Psoriasis Associated with Opisthorchiasis under Conditions of Anthelmintic Therapy

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Biopsy specimens from patients with psoriasis concomitant with chronic opisthorchiasis were examined. Severe clinical course of combined disease was associated with degenerative changes in epidermocytes, keratinization disorders, and diffuse inflammatory cell infiltration of the derma. Combined therapy including anthelmintic agents produced a positive effect: decreased the degree of acanthosis, increased intracellular regeneration of epidermocytes, and suppressed inflammatory reaction of the derma and hyperplasia of immunocompetent cells. These data attested to an important role of opisthorchiasis in the pathogenesis of psoriatic disease.

Key Words: *psoriasis; opisthorchiasis; skin biopsy; helminthocidal agents; electron microscopy*

Chronic opisthorchiasis ranks among the most prevalent diseases in the structure of regional pathology in West Siberia and especially in the Ob'-Irtysh Basin [1,5]. Opisthorchiasis often runs a latent course, in many cases is characterized by a stubborn wave-like course with periods of exacerbations and remissions, with predominant involvement of the gastrointestinal organs. Opisthorchis invasion is often detected only after development of severe complications [2,13]. In recent years opisthorchiasis acquired a pattern of a systemic disease even under conditions of low intensity of invasion [8,9]. Opisthorchiasis remains a pressing problem because of inefficiency and toxicity of modern anthelmintic agents.

Psoriasis is also a systemic condition (psoriatic disease) [3,4,12], which is due to the involvement of not only the skin, but also the viscera and locomotor system [14]. Dermatoses in the West Siberian region endemic for opisthorchiasis are characterized by severe clinical course and are often resistant to therapy [7]. Therefore, the study of association of opisthorchiasis and psoriasis is important not only for regional pathology of West Siberia, but also for understanding of the pathogenesis of combined total systems diseases.

We studied structural changes in the epidermis and derma in psoriasis concomitant with chronic opisthorchiasis during therapy with anthelmintic drugs.

MATERIALS AND METHODS

Forty-two patients with psoriasis concomitant with chronic opisthorchiasis were examined. Twenty-three patients presented with exudative psoriasis, 19 with the vulgar form; 34 patients had progressive stage of the disease and 8 had stationary stage. After a course of therapy for dermatosis one of helminthocidal drugs was prescribed: chloxyl (n=9), biltricide (n=10), or poputril (70% extract of aspen bark; n=17); 6 patients received no anthelmintic treatment.

Biopsy specimens were collected from areas of involved skin under local anesthesia before treatment and 1 month after the start of combined therapy. The greater part of the skin biopsy specimen was fixed in

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10% neutral formalin, paraffin sections were stained with hematoxylin and eosin in combination with Perls reaction, by Van Gieson method with post-staining of elastic fibers with Weigert resorcin-fuscin, and periodic acid-Schiff reaction was carried out. For electron microscopy the fragments of biopsy specimens were fixed in 4% paraformaldehyde, postfixed in 1% OsO_4, and embedded in epon and araldite mixture. Semithin sections were stained with Schiff reagent and Azur II; ultrathin sections were contrasted with uranyl acetate and lead citrate and examined under a JEM 1010 electron microscope.

RESULTS

Psoriasis was associated with disseminated efflorescence on the hairy part of the head, skin of the trunk, upper and lower limbs occupying not only flexion, but also extension surfaces. The mean area of the skin involved in the pathological process was 26.3±0.8%. Exacerbation of psoriasis started spontaneously in 72% patients with psoriasis and opisthorchiasis, 56% patients noted that the exacerbations were more frequent, did not depend on the season, were severe and drug resistant. After anthelmintic therapy the progressive stage of psoriasis transformed into regressive, the most part of psoriatic elements (mainly on the shins and knee joints) were completely resolved. Signs of acute inflammation disappeared, infiltration and desquamation decreased, the total area of involved skin markedly decreased; the best effect was observed after poputril therapy.

Under light microscope skin biopsy specimens before treatment showed hyper- and parakeratosis of different degree, acanthosis, and epidermocyte degeneration. Plethoric vessels of the papillary layer, perivascular edema and diffuse polymorphonuclear cell infiltration were observed in the derma (Fig. 1, *a*). In some biopsy specimens the infiltrates contained numerous polymorphonuclear leukocytes disseminating into the epidermo-dermal conjunction area and actively penetrating into the epidermis, forming Munrow microabscesses. The number of elastic fibers sharply decreased in the derma, especially in the papillary layer, and their tinctorial characteristics were modified in many cases.

