EXTRATHYMIC DISTRIBUTION OF THYMALIN-POSITIVE CELLS IN EPITHELIA OF ORGANS CLOSE TO THE THYMUS MORPHOGENETICALLY DURING HUMAN PRENATAL DEVELOPMENT

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Proliferation and differentiation of T lymphocytes from precursor T cells, originating in hematopoietic organs, take place in the thymus, the central organ of the immune system. This process involves hormones secreted by the reticuloendothelial cells of the thymus. Several hormones have now been identified in the thymus, of which three have been synthesized and purified: thymopoietin [8], thymulin [6], and thymosin-α_1 [9]. Monoclonal antibodies against these hormones have enabled them to be located in the epithelial cells of the thymus. Two new Soviet hormonal preparations of the thymus have now been obtained: T-activin [1] and thymalin [3]. Thymalin is a polypeptide complex with mol. wt. of 5000 ± 500 daltons, used clinically in the correction of immunodeficiency states. The presence of thymalin-positive cells was established previously in the human embryonic thymus at 6 weeks of development, before colonization of the gland by lymphocytes, and the dynamics of the distribution of thymalin-expressing cells in the thymus has been monitored during human prenatal ontogeny [5].

The aim of the present investigation was to discover whether epithelial cells containing thymalin are present in the epithelium of other organs similar in their origin to the epithelium of the thymus. Such organs include those of the respiratory system and the proximal part of the digestive system which, like the thymus, develop in the region of the embryonic foregut. The foregut lies at the cranial end of the embryo, at the boundary between ectoderm and entoderm, and the epithelium arising from this anlage possesses the properties of both of these embryonic rudiments [2, 4].

EXPERIMENTAL METHOD

The test material consisted of epithelium of the thymus, epiglottis, larynx, trachea, lung, esophagus, skin, intestine, and liver of 20 human fetuses at 20-25 weeks of development, obtained as a result of spontaneous abortions from clinically healthy women.

Thymalin was determined by the indirect immunofluorescence method, using specific antiserum to thymalin obtained from G. A. Ryzhak, Leningrad Research Institute of Vaccines and Sera, Ministry of the Medical and Biological Industry of the USSR, to whom the authors are grateful. Frozen sections were fixed for 5-10 min at 4°C in absolute acetone, washed with buffered physiological saline, and incubated in a humid chamber consecutively with rabbit antiserum containing antibodies to thymalin (titer in the indirect agglutination test 1:3200, dilution 1:4) and with donkey serum to FITC-labeled rabbit globulin, prepared at the N. F. Gamaleya Research Institute of Immunology, Epidemiology, and Microbiology, Academy of Medical Sciences of the USSR (titer 1:64, dilution 1:4). To reduce nonspecific adsorption of proteins the conjugates were treated with acetone liver powder before incubation with the slices. Control frozen sactions were treated with intact rabbit serum or with buffered physiological saline instead of the antithymalin serum. The preparations were studied in a Lyumam-RZ microscope.

