DISTRIBUTION OF CROSS-REACTING ANTIGEN COMMON TO GROUP A STREPTOCOCCAL POLYSACCHARIDE AND STRATIFIED SQUAMOUS EPITHELIUM IN HUMAN ORGANS

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Immunological cross-reactions between group A streptococcal polysaccharide (polysaccharide A) and an antigen of epithelial cells of ectodermal origin were described previously [1-6]. The localization of the cross-reacting antigen (CRA) in the cytoplasm of cells in the stratum basale of the skin epithelium and epithelial reticulum of the thymus has been demonstrated by the indirect immunofluorescence method, using a preparation of antibodies against streptococcal polysaccharide, in mammals of various species (man, rabbit, guinea pig, mouse). The distribution of CRA in organs containing stratified squamous epithelium (esophagus, oral cavity, vagina, distal end of the rectum, sclera of the eye, etc.) has been studied in mice. CRA has also been found in cells of transplantable mouse tumors connected histogenetically with the epithelium carrying the antigen [2]. Tissue reactions with CRA have been found only on testing antibodies with high affinity for polysaccharide A and have not been found on testing preparations containing antibodies with low affinity. Investigation of cross-reactions between antigens of the microorganism and antigens of various mammalian tissues is interesting in connection with the study of autoimmune reactions associated with an infectious process [4]. Determination of the localization of CRA characteristic of stratified squamous epithelium in various human tissues may also help to solve a number of problems in histogenesis and could lay the foundations for development of a method of differential diagnosis of tumors arising from stratified squamous epithelium.

The object of this investigation was to study the distribution of a CRA common to polysaccharide A and stratified squamous epithelium in tissues of various human organs.

EXPERIMENTAL METHOD

Tissues from organs of clinically healthy persons with blood group O aged from six to 28 years, dying from acute trauma, and tissues of human fetuses between eight and 27 weeks of intrauterine development (blood group O) were used. Material was taken not more than 18 h after death. Sections 5 μ thick were cut in a cryostat (−20°C) from tissue frozen to −76°C (with a mixture of dry ice and acetone), kept for not more than 24 h, and used in the unfixed form. The sections were processed by the method described previously [4, 5]. Tissues of the mucous membrane of the oral cavity, esophagus, stomach, rectum, large and small intestines, heart, liver, kidney, spleen, urinary bladder, and other organs were investigated. Sections of human skin and thymus, in which CRA was revealed in previous investigations [1, 3, 6], were used as the control. Four series of a preparation of antibodies with high affinity for polysaccharide A, obtained by the method described previously, were used. The antibody preparations contained 0.5-1.7 mg protein/ml. The antibodies were inhibited by mixing equal volumes of antibodies (2-3 mg/ml) and polysaccharide A (200-300 mg/ml). Antibodies against mouse immunoglubulins, isolated from rabbit sera (protein content 1.6

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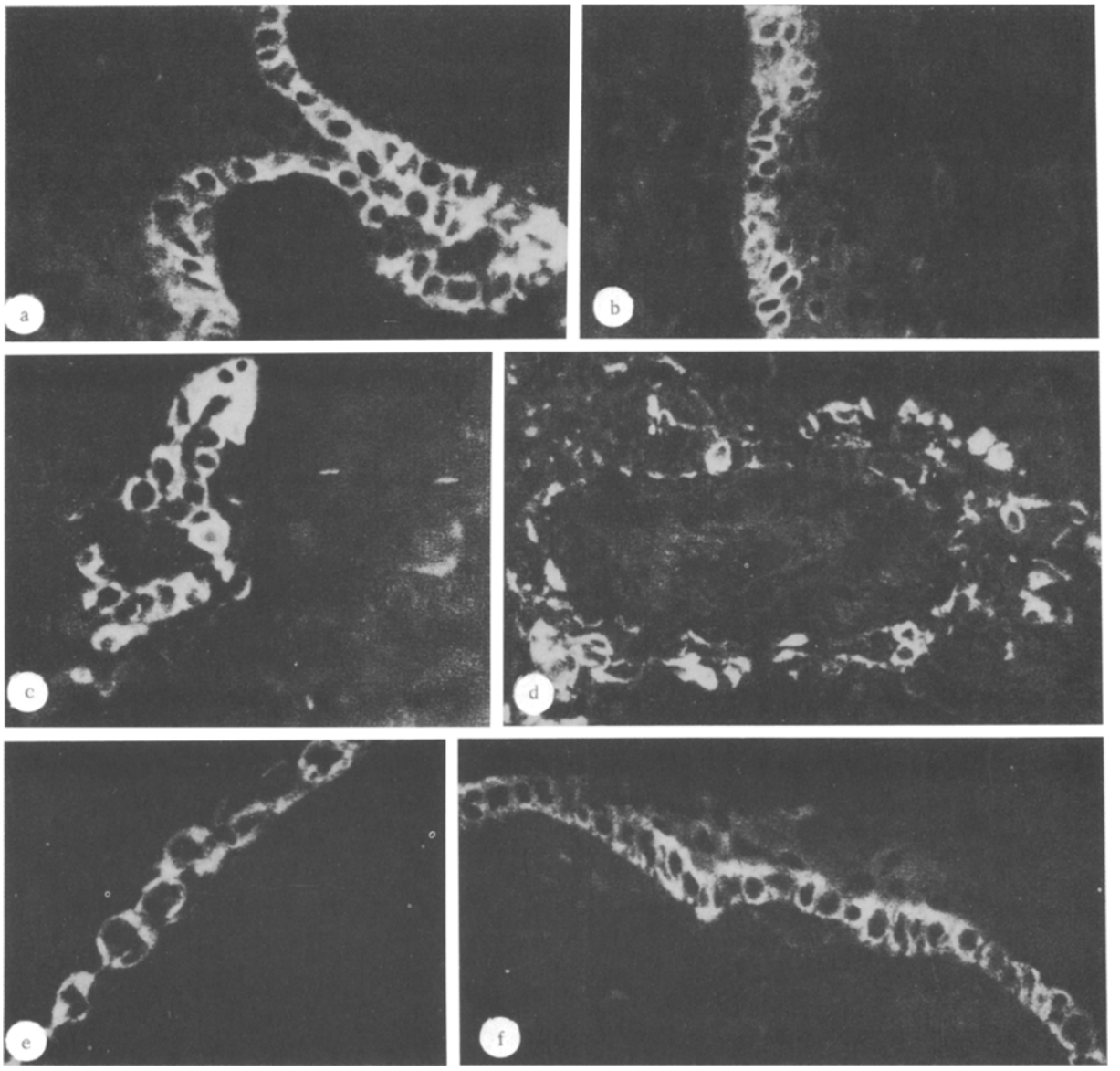

