Forensic Science and Criminology

Review Article

Forensic histopathology of the carotid body

Andrea Porzionato*, Maria M. Sfriso, Veronica Macchi, Martina Contran, Anna Rambaldo, Lucia Petrelli, and Raffaele De Caro

Department of Neuroscience, University of Padova, Padova, Italy

Abstract

The aim of the present study is to provide a review of main histopathological changes of the carotid body with potential forensic interest. Developmental changes in the carotid body have been reported in Sudden Infant Death Syndrome. SIDS victims frequently show alterations in respiratory regulation which may partly be ascribed to peripheral arterial chemoreceptors. Histopathological findings regarding cellular populations, connective components and inflammatory infiltrates have also been observed in opiate-related deaths. Better awareness about the structure of the carotid body and possible histopathological changes may be useful also for histopathological investigations in other cases of forensic relevance.

Introduction

The carotid body is the main arterial chemoreceptor directly involved in the control of respiratory and cardiocirculatory functions. It is located at the carotid bifurcation and consists of lobules separated by connective tissues, each one is organized in clusters of two different populations of cells (Figure 1). The first one is represented by type I (or chief) cells, in turn classified into light, dark and pyknotic cells. They are the real chemoreceptors which store and release neurotransmitters and neuromodulators, which are contained in dense-cored granules (Figure 1C-D). The second type is made by type II (or sustentacular) cells, which are considered supportive cells [1-3]. The carotid body is highly susceptible to reductions in pO_2 pressure and pH and to increases in pCO_2 pressure, in response of which rises the frequency and the volume of ventilation [4-6]. The sensory innervation of the carotid body is given by the carotid sinus nerve, a branch of the glossopharyngeal nerve. Moreover, the carotid body receives post-ganglionic sympathetic nerve fibers from the superior cervical ganglion, mainly acting on the microvascularization, and some parasympathetic fibers [6,7].

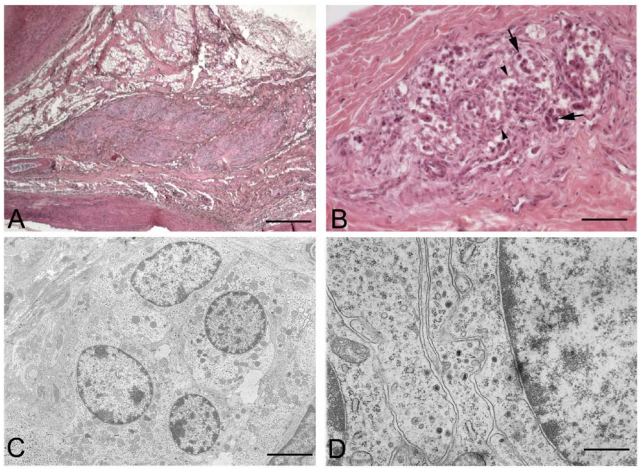

Figure 1. Normal structure of the carotid body. A: Carotid body of an adult human subject. B: Higher magnification of a lobule, showing the coexistence of roundish type I cells (arrows) and elongated type II cells (arrowheads). C-D: Electron micrographs of carotid body of 2-weeks-old rat showing a cluster of type I cells (C) and many dense-cored granules in the cytoplasms of adjacent type I cells (D). (Scale bars: A: 1 mm; B: 75 µm; C: 2.5 µm; D: 1 µm).

The carotid body may undergo structural and functional modifications in response to a series of environmental stimuli, some of which may show forensic implications. The carotid body, for instance, may be affected by chronic hypoxia, a condition which may involve humans living at high altitudes and therefore exposed to low atmospheric air pressure. The adaptive response mainly produces glomic hypertrophy due to increased number of type I cells. In particular, it has recently been highlighted that, as a consequence of a chronic hypoxic stimulus, type II cells may differentiate into precursor neural cells (also expressing nestin) which then give rise to mature glomus cells [8,9]. In this sense, type II cells are considered the stem cells of the carotid body [10].

The structure and function of the carotid body has also been reported to change along postnatal development and ageing. In particular, during the postnatal period, it has been demonstrated an increase of the total volume of the carotid body, accompanied by a progressive increment in vascularization [4,11]. Furthermore, ultrastructural studies revealed increased numbers of dense-core granules of type I cells and type I-type II cells synapses. The innervation of the carotid body has also been reported to develop in the postnatal period, due to an increase in afferent nerve endings and a decrease in the efferent ones [11].

The carotid body in sudden infant death syndrome

In contrast, defects in carotid body development or maturation have been associated with several neonatal respiratory deficiencies, such as sudden infant death or congenital central hypoventilation syndrome.

Correspondence to: Andrea Porzionato, Department of Neuroscience, University of Padova Via A Gabelli 65, 35127 Padova, Italy, Tel +39 049 8272327; Fax +39 049 8272328; E-mail: andrea.porzionato@unipd.it

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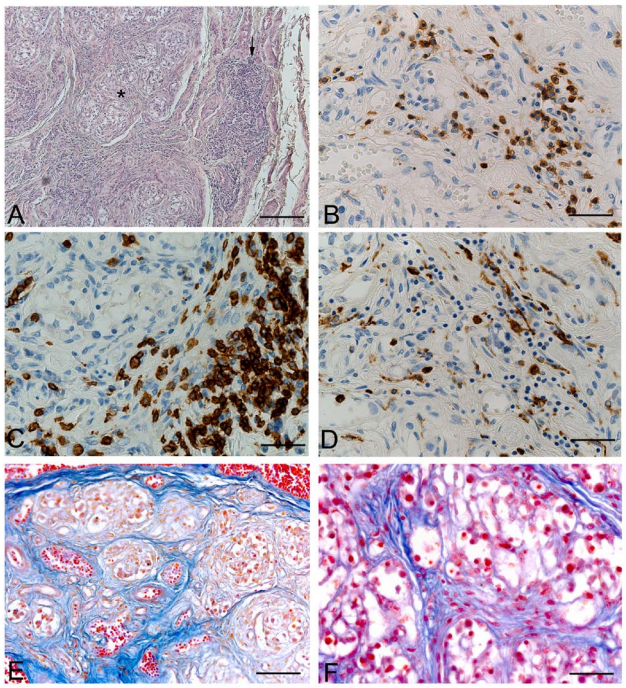