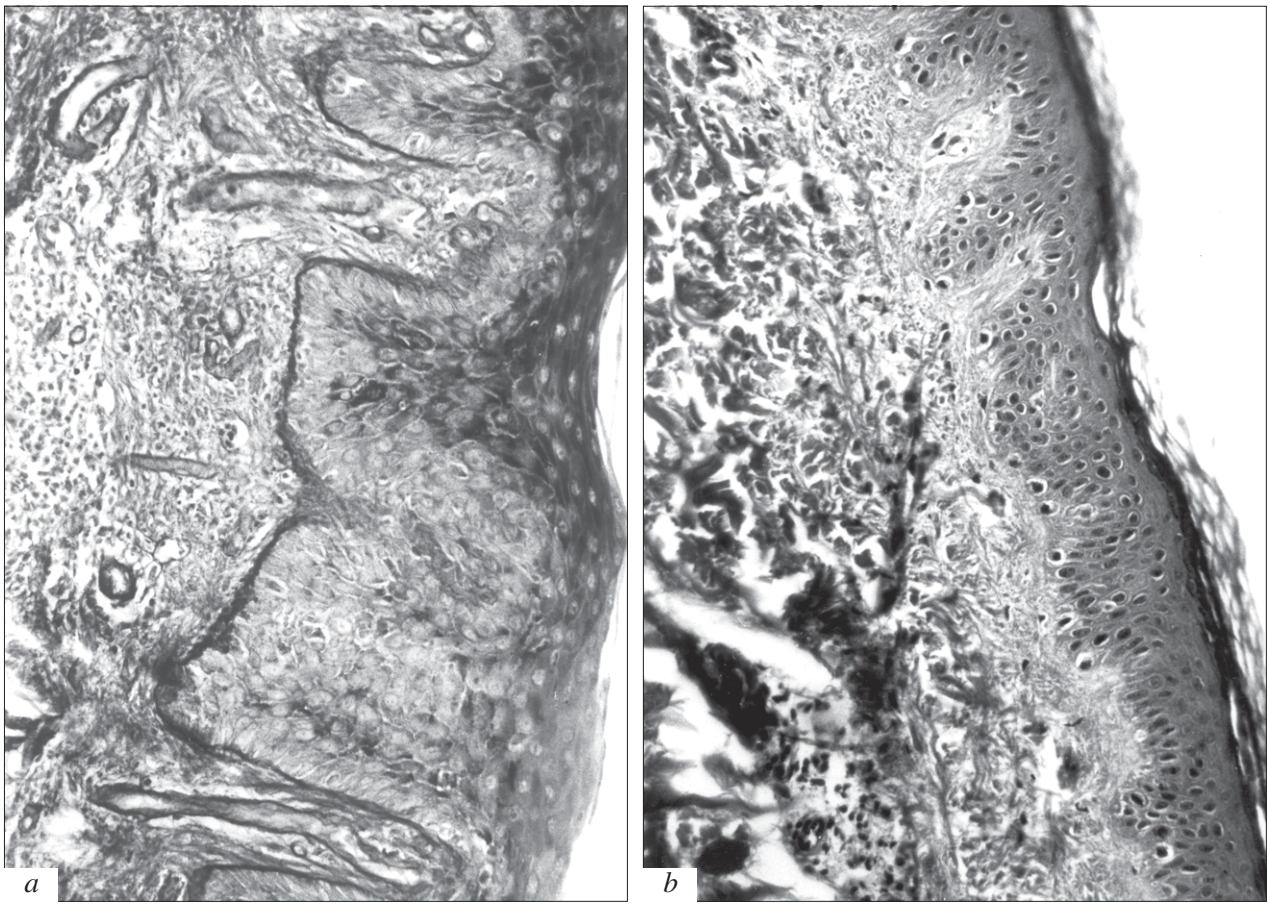

Fig. 1. Light microscopy of skin biopsy specimens in psoriasis concomitant with opisthorchiasis during combined therapy, ×320. *a*) before therapy: acanthosis and pronounced inflammatory cellular infiltration of the derma. Periodic acid-Schiff reaction; *b*) after therapy: reduction of acanthosis and minimum cell infiltration of the derma. Hematoxylin and eosin staining.

Pathomorphological study of biopsy specimens of involved skin sites after combined therapy including helminthocidal drugs showed an appreciable reduction of acanthosis severity (Fig. 1, *b*). Few degenerative keratinocytes were located mainly in the prickle layer. The severity of vascular disorders decreased; hyperemia, edema, and inflammatory cell reaction of the derma were reduced. Cell infiltrates consisted mainly of lymphocytes and was located perivascularly; no intraepidermal microabscesses were seen.

