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Perspective

Immunity Participation in the Hypertension Pathology

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Research that have led to immune system participation in the pathology of Hypertension are relatively new.

Association between HTA and renal disease was reported on 1879 [2] and the first description of autoimmunity as producing morbid situation appeared on 1904 when the antibodies description causing hemolytic anemia in the crio hemoglobin paroxysmic [2] where the end of the stated situation by Paul Erlich who established that the organism didn't hurt himself (horror autotoxicus) [3].

Pioneer observations about participation in experimental models in HTA started to re appear at the end of the last century [4], however it has been in the last few decades when an increasingly number of researches [5] have led to stablish in an unmistakable manner the critical role of autoimmunity in the complex etic pathogenic mechanism which results in the elevation of HTA [6-8].

Inflammation as manifestation of the immune reactivity of hypertension arterial

Inflammation as a demonstration of the immune reactivity of Hypertension Arterial. It is very well stablished that the kidneys inflammation, in the arterial wall and the central nervous system helps development and increases severity of the hypertension.

The potential hypertensive of the inflammation in this target organs has been demonstrated in the studies in which the inflammation has been reduced with a range of immunosuppressors treatments which result in the prevention or improvement of hypertension in practically all of the hypertense ceps of mice. Even more, the experimental induction of the renal inflammation is associated with the increase of the arterial hypertension [7].

Renal inflammation induces hypertension as a result of the reduction of the natriuresis by pressure, which is the response of the renal adaptation to a sodium positive balance. The reduction of the natriuretic response by the increase of the pressure of renal perfusion which is caused by the tubulointerstitial inflammation of the release of oxidative stress with reduce of nitric oxide, increase of the angiotensin activity and the effects profibrotic with losses peritubular capillary. In the arterial wall, inflammation increases the local produce of reactive species of oxygen, increases the vasoconstrictor tone and suppresses the endothelial vasodilatation response. In the central nervous system, the inflammation of the areas in the third ventriculus helps lymphocyte migration to the arterial wall (originator of the vascular inflammation) and stimulates the activity of the sympathetic nervous system which carries not only the increase of the vasoconstrictor tone, cardiac expense and the reabsorption tubular of sodium, but also, induces the stimulation of various aspects of the immune system.

Lymphocytes participation in the pathology of hypertension arterial

Lymphocytes paper in the pathology of hypertension was initially found in pioneer experiments of Svendsen [4], who demonstrated that the malnourished mouse didn't develop hypertension depending of salt in the model DOCA (deoxycorticosterone). Hypertension de-

velopment capacity in this phase of the experimental model was recovered with the lymphocytes transfer. Guzik., *et al*. [10] demonstrated that induced hypertension by angiotensin II was surprised in mice Rag 1 -/-, lacking lymphocytes, and that the response to angiotensin was restored with the adoptive transfer of lymphocytes T. same resistance to hypertension was demonstrated in mice Dahl nulls for Rag 1 [11]. Lymphocytes B paper was demonstrated by Chan., *et al*. [12] who used mice BAFFR -/- (lacking B cell activation factor-receiver).

Inherent immunity, acquired and autoimmunity in hypertension arterial

Inherited immunity acquired immunity and autoimmunity have a real important role in hypertension arterial. There is evidence that the activation of inflammasome NLPR3 in induced hypertension by salt [13] and in other hypertension experimental types. In hypertension patients has been evidence demonstrated of activation of inherited immunity, including increase of the receptors toll-like (TLR) 2 and 4 in monocytes of peripheral blood [14] and increase in plasmatic levels of IL-1Beta and of IL-18 [15,16].

All aspects of immunity acquired have been demonstrated in experimental types of hypertension, including incorporated antigens in cells presenting antigen *in situ* and circulating [17], coestimulation [18] and cell T release of immune memory [19]. In patients with essential hypertension have been detected antibodies directed to antigens of pathological potential [20,21].

Even the hypertensive patient doesn't have hypernatremia, increase of concentration of sodium inside the range do not exceed physiological levels is able to polarized T cell indifferent towards generation of IL-17 cells through activation of SGK1 (serum and glucocorticoid regulated kinase 1) [22,23]. Generation of IL-17 helps autoimmunity, inflammation and over regulated cotrasporter Na-K-2CL.

The importance of IL-17 generation by increase of the sodium concentration must be considered in the context of increase levels chronic in the concentration of sodium (≥3 mMol/L) which stimulate the central nervous system and increase the arterial pressure [25].

On the other hand, overload sodium causes high concentration in subcutaneous tissue led to glycosaminoglycans.

This tissular increase of sodium, without systemic repercussion, induces stimulation of TonEBP (tonicity-responsive enhancer binding protein) which increases infiltration of macrophages with generation of VEGF-C (vascular endothelial growth factor-C) and increase in the subcutaneous lymphatic network [26].

Subcutaneous levels of sodium in these conditions are inside range which could help generate IL-17 [22,23].

Autoantigens which evidence base experimental are being object in human studies are modified proteins by generation of isoketales which result in peroxidation of lipids [17] and stress proteins 70 (HSP70) [27]. Participation of the last one can be induced by over expression and mobilization to extracellular space or make its protection function and antigen transport to major complex of histocompatibility of cells with antigen [28].

A look towards the future

Possibility of eliminate or avoid lead elements of the immune reactivity with the objective of prevent or treat hypertension arterial is subject to identification of factors that most likely are multiple and variable in different habitats, groups of different age and different sex.

Potential antigen assessment and its generation pathologist and physiologist are a great part of current research about immune pathology of hypertension and they promise results in the near future.

On the other hand, possibility of an immunosuppressor being a valid therapeutic option in resistant severe hypertension to treatment needs to be explored.

Various studies have shown high levels of cytosines in hypertensive patients, and recently Chen., *et al*. [29] assessed a reasonable number of patients with renal insufficiency who had resistant hypertension and they found an important increase of TNF α and IL-6 and reduction of TGF β levels. In studies of 6 - 7 years following those patients they had an increase in mortality and cardiovascular diseases.

Recently, it has been highlighted in an editorial [30], these results open the option to use treatment of anti-IL-6 o anti- TNF α.

There is a report of a short treatment course with mycophenolate mofetil which resulted in change of severe hypertension resistant to treatment in a patient with easy control [31].

There is the need of meticulous studies which can clarify the clinical characteristics and the values of cytosines which can allow to predict a potential good result of the immunosuppression in transitory essential hypertension.

Conflict of Interest

None.

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