Figure 2. Carotid bodies of opiate-related deaths. A: Chronic carotid glomitis, characterised by an inflammatory aggregate (arrow) partially infiltrating a glomic lobule (star) (H.E.). B-D: Carotid body sections immunohistochemically stained with anti-CD45 (B), -CD8 (C), and -CD68 (D), showing inflammatory aggregates mainly composed of CD8-positive cytotoxic lymphocytes with macrophagic component. E-F: Increased interlobular and intralobular connective components of carotid bodies of opiate-related deaths. (Scale bars: A: 150 μm; B-D, F: 37.5 μm; E: 75 μm).

Hypotheses of alteration of reflexes triggered by peripheral arterial chemoreceptors have also been reported for Sudden Infant Death Syndrome (SIDS), a condition which is frequently put in differential diagnosis with homicide or accidental death [4,5,12]. It has been evidenced, for instance, that the period of postnatal maturation of the carotid body seems to correspond with the age range in which the risk of SIDS is highest [13,14]. Moreover, a series of cytochemical findings have been reported in the carotid bodies of SIDS victims [4,5,15].

The Sudden infant death syndrome (SIDS) is the sudden unexpected death of infants under 1 year of age, which remains unexplained after a thorough investigation, including performance of a complete autopsy and review of the circumstances of death and the clinical history [16]. Since the carotid body plays a pivotal role in the control of cardiorespiratory functions, prolonged sleep apnea, excessive periodic breathing and reduced hyperventilatory activity under hypoxic conditions (conditions increasing the risk of SIDS) could be ascribable to defective carotid body development. In literature, animal experimental studies have reported that carotid body denervation in the first postnatal period may cause the alteration of rhythmic ventilation and possibly unexpected deaths [17].

From a morphological point of view, conflicting observations have been reported about possible increases or decreases in the volume of the carotid body of SIDS victims [18,19]. Higher percentages of sustentacular and progenitor cells have been reported by other authors [20-22]. Besides, a prominent reduction or absence of dense-cored granules has been highlighted with ultrastructure analyses [21]. As it regards the content of various neurotransmitters, some reports showed conflicting results. Perrin et al. (1984) [23] reported ten- and three-fold higher concentrations of dopamine and noradrenaline, respectively, in SIDS carotid bodies but these findings were not confirmed by another research group [24].

Histopathology of carotid body in opiate-related deaths

Ageing is another situation in which the carotid body undergoes a series of structural and functional changes. These alterations include increase in interlobular and intralobular connective tissue and in type II cells, together with presence of inflammatory infiltrates [25,26]. Similar modifications of the carotid body structure have been described also in some clinical pathologies. For example, histological analyses demonstrated a consistent enlargement of the glomic lobules due to high proliferation of type II cells resulting in an increase in total volume of the carotid body in subjects affected by cardiac hypertrophy. These hyperplastic effect has been also observed in other pathologies like bronchial asthma, chronic bronchitis and emphysema [27].

In a forensic context, particular attention has been put by our group to the histopathological changes of the carotid body in opiate addiction [6,7,25,26]. Morphometric analyses have demonstrated an increase in the total volume of the carotid body in opiate-related deaths with respect to age-matched controls. Moreover, structural changes similar to age-related changes have also been seen, *i.e.,* increases in interlobular and intralobular connective tissue, together with increased number of type II cells. These changes have been ascribed to heroin-dependent progressive arteriosclerosis of glomic arteries [24]. The above morphometric analyses also revealed histopathologic alterations specific of opiate-addiction and not present in ageing, i.e., decreased percentage of light cells. Apart from increased content in connective tissue, the disposition and complexity of the connective components have also been recently evaluated with reference to novel image analyses based on analysis of dispersion (Morisita's index), gray level co-occurrence matrix (entropy, angular second moment, variance, correlation) and fractal (fractal dimension, lacunarity) parameters. Significant changes were found in all the above morphometric parameters with respect to age-matched controls, indicating higher complexity and irregularity of the connective tissue disposition. It was also intriguing that carotid bodies of opiate-related deaths showed higher fractal dimension and lower lacunarity also with respect to aged cases, confirming a branching of the connective components even more irregular than in aging [6].

Apart from the above histopathological changes in the parenchymal and connective components of the carotid body, we also demonstrated in opiate-addiction an higher incidence of chronic carotid glomitis, a pathological condition defined by the presence of lympho-monocyte aggregates throughout the carotid body. Such alterations have been previously reported only in aged persons and furtherly support the hypothesis of degenerative mechanisms in the carotid body of opiate addicted. In particular, in heroin addict subjects, chronic carotid glomitis could arise as inflammatory response against infective agents, heroin itself and other drugs, resulting in modification of the excitability of the glomus cells as well as their survival, proliferation and differentiation [5,7]. Inflammatory infiltrates resulted to be preferentially T cells (CD3+), in particular CD8-positive T suppressor/cytotoxic cells even if T helper lymphocytes, Natural killer cells and macrophages have also been detected [7] (Figure 2).

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