

Mast cells in the human carotid body

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SUMMARY Mast cell counts were carried out on sections of human carotid bodies from 39 subjects showing one of four stages of histological change associated with aging, and in five subjects showing different forms of histopathology in the carotid body associated with disease. There was no relation between mast cell density and age or the histological changes associated with aging of glomic tissue. The normal range of mast cell density calculated in terms of the 80% confidence limits was 18.5 to 67.5/mm². In three middle aged subjects with carotid bodies of normal histological appearance there was an abnormally high density of 83 to 96/mm². In two elderly subjects showing age changes of fibrosis and accumulation of lymphocytes there was an abnormally low density of 12/mm² or less. Mast cell density was not related to different types of carotid body hyperplasia. The mast cells were essentially stromal in location, usually closely applied to the walls of small glomic blood vessels, and were rarely found in intimate association with glomic chief cells. This suggests that mast cells are not directly concerned with the functions of glomic cells but does not preclude the possibility that they may have some effect on regulating glomic blood vessels and thus participate in the distribution of blood supply within the carotid body.

It is becoming clear that a range of histological appearances may present in carotid bodies studied routinely at necropsy. Some of these may be ascribed to normal age change; others are abnormal and found in diseases usually associated with either chronic hypoxaemia or systemic hypertension. Mast cells are common in the human carotid body, and we thought it would be of interest to see if mast cell density in the organ is related to age and the consequent histological changes in glomic tissue, or to different types of carotid body hyperplasia.

Material and methods

Forty four cases were studied and divided into eight groups based on the histological appearance of the glomic tissue.

GROUP 1

The group comprised 11 subjects, ranging in age from 16 to 59 years, who were free of cardiopulmonary disease and who showed no age change in the carotid bodies. The normal glomic tissue consisted of clusters comprised of inner cores of chief (type I) cells with a covering of sustentacular (type II) cells. Type I cells contained catecholamine with clear oval nuclei and copious faintly eosinophilic cytoplasm; type II cells

resembling Schwann cells, were elongated and closely associated with nerve axons.

GROUP 2

This comprised four subjects, ranging in age from 20 to 40 years, who were free of cardiopulmonary disease. The carotid bodies showed undue prominence of the dark variant of chief cells,¹ commonly found in the young.²

GROUP 3

This comprised 11 subjects, ranging in age from 68 to 93 years who were free of cardiopulmonary disease. The carotid bodies showed undue prominence of the sustentacular cells,¹ commonly found in the elderly as a normal age change.²

GROUP 4

This group comprised 13 subjects, mostly in the age range of 70 to 100 years, but with three exceptions ranging in age from 46 to 62 years. They were all free of cardiopulmonary disease. The carotid bodies showed fibrosis with diffuse or focal collections of lymphocytes and there was fibrous occlusion of branches of glomic arteries. Such normal age changes are commonly found in the elderly and aged.²

GROUP 5

This group comprised two subjects, aged 67 and

74 years. The first had right ventricular hypertrophy and chronic hypoxaemia complicating panacinar emphysema. The second had left ventricular hypertrophy secondary to systemic hypertension. Both showed carotid body hyperplasia with a proliferation of sustentacular cells compressing the surrounded clusters of chief cells; both met the criteria for this condition, which we have set out elsewhere.^{3,4}

GROUP 6

This comprised one subject, aged 61 years, with a congenital coarctation of the aorta, who showed gross proliferation of sustentacular cells with compression, distortion, and ablation of the cores of chief cells.⁵

GROUP 7

This contained only one subject, aged 62 years, with a ventricular septal defect and late reversal of shunt, leading to acute hypoxaemia and early proliferation of dark cells in the carotid bodies.⁶

GROUP 8

This also comprised one subject, aged 80 years, who had systemic hypertension, enlargement of the carotid bodies, and pronounced focal hyperplasia of the dark variant of chief cells superimposed on sustentacular cell hyperplasia.⁷

The carotid bodies were dissected out at necropsy and fixed in 10% formalin. Paraffin sections 5 μm in thickness were stained with a solution of 2% toluidine blue in 5% aluminium sulphate to show mast cells. We used this technique because Heath in 1961 showed that by preparing certain basic dyes, such as the thiazines toluidine blue and methylene blue in aluminium sulphate, a highly specific stain for the detection of sulphated mucopolysaccharides in tissue sections could be produced.⁸ Using this method mast cell granules stain deeply metachromatically. We selected formalin as this is the fixative used routinely for post mortem histology. In human tissues, in contrast to those of the rat, some of the metachromatic granules of the mast cell may dissolve out in such aqueous fixatives, especially after prolonged immersion. Because of this, we have previously used methanol fixation for human tissue when we wished to determine with precision absolute mast cell counts.⁹ In the present study, however, we wanted to establish, for purposes of comparison, base lines for mast cell counts in tissues processed routinely with other organs for post mortem histology.

