Immunopathogenesis of psoriasis

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Abstract: Psoriasis is a common inflammatory disease affecting 1% of the Brazilian population. Th17 and Th1 cells are involved with the immunopathogenesis of psoriasis. In this article it is discussed the interaction between the innate immunity (especially dendritic cells and keratinocytes) and adaptive immunity (T lymphocytes) in the pathogenesis of psoriasis.

Keywords: Allergy and immunology; Cytokines; T-lymphocytes; Psoriasis; Psoriasis/etiology

Resumo: A psoriase é doença inflamatória comum, afetando cerca de 1% da população brasileira. Os linfócito T auxiliares (Th17 e Th1) estão envolvidos na imunopatogênese da psoriase. Neste artigo é discutida a interação entre a imunidade inata (especialmente células dendríticas e queratinócitos) e adquirida (linfócitos T) na patogênese da psoriase.

Palavras-chave: Alergia e imunologia; Citocinas; Linfócitos T; Psoriase; Psoriase/etologia

IMMUNOPATHOGENESIS OF PSORIASIS

The immunopathogenesis of psoriasis is complex and involves alterations in the innate immunologic system (keratinocytes, dendritic cells – DC, histiocytes, neutrocytes, mastocytes, endothelial cells) and acquired (T lymphocytes).

Initially there is activation of the cells of the innate immunologic system (IIS) when activated produce growth factors, cytokines and chemokines that act upon the cells of the acquired immunologic system (AIS) and vice-versa.

Mechanically trauma, e.g., can activate keratinocytes, that begin to release cytokines, (IL-1 and the TNF-α) and proteins of thermic shock. These substances activate the DCs (Langerhans cell - LC – and resident DCs) in the epidermis and dermis. The linkage of antigens of infectious agents to the toll like receptors in the DCs and keratinocytes may also lead to the activation of these cells. The DCs and the activated keratinocytes produce inumerous chemokines, cytokines and growth factors.

Once activated, the DC processes an antigen (environmental or endogenous, not defined yet) and migrates to the regional where the antigen is presented to the T lymphocytes (TL). In order to activate the TL it is necessary the linkage of the antigen (coupled to the main molecule of histocompatibility on the membrane of DC) to the receptor of the TL, besides the linkage of proteins of the plasmatic membrane of DC (ICAM-1; LFA-3; CD80/CD86) to the proteins of the membrane of TL (respectively LFA-1; CD2; CD28). Therefore, to occur the lymphocyte activation there should be established an “immunologic synapse” among proteins of the membrane of the cell that presents the antigen (APC) and of the TL.

The activated TL of patients suffering from psoriasis differ preferentially in LTCD4+ type1 (LT1; producers of INF-γ, TNF-α and IL-2) and type 17 (LT17; producers of IL-17, TNF-α, IL-6; IL-22) and LTCD8+ type 1 (L1; producers of TNF-α, INF-γ, perforins and granzyme B).

The activated TL migrate to the skin through the linkage of molecules of adhesion expressed in its plasmatic membrane (CLA and LFA-1) to the molecules of adhesion present in the membrane of the activated cutaneous endothelial cell (E-selectina and...
ICAM-1). The LTc1 concentrate themselves in the epidermis and the TLh in the dermis.¹,⁵

In the dermis the TLh meets and interacts with the DCs and histiocytes forming new “immunologic synapses”. The interaction among these cells leads to the production of inumerous cytokines that keep and amplify the inflammatory process.¹,³

The activated DCs and histiocytes produce IL-12 and IL-23.¹ The IL-12 favours the proliferation of the LTh1 and the IL-23 of the LTh17.¹,³ The proliferation of Th17 and Th1 in psoriasis is also attributed to the decrease of regulatory TL (responsible for the suppression of the activation of such lymphocytes).¹,³,⁶

In psoriasis the dermal DCs found in greater numbers are of the myeloid type (DC11c+).¹,⁵ These cells function like APC to the TLs and also as inflammatory cells (DCi), great producers of IL-20, synthetase inducer of the production of nitric oxide (iNOS), as well as of IL-23 and TNF-α.¹,³ The IL-20 stimulates the proliferation of keratinocytes and the nitric oxide the vasodilatation. The IL-23, favours the proliferation of the LTh17 and consequent production of IL22 and IL-6 (that stimulates the proliferation of the keratinocytes), besides of IL-17 and TNF-γ. The IL-17 stimulates the keratinocyte to produce defensins (proteins that impede the infection of the lesions) and IL-8. The TNF-γ stimulates in the keratinocyte the production of IL-8 and IP-10 (chemotatic proteins to neutrocytes and LT respectively), of IL-1 and of TNF-α itself, apart from growth factors that favour the angiogenesis. Therefore, cytokines Th17 stimulate the keratinocytes to proliferate and to produce inumerous inflammatory proteins (Pic.1).¹,³,⁵,⁷,⁸

The proliferation of LTh1 induced by IL-12 leads to the production of TNF-α and INF-γ. The INF-γ also stimulates the production of IL-12, IL-8, IP-10, IL-23, defensins and iNOS by the keratinocytes and DC.⁷,⁸

Interferons, TNFs and IL-20 are activators of transcription factors (STAT-1, STAT-3 and nuclear factor kB) that, in their turn, control various groups of genes that codify various inflammatory mediators in psoriasis.¹,³,⁵

Recent studies in patients treated with etanercept reveal that the TNF modulates the activation and maturation of the DCs in psoriasis.⁷,⁸ The blocking of TNF by this therapeutic agent decreases the activation and maturation of the DCs and consequently inhibits the activation of the lymphocytes and the production of cytokines, chemokines and growth factors by LT, DC keratinocytes.⁷,⁸

It is worth mentioning that the IL-6, the TNF-α and the IL-17 are cytokines involved in the pathogenesis of the atherosclerosis, what justifies a higher incidence of cardiovascular diseases and of the metabolic syndrome in patients with psoriasis.²,¹⁰

Concluding this study, the knowledge of the main alterations between the SII and the SIA is essential for a better understanding of the immunopathogenesis of psoriasis, as well as of the mechanisms of action of the immunosuppressive and biological medications used in its treatment.
REFERENCES

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