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Structure, location, function and pathological features of the human carotid body

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SUMMARY

Study of the structure, function and location of the carotid body is essential in the field of interventionist radiology since the exploration of these aspects with stents elicits a baroreceptor response, triggering in some cases unrecoverable vagotonic crises.

This matter is of dual interest because massage in this zone (the bifurcation of the carotids) is one of the manoeuvres most frequently used in primary care in cases of sinusal paroxistic tachycardia.

This organ changes with age, cellularity decreasing over time in a fashion inversely proportional to the amount of connective tissue, the cell clusters among them becoming increasingly distant from one another. In the present work, upon studying the structure of this body we observed different cell types and these could be classified as type I, or the main type, in turn divided into type A (pale) and type B (dark), surrounded by type II cells which acted as a support. As well as these, we observed paraneurons very similar to those of the autonomic nervous system. Inside these, Nissl granules were observed, in agreement with the extensive innervation to which this structure is subjected, like its vascularisation of capillaries and venules, where many contacts of glomic cells with nerves and with the vessels are observed.

The large amount of neurotransmitters inside the body, encephalin, leucine and above all dopamine, makes the carotid body a good candidate for collecting the peptide necessary for the treatment of Parkinson's diseases or similar dyskinesias.

Key words: Carotid body – Glomus – Function – Pathology – Stent – Plaque-atheroma

INTRODUCTION

The *glomus caroticum* can be defined as a paraganglion; i.e., an aggregate of chromaffine tissue distributed throughout the autonomous nerve system and sometimes formed by small, intensely fluorescent cells; the so-called SIF (small intensity fluorescent) cells.

In the past there has been considerable controversy as regards the classification of these paraganglia. Then, Pearse (1969) and Pearse and Polak (1974) discovered the APUD system, observing that they really did belong to this diffuse endocrine system. Likewise, Tischler (1990, 1997), Kohn (1903), De Castro (1951) and De Castro and Rubio (1968) also carried out interesting work on the issue.

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The carotid sinus can be considered a "fashionable" structure owing to the increase in interventionist radiology with the emplacement of blown-up balloons that produced a vagal response upon being stimulated in its baroreceptor function. Its location is also a handicap, however, because it is not constant; although it is usual to find it at the bifurcation of both carotid vessels this location may vary and may sometimes be an insurmountable problem for radiologists, apart from its intense vascularisation. Hence the high risk of such interventions.

The carotid body has also been assigned a chemoreceptor function, although this is debatable because many authors do not differentiate these structures, body and sinus, giving both a baroreceptor and chemoreceptor function.

From the embryological point of view, the carotid body develops from the mesenchyme of the III pharyngeal arch, the glosopharyngeal nerve (IX cranial pair) being the main nerve, having a specific branch for the so-called intercarotid nerve of Hering.

Material and Methods

We studied 24 carotid glomi from human cadavers of both sexes and with ages between 20 and 85. To obtain the samples, the same procedure was always followed; i.e., placing the head of the cadaver in hyperextension and making an incision between the retro-angulo-maxillary depression and the sterno-clavicular joint, separating the different muscle groups until the common carotid artery was localised, dissecting this down to its bifurcation.

The next step was to ligate below the primitive carotid and above the external and internal carotid vessels, obtaining the piece as done in medico-legal autopsies.

The material thus collected was washed with physiological saline, and fixed with 10% formaldehyde. The pieces where then dehydrated in increasing alcohol series and were embedded in polywax. Following this, 7 μm sections were obtained and stained with the Klüver-Barrera, Martins trichrome and Mayer-Eosin Hemalumbre techniques.

Results

The *glomus caroticum* is a complex structure to study because it differs widely in its location in the body; in most of our samples it was located at the carotid bifurcation, closer to the external vessel. However, the *adventitia* of this artery may also become unravelled and encompass the carotid body and participating from an external capsule (Fig. 1).

Surrounding this organ we observed a large amount of adipose tissue; an intense degree of vascularisation and abundant clusters of nerve fibres.

Inside the glomus we observed its peculiar structure; on observing it panoramically, we found cellular niches separated by septa of connective tissue (Fig. 2). At higher magnification, these niches were seen to contain cells (Figs. 3 and 4), which we classified in two types: type I, also called glomic, principal or neuroendocrine cells, could also be subdivided into those of type A (pale cells, globose, with spherical vesicles with a dense core) and those of type B (dark cells with long, fine prolongations, with pleomorphic vesicles with a dense or lucid structure)

The other type of cell was type II, these cells being for support. They were readily visualised because they encompassed from 2 to 6 type I cells, sometimes in such a pronounced way that they resembled a capsule for the pale and dark cells.