The sections of carotid body were systemically scanned and mast cell counts made using an eyepiece graticule that had been calibrated with a stage micrometer. The numbers of mast cells present in each of the 35 squares in the graticule were counted wherever possible and the density of mast cells per square millimetre of the section of carotid body was

calculated. The area of one of the squares was 0.016 mm^2 . The number of squares counted in individual cases ranged from 26 to 546, the mean number being 224. Hence the mean area studied ranged from 0.42 to 8.7 mm^2 , the mean being 3.58 mm^2 . Serial scanning of the section was carried out only within the borders of the carotid body delineated by the curved margins of the lobules of glomic tissue. Stromal tissue contained within the limits of the carotid body was included in the counts.

Results

QUANTITATIVE

Fig 1 shows the mast cell counts; the mast cell density is related to age. Mast cells were ubiquitous in the human carotid body. In most cases the numbers present ranged between 18.5 and 67.5/ mm^2 calculated in terms of the 80% confidence limits. The mast cell density was unrelated to sex or to age, there being as many mast cells in the carotid bodies of a centenarian who died from bronchopneumonia as in a boy of 16 years dying from epilepsy (fig 1). The density was unrelated to histological changes in the carotid body, whether they were normal and due to age change or abnormal as in one of the pathological conditions of glomic tissue described above (fig 1). In all these pathological conditions the mast cell density fell into the range found in normal subjects.

Unusually large numbers of mast cells, between 83 and 96/ mm^2 , occurred in the carotid bodies of four subjects. In three of them the carotid bodies showed a normal histological appearance (the subjects were between 50 and 58 years of age). An overall clinical and pathological examination of these cases with high mast cell counts did not show any features in common to suggest a basis for the large numbers of these cells in the carotid body. Counts were not carried out on other tissues to establish if they also contained large numbers of mast cells. Unusually small numbers of mast cells, 12/ mm^2 or less, were found in the carotid bodies of three elderly subjects, in two of whom the fibrosis and lymphocytic accumulation associated with old age had occurred.

Mast cell density in the carotid body was not related to the underlying disease present or to the cause of death. It was also not related to the histological appearance of the carotid body. This was exemplified by three women aged 79, 80, and 93 years, all of whom were dying from bronchopneumonia with no other pathology, and all of whom had carotid bodies of normal combined weight (15.3, 16.3, and 13.1 mg, respectively) and showed sustentacular cell proliferation. In spite of these similarities the three showed remarkably different mast cell densities in the carotid body of 34, 83, and 8/ mm^2 , respectively.

Mast cells in the human carotid body

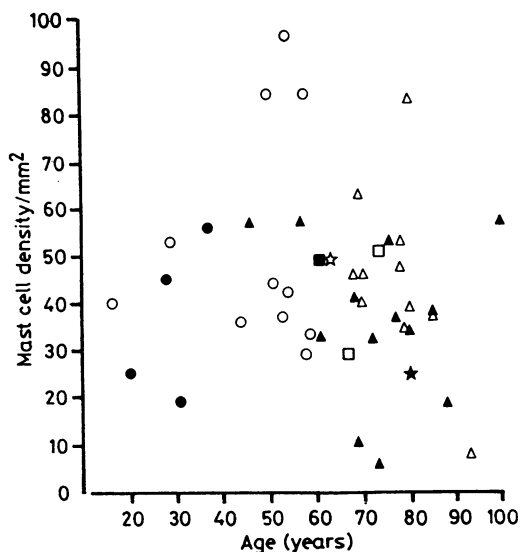


Fig 1 Relation between mast cell density (MC/mm²), age, and histological appearance in human carotid body. Eight symbols used refer to four stages of age change and four different types of histopathological change. Each subject is indicated by symbol referring to histological changes found in carotid bodies in previous studies. Basic histological pattern (group 1) ○; dark cell prominence (group 2) ●; sustentacular cell proliferation (group 3) ▲; fibrosis (group 4) ▲; sustentacular cell hyperplasia in hypoxic cor pulmonale and systemic hypertension (group 5) □; sustentacular cell hyperplasia in coarctation of the aorta (group 6) ■; dark cell prominence in ventricular septal defect (group 7) ☆; dark cell hyperplasia in systemic hypertension (group 8) ★.

QUALITATIVE

Even in those cases in which many mast cells were present, in the main they were confined to the interlobular connective tissue where they were commonly closely associated with blood vessels (fig 2). Practically no mast cells were found within the lobules of glomic cells. The few that were present were not associated within the central cores of chief cells but were closely applied to the covering shell of sustentacular cells (fig 3).