Electron microscopy of epidermocytes in skin biopsy specimens collected before therapy showed ultrastructural signs of keratinization disorders. Multilayer squamous epithelium lost clear-cut structural characteristics of different layers, the basal and prickle layers were drastically thickened. The population of epidermal basal cells was characterized by moderate polymorphism due to, primarily, different electron density of the cytoplasmic matrix. Epitheliocytes with electron-transparent cytoplasm predominated; solitary free ribosomes, small mitochondria with solitary cristae, and thin bundles of primary filaments were seen in the cytoplasm; other cells were characterized by high density of the cytoplasmic matrix. In basal cells nuclear heterochromatin formed small lumps and concentrated marginally; the nucleoli were extremely rare. In many biopsy specimens epidermocytes of the basal layer were degenerative with focal alteration of cytoplasmic organelles and contained polymorphic autophagosomes and residual structures. Extracellular spaces were dilated because of impaired specialized cell-cell contacts and filled with finely granular substrate.

Epitheliocytes of the prickle layer were characterized by most stereotypical ultrastructural organization. The main alteration in all cells was devastation of the perinuclear zone of the cytoplasm: decreased number or absence of cytoplasmic organelles (Fig. 2, *a*); thin short bundles of tonofibrils and solitary vacuolated mitochondria were seen near the cytolemma. The nuclei of some cells contained fragmented nucleoli. The zone of prickle epidermocytes was markedly extended in the majority of biopsy specimens, and signs of differentiation of the epidermal granular layer cells were markedly reduced, this resulting in the absence of zonal polymorphism.

