 1 case in which there was questionable enlargement of the jugular foramen.

Some of these tumors may be completely removed, sacrificing the 9th, 10th and 11th cranial nerves. In Stout’s case an extracranial approach sufficed for complete removal. In our case the location of the tumor within the jugular foramen made surgical treatment very difficult, particularly as the tumor could not be seen at the operation. Had the tumor been exposed by resecting the floor of the posterior fossa lateral to the jugular foramen it would have been necessary to sacrifice the 9th, 10th and 11th cranial nerves and the internal jugular vein in order to remove the tumor. This, of course, would have been a difficult and hazardous procedure and the loss of these three important cranial nerves, particularly the entire right vagus, would have seriously handicapped the patient. Nevertheless there would seem to be no alternative and should we be presented with this problem again we would feel justified in carrying out such radical surgery as a life-saving measure.

All of these tumors, like nonchromaffin paragangliomas in other locations, were
FIG. 6. Numerous cavernous channels formed by a single layer of endothelium course among the tumor cells. (Hematoxylin and eosin ×570)

quite vascular at operation with 1 exception (Stout’s case). These tumors do not seem to respond to X-ray therapy. They apparently grow slowly (1 patient had an 8-year history) and may attain considerable size. On the other hand, some of them, though very small in size, may damage the 9th and 10th nerves so severely as to render the patient helpless with continuous vomiting.

SUMMARY

A case of nonchromaffin paraganglioma of the paraganglion intravagale of the ganglion nodosum is reported. It produced the typical clinical syndrome of the jugular foramen and continuous vomiting. A review of the literature disclosed that only 4 similar cases have been reported. All of these tumors are similar, histologically, to the tumors of the carotid body. It is believed that they have arisen from the paraganglion intravagale of the ganglion nodosum of the vagus nerve. Surgical treatment is difficult and hazardous and complete removal requires that the 9th, 10th and 11th cranial nerves and the internal jugular vein be sacrificed.

REFERENCES

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