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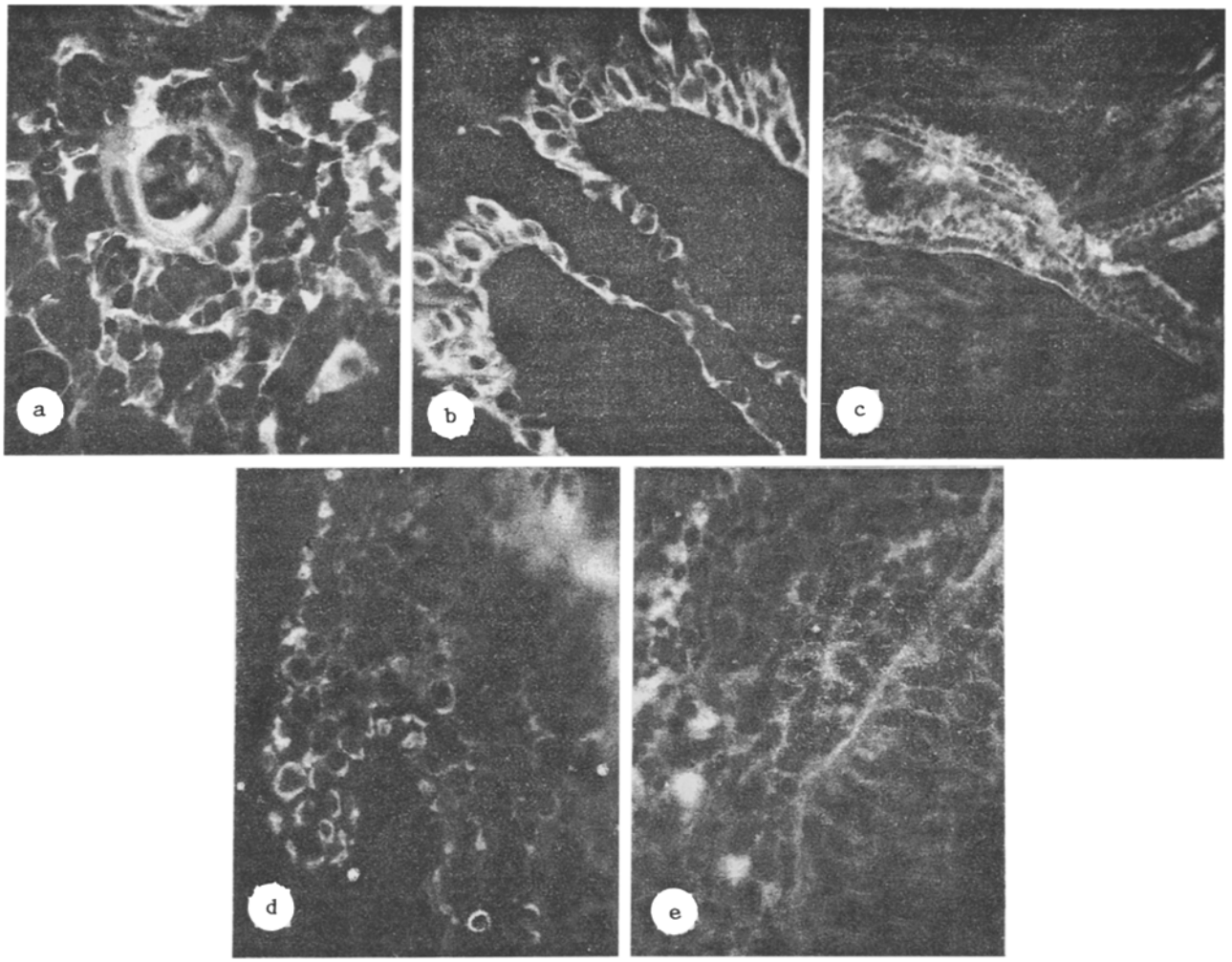

Fig. 1. Indirect immunofluorescence test with antibodies to thymalin polypeptides: a) network of thymalin-positive cells in medulla of thymus. 800×; b) thymalin-expressing cells in stratified prismatic epithelium of trachea. 800×; c) thymalin-expressing cells in stratified squamous epithelium of esophagus. 400×; d) thymalin-expressing cells in epidermis of skin. 800×; e) no thymalin-expressing cells present in intestinal epithelium. 800×.

EXPERIMENTAL RESULTS

Thymalin-positive cells were identified (Fig. 1) not only in the thymus but also in the epithelium of the epiglottis, larynx, trachea, tongue, esophagus, the skin of the head and back, and in the salivary gland epithelium. No thymalin positive cells were found in the epithelium of the small and large intestine or in the liver, i.e., organs developing from the entodermal embryonic anlage. The fluorescent cells in the above-mentioned organs were the younger epithelial cells. In the air passages these were basal and intermediate cells of stratified epithelium, and in the esophagus and skin they were 1 or 2 layers of the stratum germinativum of the epithelium. Intense fluorescence was observed in the epithelium of the skin and trachea, weaker in the epithelium of the esophagus and salivary glands. No fluorescence was present in control sections cut through all organs mentioned above.

It can be concluded from analysis of the results that the presence of thymalin is a feature not only of the epithelial cells of the thymus, but also of the epithelium of other organs, derivatives of the foregut, namely the organs of respiration, of the proximal part of the digestive tract (before the stomach), and the skin and its derivatives. Thymalin-positive cells are absent in the epithelium of the gastrointestinal tract and of the large digestive glands. Recent studies have demonstrated the presence of prothymosin-α [10] and parathymosin-α [11], which are very similar in their molecular structure to thymo-

sin, differing from it in their higher molecular weight and larger number of amino acid residues, in certain organs of the rat. Other workers [7, 12] have shown that thymopoietin is present in the basal keratinocytes of the skin.

The extrathymic distribution of thymalin-expressing cells was thus demonstrated in the epithelium of the epiglottis, larynx, trachea, lung, and esophagus of the human fetus, which is related morphogenetically to the epithelium of the thymus, and together with reports in the literature on the presence of other thymic hormones in certain animal organs, this indicates the need for further research in this direction with the aim of re-evaluating the role of the hormone-like substances of the thymus in the body. The epithelium of organs genetically closely related to the thymus, such as the skin, may perhaps participate in the histophysiology of the immune system.

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