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ABH Histo-Blood Group Antigens are Differentially Expressed in Involuted Human Thymus

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Although ABH histo-blood group antigens (HBGA) have a wide tissue distribution, their role in pathological conditions is still disputable. The present work examines the expression pattern of ABH HBGA in the process of aging of human thymus. Glands from senile and young individuals were studied by routine histology and immunohistochemistry. Involuted thymus exhibited scattered epithelial cells (EC), positive for HBGA. Endothelial cells of blood vessels and erythrocytes were always immunopositive. Only single lymphocytes possessed HBGA. The epithelial framework reorganization during senile thymus involution involves differential expression of ABH antigens. In the gland of young individuals, in contrast with senile thymus, all lymphocyte populations and the Hassall's corpuscules expressed HBGA. The reduced reactivity for ABH antigens in the lymphocytes of the senile gland might reflect the damaged communication between these two cell types. New evidence for differential expression of HBGA in thymic ontogeny is presented.

Key words: histo-blood group antigens, thymus, involution, aging.

Introduction

ABH histo-blood group antigens (HBGA) are glycoproteins present in different cell types apart from red blood cells [3]. It is believed that they participate in cell differentiation [8], cellular adhesion [11], cancer metastasis and angiogenesis [5]. The epithelial cells (EC) comprising the thymocyte microenvironment play an important role in the ontogeny of the thymus [9]. The thymus undergoes age-related, physiological involution during normal human development [1, 4]. We present a new outlook on the expression pattern of ABH HBGA in senile thymus related to the process of aging.

Material and Methods

Normal thymus glands with no pathological alterations were taken from autopsy samples of senile (aged 65-80 years; n=10) and young (aged 2-16 years, n=8) individuals (Department of General and Clinical Pathology, Medical University, Sofia,

Bulgaria). The blood group phenotype was determined by direct agglutination. The study was approved by the Ethics Committee of the hospital. Routine microscopy was performed prior to the immunohistochemical study. The indirect immunoperoxidase technique with the universal LSAB-2 kit (DAKO) with chromogen AEC was carried out on paraffin sections according to previously described protocols (12). As primary antibodies were used monoclonal antibodies with defined specificity to human HBGA A and B (BulBio; Cat. N: 780001, 780002). Negative and positive controls were examined in parallel. Specific reactivity for EC in positive controls was evaluated on serial sections by anti-pancytokeratin antibody (Sigma Chemical Co; Cat. N: C1801). Immunoreactivity was assessed by a semiquantitative scale ranging from (3+) to (—).

Results

A complete match between blood group phenotype and tissue immunoreactivity for HBGA was detected. Senile thymus exhibited large areas of adipose tissue containing scattered EC and lymphocytes. Stromal EC, positive for HBGA, revealed different size, morphology and intrathymic localization. Endothelial cells of blood vessels and red blood cells were intensely stained for HBGA (Fig. 1). Almost no Hassall's corpuscules (HC) were detected in the medullar part of the involuted gland. Only single scattered lymphocytes possessed HBGA.

In control normal thymus from young individuals the lobulated structure of the gland was preserved. EC were organized as a supporting framework for lymphoid cells. HBGA were discovered in endothelial cells and erythrocytes. EC were also positive for ABH antigens. In contrast with senile thymus, most lymphocyte popula-

