GRANULOMATOUS MYCOSIS FUNGOIDES: THE ROLE OF TISSUE MACROPHAGES

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Four cases of granulomatous mycosis fungoides (GMF) were analyzed by histological, immunohistochemical and molecular methods.
Patients were adult males 18 to 40 years old presenting several plaques and nodules. Complete haematological staging was negative at presentation. The patient was treated by polychemotherapy and radiotherapy. Two patients developed systemic CD30+ lymphoma or disseminated pleomorphic T-cell lymphoma and died of disease. Skin biopsies showed a dermal infiltrate formed by isolated multinucleated giant cells or sarcoid-like granulomas surrounded by atypical lymphocytes, forming rosette-like features and showing focal epidermotropism. Tumor cells were CD2+, CD3+, CD4+, CD5-, CD7-, CD45RO+, IL-17-. Multinucleated giant cells were interleukin (IL)-17+, interferon (IFN)-γ+ and tumour necrosis factor (TNF)-α+, CD68-KP-1+ and CD163+. Interestingly, neoplastic cells rosetting around and located into the multinucleated giant cells, as the epidermotropic lymphocytes, lost the CD5 marker and were proliferating (Ki-67+), while macrophages were hyperplastic forming a nourse-like features. Molecular analysis revealed a T cell clone in all cases and in one case genotypic studies by microarrays CGH showed a loss of 5q33.1, only containing IL-17β and PCYOX1L genes. Recently, genetic alterations with reciprocal translocation t(3;9)(q12;p24) and trisomy of chromosome 8 have been reported in two cases of GSS, which may indicate predisposition to granuloma formation. In our case one of the 2 genes deleted is IL17B, involved in the regulation of IL-17 expression. Immunohistochemical stains showed that tumor lymphocytes do not express IL-17, but a strong expression of IL-17 was detected in the multinucleated giant cells. IL-17 has been reported in cutaneous T-cell lymphomas as a cytokine that represents an early event in the development of the inflammatory reaction within the tumour microenvironment, a process that may influence tumour phenotype and growth. Conclusion: Four cases of granulomatous CTCL was analyzed showing characteristic histopathologic, immunohistochemical and molecular features, the loss of IL-17-β could be considered to play a key role in granuloma formation and tumor microenvironment reaction.