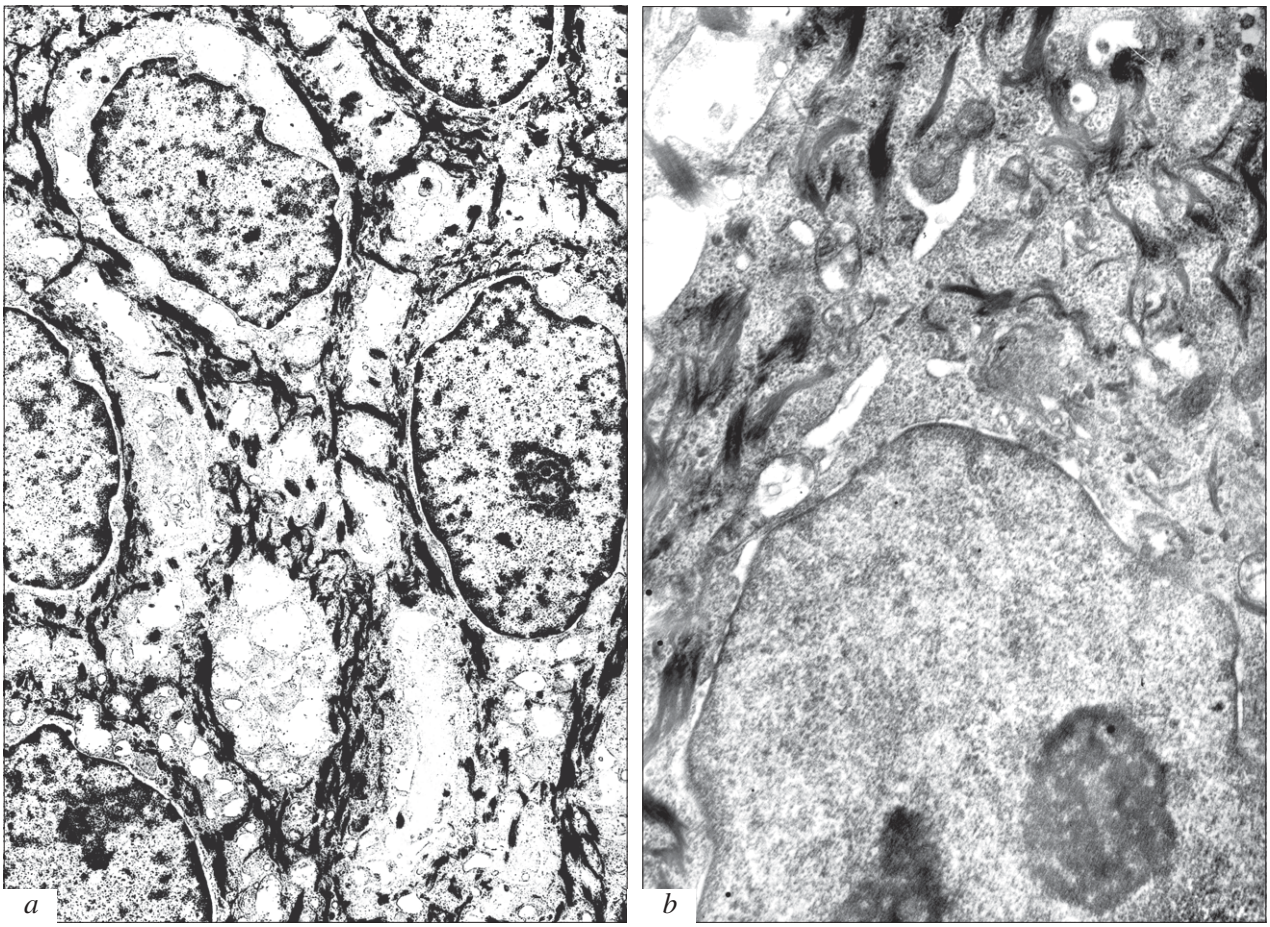

Fig. 2. Ultramicroscopic characteristics of the prickle layer epidermocytes in psoriasis concomitant with opisthorchiasis. Electronograms. *a*) before treatment: perinuclear devastation of cytoplasm, vacuolation of mitochondria, fragmentation of nucleoli, ×3000; *b*) after combined therapy: numerous free ribosomes and tonofibril bundles in cytoplasm, large nucleoli, ×10,000.

Small heterogeneous granules of keratohyalin formed in just solitary cells of the granular layer, but no true keratinization was observed. Euchromatic nuclei without signs of degradation, mitochondria, and individual elements of granular cytoplasmic reticulum were retained in epitheliocytes; many cells contained short bundles of tonofilaments with minimum trend to concentration and aggregation. Horny layer cells also retained nuclei, but they exhibited signs of degradation; cell cytoplasm retained its structure without elements of hornification intrinsic for this layer.

Combined therapy including helminthocidal agents led to recovery of the ultrastructural organization of epitheliocytes in all layers of the epidermis, which was paralleled by induction of full-value keratinization with clear-cut morphological stratification of the layers. The basal layer epidermocytes became more monomorphic, contained euchromatic nuclei with irregular contour, unevenly dilated nucleolemma, and large nucleoli. The cytoplasmic matrix was characterized by moderate electron density and greater saturation with not only free ribosomes, but also with membrane organelles, including the cytoplasmic reticulum elements. The density of intracellular ultrastructures was also due to numerous diffuse primary filaments and the solitary osmiophilic bundles of tonofibrils formed by them.

The prickle layer cells became larger and more polymorphic, many of them had long cytoplasmic processes integrating with the neighboring epitheliocytes by means of numerous desmosomes. The nuclei contained a lesser number of heterochromatin lumps, with 1-2 large nucleoli discernible. The perinuclear zone of the cytoplasm was characterized by high density of cytoplasmic organelles, including protein-producing structures, and by increased number of diffusely located tonofibril bundles (Fig. 2, *b*). Aggregation of filamentous structures was observed near the granular layer in many prickle epitheliocytes, and large osmiophilic granules formed in the granular layer of the epidermis, which, in parallel with degradation of the epitheliocyte cyto- and nucleolemma, provided full-value keratinization, regarded as the process of terminal cell differentiation of the epidermis.

Hence, combined therapy (including helminthocidal agents) of patients with psoriasis concomitant with opisthorchiasis promoted induction of intracellular regeneration and differentiation of epidermocytes, which led to recovery of hornification process without epithelial hyperplasia. The best effect was observed after therapy with aspen bark extract (poputril) due to its lowest toxicity in comparison with chloxyl and biltricide.

Presumably, interorgan interactions as the basis of systemic reactions in health and disease are the key factor in the pathogenesis of psoriasis concomitant with opisthorchiasis. Metabolic reactions can be considered as the main aspects. The dominant of plastic support of continuous degradation and proliferation of the epidermis in psoriasis [10] creates a deficit of plastic resources for other organs and tissues, particularly under conditions of parasitic invasion [11]. Disorders in plastic metabolism augment in psoriasis concomitant with parasitic invasion, being paralleled by profound disintegration of functions with development of severe forms of the dermatosis. The effect of plastic deficit in combined disease is particularly obvious in rapidly regenerating tissues. For example, a complex of structural and functional changes develops in the gastrointestinal mucosa in psoriasis concomitant with opisthorchiasis: psoriatic gastrointestinopathy [8], one of manifestations of the universal regeneratory plastic failure syndrome [6].

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