Intracranial Pheochromocytomas (Active Glomus Jugulare)

Case Report

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Certain cells from the primitive neural crest become glands instead of neurons. These glands, the largest of which is the adrenal medulla, are called chromaffin bodies or paraganglia (Fig. 1).27

In a review of some 1000 recorded tumors of these glands, 93% were in the adrenal medulla and the other 7% along the aorta and its major branches. Less than 1% are above the diaphragm.14,41 Grossly these tumors are well-demarcated, soft, dark, lobulated, vascular masses usually weighing less than 50 gm.16,33 Microscopically they consist of intertwining cords of large irregular polyhedral epithelial cells with faintly granular cytoplasm and large hyperchromatic, centrally placed, round or oval, vesicular nuclei. Occasionally one of these cells resembles a neuron. The stroma is scanty, loose, and contains occasional nerve fibrils. Vasculature is abundant and thin walled, with occasional clumps of epithelial cells bulging directly into the vessel lumen. Mitoses are rare, and malignancy is a clinical rather than a pathological diagnosis.6,8,12,13,16,32,35,40

The more common terms applied to these tumors are; "pheochromocytoma," because of the dark color; "chromaffinoma," because of the chromium salt affinity histologically; and "paraganglioma," because of their anatomical location.4,6,36,37 None of these terms specifically designates the 10% to 30%1,10 of these tumors having the unique property of producing excesses of catecholamines3,7,11 resulting in the dramatic clinical picture of hypertension (paroxysmal or sustained), pallor, sweating, malaise, headache, weight loss, and occasionally associated diabetes mellitus and hyperthyroidism.3,12,30,32,33,42,47 Grossly and microscopically these secreting tumors are indistinguishable from the nonsecreting tumors22 with one controversial exception. Some claim the secreting tumors all stain with chrome salts and are thus distinguished from the nonsecreting tumors.6,36

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In discussions of these glands and their tumors, the carotid body (ganglion minutum)45 and the glomus jugulare are customarily omitted on the debatable basis that they are of different origin and that they do not stain with chrome salts. Some anatomists are quite emphatic in stating that they are not derived from the chromaffin chain.26,50 but more recent workers believe that they are of the same origin as the abdominal and thoracic paraganglia.2,11,54

At least two secreting tumors32 of the carotid body exist in the world literature. The patients, a 66-year-old man5 and a 12-year-old boy,17 both died following removal of a tumor that in each instance was clinically, grossly, microscopically, and biochemically a secreting pheochromocytoma. One was called an "active chemodectoma" and the other a "nor-adrenalin, adrenalin producing non-chromaffin paraganglioma."

The glomus jugulare was described
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grossly by Valentin45 in 1840 and microscopically by Luschka25 in 1862. Tumors of the glomus jugulare were described by Golgi in 186918 and Krause24 in 1878. The latter also remarked on the similarity of this structure to the carotid body. The tumors have been called hemangiomas, hemangiendotheliomas, chemodectomas, hemangiofibroendotheliomas, and non-chromaffin paragangliomas.16,21,24 In 1943 Watzka40 suggested the term “non-chromaffin paraganglioma” for the carotid body tumor, and in 1948 Lattes and Waltner24 suggested this term for tumors of both the carotid body and the glomus jugulare. Winship, et al.,23 in 1948 reported that they thought all these tumors were glomus tumors. Sjoerdsma et al.,41 and Zak12 suggested that all these tumors were part of a multicentric glomus neoplasia along with von Hippel-Lindau’s and von Recklinghausen’s tumors.26,37,39 Huppler et al.,21 in 1955 suggested that they were all chemodectomas and that they might have a secretory function in addition to being sensory receptors. Steinberg and Holz,43 Pryse-Davies, et al.,24 and Boyd, et al.,7 suggested in addition that there might be a slight increase in catechols in these tumors.

The signs and symptoms of the tumors of the glomus jugulare predictably are those of cranial nerve deficits starting with the ninth, tenth, and eleventh, the nerves passing through the jugular foramen. The seventh, eighth and finally the twelfth nerves may be involved. There is often erosion of the petrous pyramid, and there may be a vascular pulsating protrusion in the external auditory meatus.8,40

In 1966, Duke et al.,45 reported a secreting tumor of the glomus jugulare. A careful review by them at that time would have indicated it was the only reported case to date. (Terracol and Guerrier44 had reported a case from France in which the blood pressure was “fluctuating” during manipulation of the tumor.) Duke’s case was a 33-year-old woman whose presenting complaint was progressive hoarseness. She had been troubled with hypertension during two previous pregnancies. The diagnosis of a glomus jugulare tumor was made and an extracranial exploration carried out. The tumor was deemed inoperable, and closed without a biopsy. She later returned with paroxysmal hypertension, pallor, sweating, and an elevated urinary vanillylmandelic acid, all diagnostic of an active pheochromocytoma. She had an abdominal exploration and then a thoracotomy in search of the pheochromocytoma. She then had selective venous catheterizations and finally the right jugular vein yielded an excess of nor-adrenalin. The right glomus tumor was reexplored and a portion removed extracranially; this was histologically and biochemically a secreting pheochromocytoma and so called by the author. It did not stain with chrome salts.

