Multicentric Chemodectomata at High Altitude

A CASE REPORT AND REVIEW OF THE LITERATURE

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SUMMARY

Multicentric chemodectomata in the right glomus intravagale and both carotid bodies were excised from a 74-year-old woman. These are rare tumours. The patient was born and lived at an altitude of 1 800 m above sea level. The effects of altitude and chronic hypoxia on the carotid bodies are discussed. Some chemodectomata may, in fact, be extreme examples of hypoxia — induced hyperplasia of chemoreceptor tissue.

S. Afr. Med. J., **48**, 1715 (1974).

The chemodectomata are rare tumours of non-chromaffin paraganglia. They occur most often in the head and neck, particularly in the carotid bodies, the glomus jugulare and the glomus intravagale, but rarer sites of occurrence in the thorax and abdomen have been described.[1,2] Glomus intravagale tumours have been reported in only 44 patients.[2]

Multiple chemodectomata have been described arising synchronously or metachronously in various parts of the paraganglionic system. This multicentricity rarely involves glomus intravagale tumours, only 6 such instances having been recorded.[3]

Recent work has shown that chemoreceptor tissue in the carotid bodies of animals[4] and of man[5,6] manifests significant hyperplasia at high altitudes. The incidence of chemodectomata at high altitude is significantly greater than at sea level.[2,7] This report concerns a case of simultaneously occurring chemodectomata in both carotid bodies and the right glomus intravagale in a patient who had lived all her life at high altitude.

CASE REPORT

The patient, a 74-year-old female, presented with a progressively enlarging, painless swelling, close to the angle of the mandible on the right. The swelling had been present for 10 years. Apart from arterial hypertension, which was untreated, she was asymptomatic.

On examination the blood pressure was 180/115 mmHg. The swelling was smooth, firm, situated in the carotid triangle on the right, 5 × 5 cm in diameter, and not attached to the sternomastoid muscle. It was mobile horizontally, but not vertically. There was quite marked arterial pulsation both anterior and posterior to the mass, with a loud overlying systolic bruit. The parotid glands on both sides were slightly enlarged. There was no cervical lymphadenopathy. The cranial nerves were intact. The eardrums were normal. The mouth, pharynx and larynx (by indirect laryngoscopy) showed no evidence of tumour. There was no evidence of cardiac or respiratory decompensation.

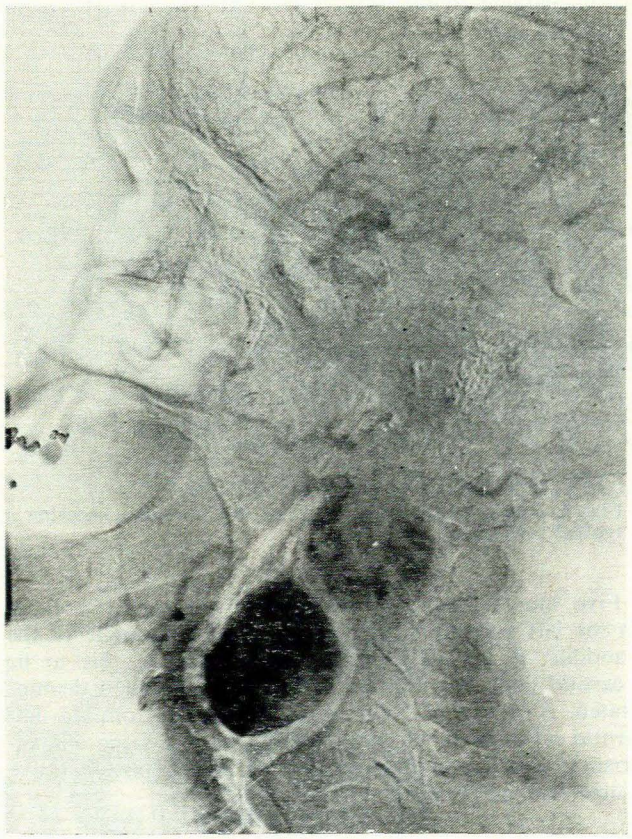

Fig. 1. Right carotid arteriogram, showing the internal and external carotid arteries splayed at their origin by a vascular tumour.