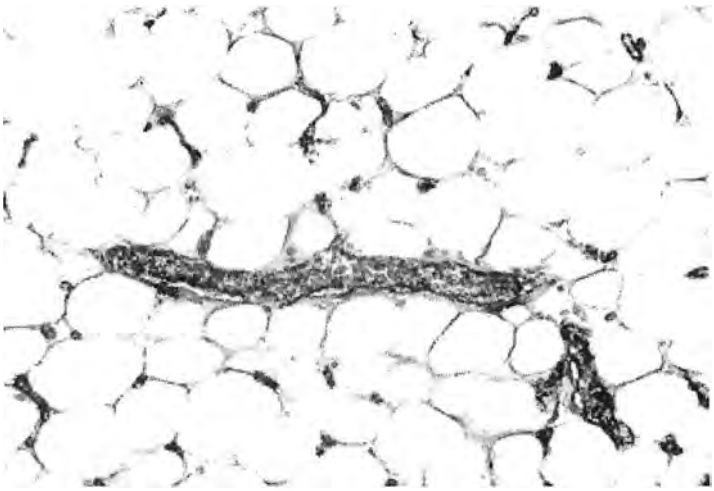

Fig. 1. Expression of HBGA B in erythrocytes and endothelial cells of thymic capillaries in senile human thymus (78-year-old male). Single stromal EC positive for HBGA B. Biotin-streptavidin-peroxidase technique. × 400

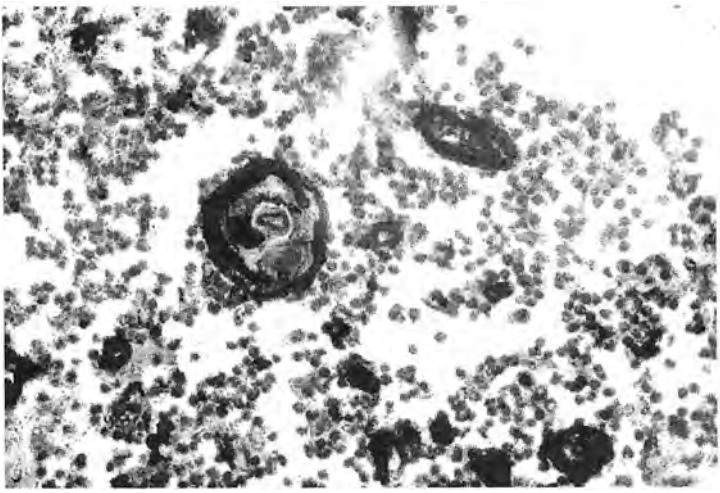

Fig. 2. Expression of HBGA A in Hassall's bodies, single lymphocytes and EC in young normal human thymus (6-year-old boy). Biotin-streptavidin-peroxidase technique. × 630

tions in the gland of young individuals expressed HBGA but with varying intensity. Lymphocytes in close proximity to hyperexpressing HC were strongly positive, while those near to the scattered immunoreactive EC revealed low staining intensity (Fig. 2).

Discussion

Our study indicates that in both aged and young thymus glands a permanent reactivity for HBGA was detected in endothelial cells of blood vessels and in red blood cells. That immunostaining pattern served as a positive internal control, as these cell types are known to be constantly positive in normal human tissues [6, 7].

It has been suggested that the blood group related antigen Le-Y may be associated with intercellular adhesion between lymphocytes and high endothelial venules in lymphoid organs [10]. Interestingly, our observations reveal that ABH HBGA are preserved in aged human thymus, although demonstrating a different pattern of reactivity compared to young individuals. We have detected previously HBGA A in desmosomal contacts between cortical EC and in zones of close contacts between thymic EC and lymphocytes [8]. It is quite possible that these glycoproteins serve as adhesion molecules in human thymus. Although the number of EC diminish in the course of involution, those which are still present in the senile thymus preserve their HBGA. The epithelial framework reorganization in aged human thymus possibly involves a differential expression of ABH antigens as shown in the present study. Probably these molecules are required by thymic EC to maintain the reduced but important crosstalk with lymphocytes during involution. Alternatively, lymphocytes also need HBGA, as most of them express ABH molecules in the young thymus. The diminished reactivity for ABH antigens in the lymphocytes of aged thymus might reflect the impaired communication between these two cell types.

The number of HC in the senile thymus was quite reduced because of the involution process. Almost none of them was immunopositive in contrast with the in-

tensely stained HC in the young gland. As these structures are regarded as components providing developing thymocytes with signals to ensure their proper functional maturation (2), HBGA might be part of these signalling molecules.

Our study presents new immunohistochemical evidence for differential expression of ABH antigens during age-related human thymus involution in reorganized EC and in single lymphocytes. These glycoproteins might be implicated in the complex cellular interactions during the ontogeny of the thymus gland.

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