The most striking observation in the *glomus caroticum* was its rich vascularisation (Fig. 5) by arteries from the division of the carotid vessels, three types of differences being observed, depending on whether the sample was from young subjects, in which the glomi were very compact with little connective tissue between the cellular niches, such niches being close to one another.

As in all organs, the glomus is affected by age, in elderly people we observed that the collagen septa became progressively thicker, the cell niches being differentiated, and where we even saw phenomena of cellular degeneration, with a decreasing cellularity of these compartments surrounded by a sea of support tissue (Fig. 2). Between these two states, there was a third, observed in middle-aged people.

Finally, we observed the close relationship between the glomus and the nervous system since it was common to note neuronal contacts with glomic cells and also neurovascular contacts (Fig. 6), such that its deep innervation could be deduced; so much so, that not only were many vegetative cells seen interacting with the cells of the carotid body but also the existence of many paraneurons very similar to

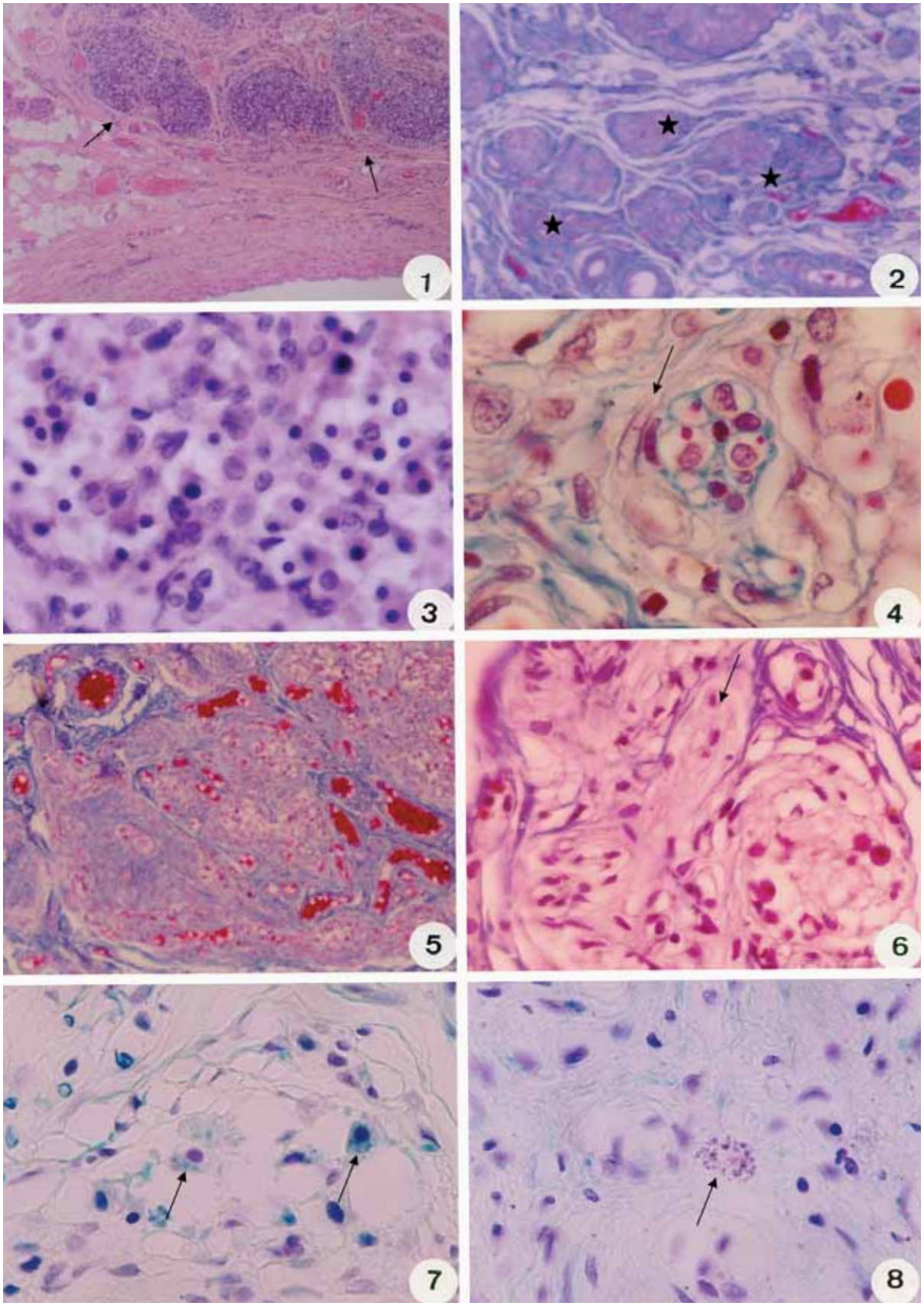

Fig. 1. Note the glomus (arrows) in a panoramic view in a young person (25 years old). H-E. x 4.
Fig. 2. Note denser and more compressed corpuscles (stars), surrounded by septa of connective tissue, that are intensely vascularised in an elderly person (84 years of age). Martins trichrome. x 4.
Figs. 3 and 4. Note variety of type 1 cells (neuroendocrine or principal) and as a subdivision pale, globose cells(arrow), together with dark cells, and type II (support) cells, with their lamellar prolongations encompassing groups of type I cells. Fig. 3: H-E. x 60; Fig. 4: Martins trichrome. x 60.
Fig. 5. Note strong degree of vascularisation shown up with the Martins technique. x 10.
Fig. 6. Nerve bundles of the Hering or De Castro nerve (arrow) forming neurovascular contacts. x 60.
Fig. 7. In the histological field, note the numerous neuroendocrine cells (arrows) stained with the Klüver-Barrera method. x 20.
Fig. 8. Note Nissl bodies in the "paraneurons" (arrow) stained with the techniques cited in Fig. 7, recently described in the human carotid body. x 20.

those of the nervous system, with their Nissl granules (Fig. 8) pointing to their activity in the vegetative nuclei at the level of the hypothalamus and hippocampus.

Discussion

This study carried out by us on 24 cadavers of different ages and of both sexes allows several conclusions to be drawn. One striking observation was the variability in location, size and versatility of the carotid body since although the usual situation is for the carotid body to be located at the bifurcation of the carotid vessels, closer to the external carotid, it may also do so behind the internal carotid vessel or the tunica adventitia may even unravel from one of these large arteries and include the carotid body.

