Changes in human lymphocyte subpopulations in tonsils and regional lymph nodes of human head and neck squamous carcinoma compared to control lymph nodes

ABSTRACT

Human secondary lymphoid organs react with an increase in the proportion of B lymphocytes and a decrease in the number of CD45RA+ T cells (naive). In tonsils, this is due to chronic pathogen stimulation, whereas in lymph nodes draining head and neck carcinomas the reaction is prompted by surrounded tumors. During this process, secondary lymphoid organs develop secondary follicles with a special organization of T and B cells in consecutive layers, that are described here by confocal microscopy. This pattern of cellular distribution may suggest a model of cell migration into the secondary lymphoid follicles.

INTRODUCTION

Background Efficient interactions between T, B and antigen-presenting cells in T-dependent immune responses take place at the secondary lymphoid organs. T cells are located mainly in the paracortical zone, which includes the interfollicular regions. B cells are placed in small primary follicles in the cortex, which become secondary follicles or germinal centres (GCs) after antigenic stimulation. Most recent studies of the GC reaction focused either on B cells, centroblasts and centrocytes, or on follicular dentritic cells. It is known that T cells have a crucial role in the development of the GC reaction, mediated by both cellular contacts and humoral factors (interleukins). GC T cells express CD40L (CD154), a molecule which allows the interactions with CD40+ B-lymphocytes. High affinity B cells, selected by antigen retained in the surface of follicular dendritic cells (FDCs), become antibody producing plasma cells or memory B cells. This distinction is determined by the signals of the CD40/CD40L interaction and by the type of interleukins secreted by T cells. Non-selected B cells, however, die by apoptosis. The activation and generation of memory T cells in the secondary follicles of lymphoid tissues remain unclear, although much is known about these processes in B cells. Some authors have shown that, in mice, T cells migrating to follicles are also able to proliferate the developing GC. During the GC reaction, T cells become concentrated both, at and near the junction of the follicular mantle with the light zone. Some cells remain there after the end of the GC reaction. The origin, migration and role of intra-GC T cells in human follicles is not accurately known, as it is not possible to study the kinetic of the GC reaction in humans. This study compares control lymph nodes with human tonsils and tumour reactive lymph nodes from patients with head and neck's carcinomas. The identification and distribution of cells in these nodes has been achieved through the study of several markers and other membrane antigens. The markers used were CD69, which is a very early activation antigen, CD45RA, a marker mostly associated to virgin cells and CD45RO, a marker associated to memory cells. In addition to the differences between control and reactive lymph nodes, an interesting distribution of the B and T cells in several layers was found, when tissue sections were performed. These results suggest a speculative model of the cellular traffic into the GC, giving a crucial role to the T cells in the regulation of the GC reaction.

CONCLUSION

Conclusions Human control lymph nodes have a higher number of T

lymphocytes than tonsils or tumor reactive lymph nodes. These are mostly T cells with naive phenotype (CD45RA+). Histologically, control lymph nodes only show primary lymph follicles. Tonsils and tumor reactive lymph nodes display an increase in the number of B cells and a decrease in the number of CD45RA+ T lymphocytes. Studies in tissue sections show the formation of secondary lymphoid follicles with a very organized structure constituted by alternative layers of subpopulations of B and T lymphocytes: CD19bright B cell zone, CD69bright CD45RO+ intra- GC T cell layer, a follicular mantle B cell layer and an external T cell zone. The characteristics of mantle B cells are nearly identical to the primary follicle B cells. We propose a hypothetical model of lymphocyte migration in the GC.