Discussion

Our findings confirm the observations of previous authors^{10 11} that mast cells are common in the carotid bodies. Indeed, we found them to be present constantly and without exception, and in four cases there was a high mast cell density exceeding 83/mm². Mast cells are also common in the carotid bodies of other mammals; their numbers vary in different species, being particularly common in cattle.¹² Although mast cells are plentiful in human carotid bodies, they

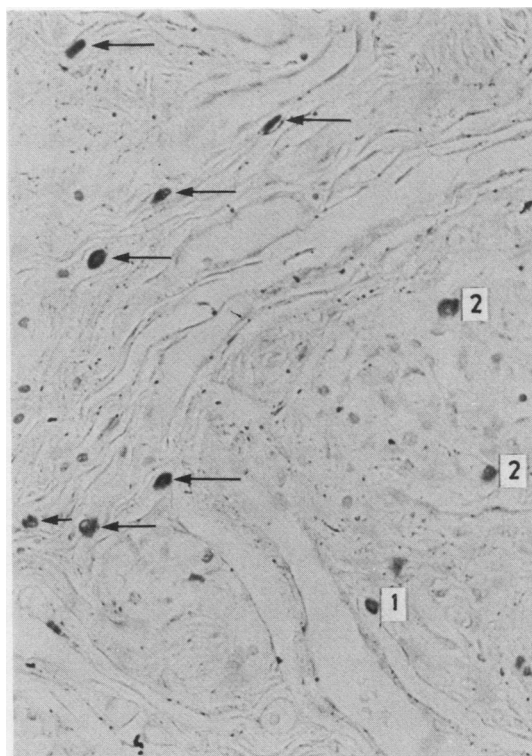


Fig 2 Section of normal carotid body from man of 54 years who died in a road traffic accident, showing characteristic distribution of the mast cells. Most (arrowed) lie in stromal connective tissues between lobules of glomic tissue. One mast cell (1) is seen closely adjacent to wall of blood vessel; two others (2) lie at edge of glomic lobule where they are situated at junction of chief (type I) and sustentacular (type II) cells. (Toluidine blue) × 375.

are largely confined to the interlobular connective tissues where they are often closely applied around small blood vessels (fig 2). A few are found closer to the glomic tissue itself, but even here they tend to be associated with sustentacular (type II) cells. They are not intimately associated with the chief (type I) cells of the central cores of glomic clusters (fig 3). Such findings suggest that mast cells are not directly concerned with the functions of glomic cells themselves, although this does not preclude the possibility that they may play a part in the regulation of the small glomic blood vessels and hence with the distribution of blood supply within the carotid bodies.

There is no evidence to show that mast cell density in the human carotid body is related to age or to the different histological appearances that develop with increasing years. Our study has shown, in fact, that throughout life the mast cell density remains constant—in the range of about 20–60 mast cells/mm², and pre-

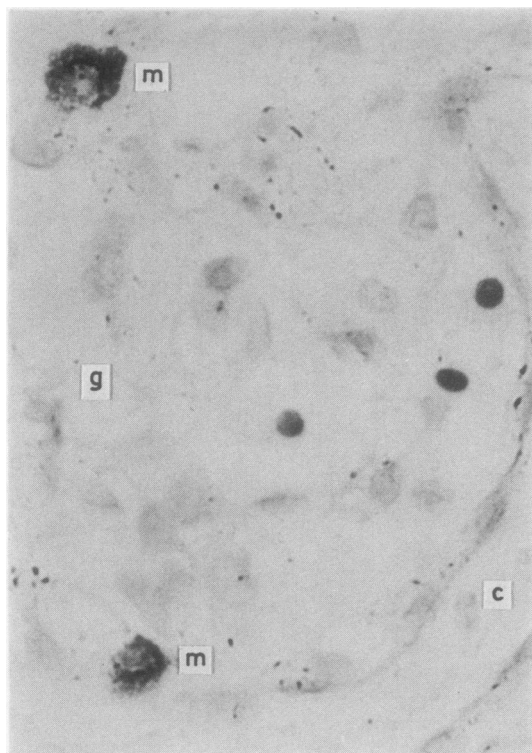


Fig 3 Part of preceding figure at higher magnification to show two mast cells (m) at edge of lobule of glomic tissue, (g) where they lie at junction of chief and sustentacular cells. Blood capillary (c) is seen skirting lobule. (Toluidine blue) $\times 1280$.

dominantly in the narrower range of 30–60/mm². A minority of subjects in middle age with histologically normal carotid bodies in our study showed a profusion of mast cells to reach a density between 80 and 100/mm². In contrast, with the onset of old age a minority of subjects showed a substantial fall in mast cell density to less than 20/mm², which was associated with the progression of age change fibrosis and the accumulation of lymphocytes in the substance of the carotid body.

Mast cell density does not seem to be related to the various forms of histopathology that may occur in the

carotid body. These include the sustentacular cell hyperplasia, which occurs in chronic obstructive lung disease and systemic hypertension,^{3,4} or in coarctation of the aorta,⁵ or the dark cell proliferation, which may become superimposed on it.⁷ We found that in these different types of histopathology the mast cell density remained in the normal range of 20–60/mm². This strongly suggests that they do not have a specific role in the pathology of glomic parenchyma.

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