MORPHOLOGY AND PATHOMORPHOLOGY

Extra- and Intracellular Collagen Resorption by Macrophages and Fibroblasts in Postpartum Uterine Involution

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Localization of catepsin B in rat uterus during postpartum involution was studied by electron microscopy using histochemical methods. The product of histochemical reaction was found in collagen-containing vacuoles in macrophages and fibroblasts, on their cytolemma and adjacent collagen fibrils, which indicated the involvement of these cells into intra- and extracellular collagen resorption in the uterus.

Key Words: *postpartum uterine involution; collagen resorption; macrophages; fibroblasts; catepsin B*

Postpartum uterine involution is a most promising model for studying connective tissue catabolism under physiological condition. More than 85% collagen accumulated in rat uterus during pregnancy degrades within 4 days postpartum [10]. Electron microscopy showed that macrophages participate in postpartum collagen resorption. They phagocytize collagen fibrils disintegrated by collagenase in the extracellular matrix [3,5,6]. Biochemical studies demonstrated the involvement of lysosome proteinases in collagen lysis [2,8,9]. An important role in collagen resorption is played by cysteine proteinases, in particular, catepsin B [1,4].

In the present study localization of catepsin B in rat uterus during postpartum involution and the role of connective tissue elements in this process are studied using electron histochemical technique.

MATERIALS AND METHODS

Rat uterus was studied 2 and 3 days postpartum. Catepsin B was visualized histochemically [7] using Z-Ala-Arg-Arg-MBNA (Bachem) as the substrate. Control samples were incubated under the same conditions without substrate or in the presence of the inhibitor p-chloromercuribenzoate. Ultrathin sections were not contrasted.

RESULTS

Examination of the myometrium 2 and 3 days postpartum revealed numerous macrophages and fibroblasts containing vacuoles with collagen fibrils (Fig. 1, *a-c*). The product of histochemical reaction for catepsin B was seen in many vacuoles, which confirmed their phagocytic nature (Fig. 1, *a, b*). This product was also found in lysosomes of macrophages and fibroblasts. Of particular interest is extracellular localization of catepsin B activity: solitary granules of catepsin B-specific product were noted on macrophage and fibroblast cytolemma and adjacent collagen fibrils (Fig. 1, *b-d*), which confirms secretion of catepsin B by these cells to extracellular matrix.

Control samples contained no product.

Our findings suggest that macrophages and fibroblasts actively participate in intracellular collagen re-

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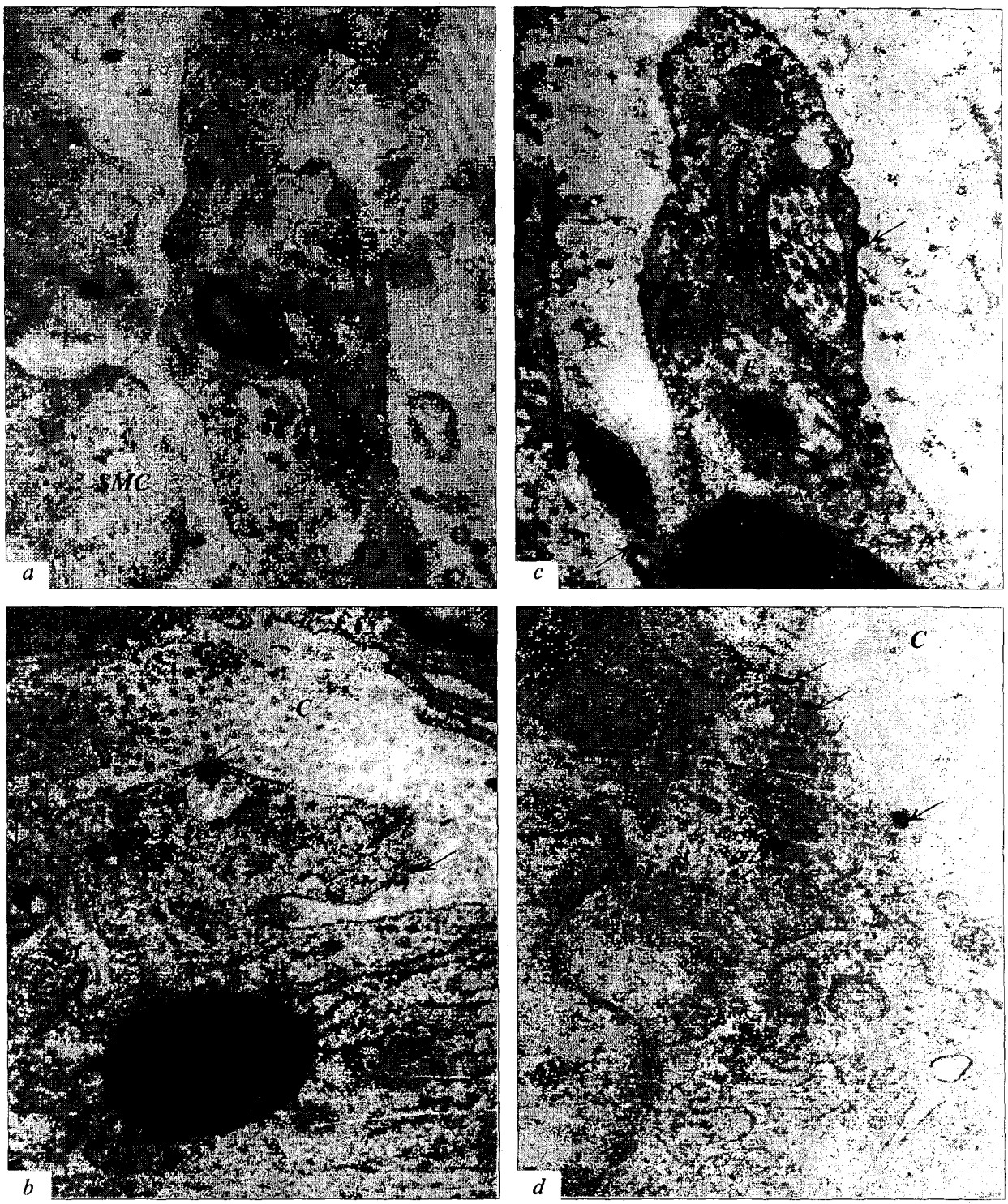

Fig. 1. Catepsin B in rat uterus during postpartum involution. *a*) postpartum day 3. Vacuoles with collagen in macrophage (M) cytoplasm. Arrows indicate collagen degradation products in vacuole. SMC: smooth muscle cell. ×50,000. *b*) postpartum day 2. Fibroblast cytoplasm (F) contains vacuoles with collagen and reaction product (arrows). Some granules containing reaction product (indicated by arrows) lie extracellularly on fibroblast cytolemma. C: collagen. ×50,000. *c*) postpartum day 3. Fibroblast cytoplasm (F) contains vacuoles with collagen (C). Reaction product (arrows) lies extracellularly on fibroblast cytolemma. ×50,000. *d*) postpartum day 2. Reaction product (arrows) lies extracellularly on macrophage cytolemma (M) and adjacent collagen fibrils (C). ×30,000.

sorption during postpartum uterine involution by phagocytizing collagen fibrils followed by their lysis in lysosomes. Macrophages and fibroblasts are also involved into extracellular collagen degradation via secretion of catepsin B and probably other lysosomal proteinases into extracellular space.

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