A right carotid arteriogram, performed by direct puncture, showed marked splaying of the internal and external carotid arteries (Fig. 1) by a large vascular tumour, typical of a carotid body tumour.

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Date received: 15 May 1974.

The tumour was approached at operation through a long oblique incision along the anterior border of the sternomastoid. A 5 × 5 cm tumour, lying in the fork of the carotid artery, was excised by sharp and blunt dissection, without interrupting blood flow in the carotid system. A further mass then became palpable and visible near the base of the skull. It had the same consistency as the tumour removed from the carotid bifurcation, and was situated in the right vagus nerve. Part of the vagus was sacrificed in removing it. This tumour measured 2 × 3 cm.

In the postoperative period a haematoma developed in the wound. At exploration, active bleeding was found coming from the partially-cut vagus nerve. The vessel was ligated. The patient subsequently manifested evidence of recurrent laryngeal nerve palsy on the right.

The histology of both tumours was the same. There were nests of cells around networks of small bloodvessels. The cells were round to polygonal, with oval, elongated nuclei, some of which were vesicular and some hyperchromatic (Fig. 2). The cytoplasm was abundant and eosinophilic. The features were consistent with non-chromaffin paraganglioma (chemodectoma).

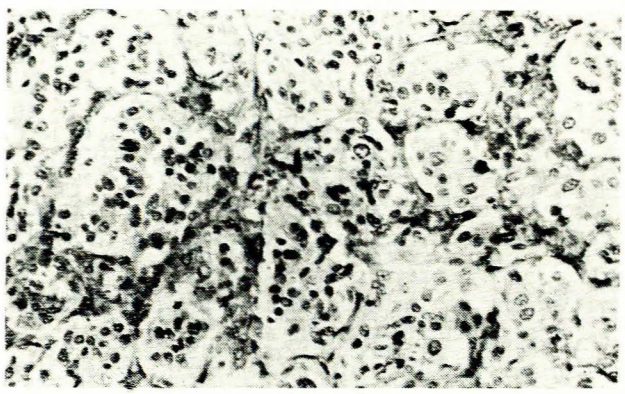

Fig. 2. Representative histology of the tumours, showing typical 'zellballen'.

Five months later the patient complained of a lump on the left side of the neck, adjacent to the angle of the mandible. A left carotid arteriogram showed this to be a carotid body tumour. No further tumours were demonstrated. A 3 × 4 cm tumour was removed from the left carotid bifurcation. Histologically it had the same characteristics as the previous two tumours. The postoperative course was uneventful.

DISCUSSION

The anatomical existence of the carotid body was reported initially by von Haller in 1743.[8] Almost 150 years passed before Marchand (1891)[9] first reported a tumour arising in this organ. Since then reports of chemoreceptor tissue occurring in different sites have appeared at regular intervals.[1,10]

In 1900 Kohn[11] reported his investigations on the morphology and embryology of the carotid body. He coined the term 'paraganglia' to describe a collection of morphologically similar cells which occurred in relationship with either the sympathetic nervous system or a branchial arch artery. The term paraganglion implied that the chief cells of the organ arose from the same cells that form the ganglion cells of the sympathetic nervous system, have an endocrine function similar to that of the adrenal medulla, and are intimately related to the autonomic nervous system. For many years it has been customary to divide paraganglia into two groups, based on their reaction to potassium bichromate. Chromaffin paraganglia exhibit cytoplasmic granules which probably contain catecholamines.[1] They are in close relationship with either adrenal medulla or sympathetic ganglia, secrete pressor substances, and are connected to an efferent nerve. Non-chromaffin paraganglia do not have cytoplasmic granules which stain with potassium bichromate. Nevertheless, catecholamines have been demonstrated in the chief cells of non-chromaffin paraganglia by fluorescent microscopic methods,[1] and these can be secreted.[12] Non-chromaffin paraganglia are usually associated with afferent nerves.[13] Because of these differences, it is increasingly common practice to call non-chromaffin paraganglia 'chemoreceptor bodies'[3] despite the fact that chemoreceptor function has not been demonstrated in all parts of the system.