Case Report

Our patient was a 17-year-old boy with a 3-year history of hospital admission for episodic headache and progressive hoarseness. He eventually developed complete seventh, eighth, ninth, tenth, eleventh, and twelfth nerve deficits (Fig. 2). It was felt he had a glomus jugulare tumor, but a consulting neurologist diagnosed syringobulbia.

On his final hospital admission erosion of the petrous pyramid was demonstrable for the first time (Fig. 3). In addition he now had severe hypertensive retinopathy with papilledema and hemorrhages and a sustained blood pressure of 250/160 which responded briskly to alpha adrenergic blocking agents (dibenzyline).27,28 The urinary vanillylmandelic acid was 48 μg/24 hrs; the upper limit of normal in our laboratory is 15. His urinary nor-adrenalin was 2375 μg/liter, over 10 times the upper limit of normal for our laboratory. Intravenous pyelogram, renal scan, aortogram, sugar tolerance, and thyroid studies were all normal. A retrograde left jugular venogram revealed obstruction at the base of the skull (Fig. 4).19 Blood from the left jugular vein contained 68 μg/liter of nor-adrenalin, and no adrenalin. Blood from the left axillary vein contained 55 μg/liter of nor-adrenalin. The normal venous catecholamine content as determined in our laboratory is 3 to 4 μg/liter, with 60% to 70% nor-adrenalin and 40% to 30% adrenalin. A vertebral angiogram58,48 showed a vascular mass in the left posterior fossa (Fig. 5). The electroencephalogram revealed widespread slow activity. Oral dibenzylle, 20 mg three times a day, reduced his blood pressure to 150/90 and produced a marked postural hypotension.

Operation. The boy was operated on in the horizontal position through a left suboc-
cipital craniotomy approach, using dibenzyline blockade. After removal of the cerebellar cap an exceedingly vascular tumor surface was encountered with a pulsatile excursion exceeding that of the adjacent brain. Digital compression of the tumor surface yielded a vigorous rhythmic thrill. Removal of the tumor down to bone and through the jugular foramen was the most vivid vascular experience we have ever encountered, requiring 6 hours and 17 bottles of blood.

Postoperative Course. The boy responded promptly, maintaining a normal level of consciousness and activity, and was up and about the ward. He continued to secrete excesses of urinary vanillylmandelic acid, how-

Fig. 2. Photographs of patient showing left facial palsy (left), left tongue atrophy (center), and wasting of left sternocleidoid muscle (right).

Fig. 3. X-ray film showing marked erosion of left petrous pyramid.
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Fig. 4. Retrograde jugular venogram, anteroposterior (left) and lateral (right) views showing rounded cutoff at level of C-1.

ever, indicating some residual tumor, presumably in the petrous bone. On the 12th postoperative day he experienced a sudden violent headache and died.

**Autopsy.** There was a massive cerebral hemorrhage from erosion by tumor tissue through the wall of the internal carotid in the foramen lacerum. The adrenals were normal, weighing 6 gm each. There were no other tumor sites. The heart weighed 380 gm and had left ventricular hypertrophy but no dilatation. Microscopically the tumor was a typical pheochromocytoma (Fig. 6). It did not stain with chrome salts. Biochemically the tumor nor-adrenalin assay was 32.6 µg, over 150 times the normal amount for an adrenal medulla. There was no measurable adrenalin. The normal adrenal medulla assays 0.1 to 0.8 µg of catecholamines per gram of tissue, and the normal ratio of adrenalin to nor-adrenalin is 4 to 1.

**Discussion**

It is thus evident that failure to stain with chrome salts can no longer be considered conclusive evidence of the absence of catecholamines or their precursors in the cytoplasm. Other factors influence this failure to stain, such as the Ph of the fixative and the state of oxidization of the tissue. The pharmacological and biochemical specificity of an endocrine producing cell greatly exceeds the specificity of ordinary histopathological techniques.
**Summary**

We have presented the second known case of active glomus jugulare tumor or pheochromocytoma of the glomus jugulare, possibly the first presenting as an intracranial mass. We have reviewed related reports and emphasized the confusion in nomenclature. Finally, we have been impressed by the fact that although the tumor in this case did not stain with chrome salts, it contained, by assay, 150 times the normal amount of noradrenalin in the adrenal medulla; this observation of course casts doubt on the traditionally conclusive reliability of chrome salts to demonstrate catecholamines or their precursors in the cytoplasm.

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