Fig. 1. Tissue sections from human organs treated with antibodies against group A streptococcal polysaccharide. a) Skin: reaction in cells of stratum basale of epidermis; b) esophagus: reaction mainly in cells of stratum basale of stratified squamous epithelium; c) mammary gland: reaction of epithelial cells of gland duct with antigen; d) thymus: reaction of epithelial cells bordering on adventitia of blood vessel in medullary zone of lobule with antigen; e) skin of 8-week human fetus: reaction of cells of simple embryonic epithelium with components; f) skin of 26 week human fetus: reaction in cells of stratum basale of stratified squamous epithelium. Indirect immunofluorescence method, objective 40× (water immersion), ocular homal 3×.

mg/ml) were used as the control.* When the indirect immunofluorescence method was used preparations of antibodies against rabbit IgG, isolated with the aid of an immunosorbent and labeled with fluorescein isothiocyanate, were used. The method of preparation of the antibodies was described previously [6].

EXPERIMENTAL RESULTS

On treatment of sections of human skin with antibodies against polysaccharide A and subsequent application of labeled antibodies against rabbit IgG to them a reaction was ob-

*The antibody preparation was obtained from E. V. Sidorova (Laboratory of Chemistry and Biosynthesis of Antibodies, Head of Laboratory Professor A. E. Gurevich).

served with cells of the stratum basale of the epidermis (Fig. 1a). In some sections a reaction also was observed in the more highly differentiated layers (stratum spinosum). The reaction was localized in the peripheral zone of the cytoplasm of cells in the stratum basale or in the perinuclear zone in cells of more mature layers of the epithelium. No reaction was observed with components of connective-tissue structures or structures of the vessel walls and nerve trunks of the dermis. Investigation of tissue sections from other organs with the aid of the antibody preparation (batch 47) revealed specific fluorescence in the cytoplasm of cells of the stratum basale of the stratified squamous epithelium of the mucous membrane of the esophagus, oral cavity, and lower third of the rectum and also of the epithelial cells of the ducts of the salivary and mammary glands (Fig. 1b, c). When antibodies were applied to tissue sections from the heart, liver, kidneys, spleen, mucous membrane of the stomach and proximal portions of the rectum, body of the uterus, and large and small intestines, no reaction could be found with the tissue cells of these organs. Treatment of sections with antibodies against mouse immunoglobulins was not accompanied by any reaction either with components of cells of the stratum basale of the epithelium or with other tissue structures. After direct treatment of the sections with labeled antibodies against rabbit IgG no reaction with the tissues was observed. Addition of polysaccharide A to the antibody preparation (batch 47) inhibited the reaction with the cells. Besides the tissues listed above, positive reactions also were observed with epithelium of the human thymus. A reaction was observed in the cytoplasm of the peripheral elements of Hassall's corpuscles and of individual epithelial cells in the medullary zone around the corpuscles. Besides cells of the medullary zone, a reaction also was observed in the cell cytoplasm in the stratum basale of the epithelium of the cortical zone, located at the periphery of the lobule. A reaction also was observed with antigens of cells of the epithelial reticulum around blood vessels in the medullary zone of the lobule (Fig. 1d). Treatment of sections through human fetal skin with antibodies against polysaccharide A (batch 47) showed that positive reactions were given by cells of the simple epithelium of the skin in 8-week embryos (Fig. 1e). During the formation of stratified squamous epithelium the corresponding antigen evidently was contained in the cells of all layers, but it gradually disappeared from the differentiated layers and by the time of complete maturation of the epithelium (16-17th weeks) it was localized mainly in cells of the stratum basale (Fig. 1f).

The study of antibodies against polysaccharide A by the indirect immunofluorescence method in tissue sections from various human organs thus showed that CRA, reacting with antibodies against polysaccharide A, is present in cells of stratified squamous epithelium (skin, mucous membrane of the oral cavity, esophagus, vagina, and other organs), and also in epithelial cells lining the ducts of the salivary and mammary glands and in cells of the epithelial reticulum of the thymus. It must be emphasized that the epithelial tissue listed above (carriers of CRA) share a common ectodermal origin. This fact is further confirmation of the view that the epithelium of the thymus has the properties of an epithelium of ectodermal genesis. The results agree with those obtained previously in a study of animal tissues [1-6] and they can evidently be used to develop a method of differential diagnosis of tumors of different origin.

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