Anatomy and Distribution

The detailed development of the chemoreceptor system has been studied extensively and has been the subject of debate for some time.[1] The fundamental question has been whether the specific cells of the system are of mesodermal or neural origin. Although this question has not finally been answered, a dual origin from mesoblastic and neural tissue would explain the presence of ganglion cells, nerve fibres and paraganglionic cells in the normal carotid body and also in the normal vagal body.[3]

Chemoreceptor tissue occurs throughout the body, both above and below the diaphragm. These sites have been identified either by standard anatomical dissection, or based on the occurrence of rare primary tumours in sites where chemoreceptor tissue had hitherto not been identified. The common denominator for chemoreceptor tissue occurring above the diaphragm is its association with cranial nerves and their ganglia, as well as with vessels of the embryonic branchial arches. The known sites of occurrence include the carotid body, glomus jugulare,[14] glomus tympanicum, auricular branch of the vagus, aortic body, glomus intravagale, ganglion ciliare, nose, lung, mandible, larynx, trachea, tongue, pineal body, heart, retroperitoneal space, walls of large arteries, pylorus, duodenum and urinary bladder.[1,2]

Histology

Chemoreceptor tissue consists of lobules of parenchymal cells, the lobules being separated from one another by a

variable amount of vascular connective tissue.[15] Within these lobules the cells are arranged in spherical clusters of '*zellballen*', which are delineated by reticulin and cellular fibrous tissue. There are two types of parenchymal cell in the carotid body, the type I or chief cell, and the type II or sustentacular cell. Chief cells exist in three forms, which are termed the light (L), the dark (D) and the pyknotic cells.

Chemoreceptor Tissue at High Altitude

The carotid and aortic bodies have been shown to respond to a decrease in blood pH, a decrease in arterial oxygen tension, an increase in arterial carbon dioxide tension, or an increase in blood temperature.[16] The effects of such a response are to vary the rate, depth and minute volume of respiration, and to affect the tone of the sympathetic nervous system. It was thus theoretically predictable that states of chronic hypoxia would produce continued excess stimulation of the carotid bodies.

Arias-Stella in 1969[17] reported that the carotid bodies of Peruvians living in the High Andes were heavier than those of people living at sea level. This was confirmed in animals from the same regions.[4] This increase in weight was due to hyperplasia, which in guinea pigs and rabbits was due to an increase in the number of light (L) cells. Similar increases in weight have been observed in other states of chronic hypoxaemia, such as chronic bronchitis and emphysema, and also in some anaemias.[15]

The effects of states of extreme oxygen deficiency on the chief cells have been studied under the electron microscope.[15] Chief cells contain granular bodies which probably contain catecholamines. These are discharged into the intercellular spaces during extreme hypoxia. The significance of this is not known.

Since these studies have appeared, there have been reports of the strikingly high incidence of carotid body tumours in people born and living at high altitudes.[2] The obvious question is whether this could be an extreme manifestation of hypoxia-induced hyperplasia of chemoreceptor tissue. However, although hyperplasia may account for some chemodectomata, some at least are true neoplasms, because metastases do occasionally occur.

Multicentricity of Chemodectomata

Multiple chemodectomata have been described arising simultaneously or sequentially in various parts of the chemoreceptor system, and are more commonly found to have a familial tendency.[18] Cases of multicentric chemodectomata which include a vagal body tumour are extremely rare, only 6 cases having previously been reported.[3] Only one of those cases had bilateral carotid body tumours. It is interesting to note in this respect that the second carotid body tumour in our case was initially missed. As the incidence of multicentricity is about 10%, this may be a pointer to the routine use of bilateral carotid angiography in the diagnostic work-up.

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