The organ also changes with age and cellularity decreases progressively, its cellular niches separating, while -in contrast- the amount of connective tissue increases.

At the beginning of the study, the first aspect to draw our attention was the intense vascularisation of the organ by arteries coming from the division of the carotid vessels and its innervation by the glosopharyngeal, vagal and sympathetic nerves.

The carotid body is an atypical structure since apart from the histological described its functionality is debated. We conclude that the carotid sinus acts as a pressure receptor and the carotid body as a chemoreceptor corroborating the reports of Rees (1975) or North et al. (2001). Hence the importance of the sinus, above all interventionist radiology since it will be stimulated by the changes in pressure produced, for example, upon expanding the stent, causing such an intense vagal response that coma and death may ensue, as reported by Maynar-Moliner (1993).

In turn, the carotid body will be stimulated when the oxygen saturation curve of haemoglobin is displaced to the right; i.e., with situations of hypoxia, hypercapnea, acidosis, diphosphoglycerate, the release of oxygen to peripheral tissues being increased.

Using Klüver-Barrera stain, in the carotid body we observed paraneurons strongly resembling those found in the nervous system, with their Nissl granules, pointing to their close relationship with autonomic nuclei at the level of the hypothalamus and hippocampus, increasing the different types of neurons cited by González (1997) and González et al. (1994, 1997, 2002), who reported dopaminergic and cholinergic neurons.

Finally, we also observed large amounts of neurotransmitter inside the carotid body, also seen by the above authors; with the strong presence of dopamine since stimulation of the body is a source of extraction for the treatment of Parkinson's disease and other dyskinesias.

Along other lines, it should be noted that during embryogenesis, the paraganglia show a considerable degree of involution. Their neurons are immature and may be seen with the Klüver-Barrera stain distorting the colouring toward luxol-fast-blue in the $6^{th}/7^{th}$ weeks of foetal life, showing an aspect very similar to the sympathicogonias of the adrenal medulla.

Sex differences. No sex differences have been reported as regards the structure and ultrastructure of the paraganglia. However, differences in function and pathology may be seen. These differences become further pronounced at high altitudes and in cases of tumours. Regarding the latter circumstance, tumours are more frequent in women than in men, and according to Parry (1970) and Parry et al. (1982) the ratio may reach as high as 6/1.

Apoptosis. Along development, histological figures of apoptosis may be found, both at the level of the central nervous system and at peripheral level. This morphological phenomenon is seen in the nuclei of the cranial pairs and in vegetative structures.

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