



EDITORIAL COMMENT

Mast cells: Promoters of myocardial fibrosis in hypertensive heart disease?



Mastócitos: promotores da fibrose miocárdica na doença hipertensiva cardíaca?

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Myocardial fibrosis – perivascular, interstitial or replacement (scar)¹ – is the endpoint of various pathological settings, often leading to dismal outcomes, including heart failure, arrhythmias and sudden death. In hypertensive heart disease, patterns of perivascular and interstitial myocardial fibrosis are common and may easily be shown and graded, in formalin-fixed samples, with histochemical stains such as Masson trichrome, elastic Van Gieson, or picosirius red.²

Experimental and human studies¹ have demonstrated that myocardial fibrosis is the result of various promoters, among which are mast cells.^{3–10} Discovered and named by the Nobel prize-winning German physician Paul Ehrlich in 1878,³ mast cells are immune cells derived from bone marrow precursors and resident in tissues. They are usually classified as typical if located in connective tissue such as the myocardium, or atypical if located elsewhere, and as MCT if their granules contain tryptase, MCC if they contain chymase or MCTC if they contain both proteases.^{3,4} Anti-chymase or anti-tryptase antibodies are used for immunohistochemical identification of mast cells in situ.⁹ Mast cells are also known to have a wide range of mediators (histamine, cytokines, growth factors and vasoactive agents) that affect tissue remodeling as pro- or anti-fibrotic

agents.^{4–7} The effect of cardiac mast cells on myocardial fibrosis may result both from degranulation and from de novo secretion of mediators common to other cells, including tumor necrosis factor alpha and beta, interleukin 4 and platelet-derived growth factor, as well as from the roles of chymase and/or tryptase.¹ The fibrogenic action of chymase may follow two pathways: the formation of angiotensin II through activation of the angiotensin-converting enzyme-independent chymase pathway, and activation of matrix metalloproteinases.^{1,4,7} Tryptase activates fibroblast proliferation and collagen I synthesis, mainly by activating protease-activated receptor-2.¹

There is controversy concerning the pro-fibrotic and anti-fibrotic phenotypes of mast cells: whether the phenotypes can switch depending on the environment and genetics, and whether fibrotic tissue can regress as a consequence of a switch to the anti-fibrotic version; what are the key points of therapeutic intervention; and other questions.

Some authors point out limitations in research into human cardiac fibrosis and its relation to mast cells, due both to the characteristics of the samples used, whether obtained from biopsy or autopsy, and to the difficulty in obtaining normal control tissue.⁷ Myocardial biopsies are limited in their size and location, although if morphological alterations are identified and appropriate complementary techniques are applied, useful data may be obtained. Furthermore, despite the difficulties in preserving autopsy material, if basic preservative measures are routinely applied, it may provide large quantities of disease samples and normal con-

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trols, as exemplified by the study by Juliano et al. published in this issue of the *Journal*.⁹

Conflicts of interest

The author has no conflicts of interest to declare.

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