Extra- and Intracellular Collagen Resorption by Smooth Muscle Cells in Postpartum Uterine Involution

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Localization of cathepsin B in rat uterus during postpartum involution is studied using electron histochemical technique. High extracellular activity of cathepsin B and accumulation of products on the cytolemma of smooth muscle cells and adjacent collagen fibrils are revealed. These findings suggest that smooth muscle cells participate in the extracellular collagen degradation via secretion of cathepsin B.

Key Words: *postpartum uterine involution; collagen resorption; smooth muscle cells; cathepsin B; electron histochemistry*

Collagen content in the uterus increases 4-5-fold during pregnancy [8], while during postpartum involution collagen is rapidly degraded and its content normalizes (within 4 days in rats) [14]. The mechanisms of collagen resorption remain unknown. It has been generally accepted that collagen degradation is an enzyme-catalyzed primarily extracellular process; collagenases cleave collages into fragments which are then phagocytized by macrophages and completely hydrolyzed in secondary lysosomes by acid hydrolases [5,12]. An important role in collagen degradation is played by cysteine proteinases [7]. The best studied cysteine proteinase, cathepsin B, degrades insoluble collagen [3] and activates procollagenase [4].

In the present study the localization of cathepsin B in rat uterus during postpartum involution is examined using electron histochemical technique. The study was focused on smooth muscle cells (SMC), since they can phagocytize collagen fibrils [2,6] and synthesize collagenase [10], which implies their involvement into collagen degradation in the postpartum uterus.

MATERIALS AND METHODS

Rat uterus was studied 2 and 3 days postpartum. Cathepsin B was visualized histochemically [9] using Z-Ala-Arg-Arg-MBNA (Bachem) as a 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.

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RESULTS

Examination of the myometrium 2 and 3 days postpartum showed that some SMC contain vacuoles with fragments of collagen fibrils (Fig. 1, *a*). Products of degradation were noted in some lysosomes and vacuoles in SMC (Fig. 2, *b*). Cathepsin B exhibited high extracellular activity at both intervals of observation. Abundant collagen degradation products in the form of solitary granules and more or less homogenous conglomerate were seen on the SMC cytolemma and adjacent collagen fibrils (Fig. 1, *b, c*). This suggests that SMC secrete cathepsin B into the extracellular space.

Control samples contained no degradation products (Fig. 1, *d*).

Thus, SMC participate in collagen degradation during postpartum uterine involution. High extracellular activity of cathepsin B suggests that collages are degraded by SMC primarily etracellularly via secretion of cathepsin B and probably other proteinases into the extracellular space. Minor amount of collagen is

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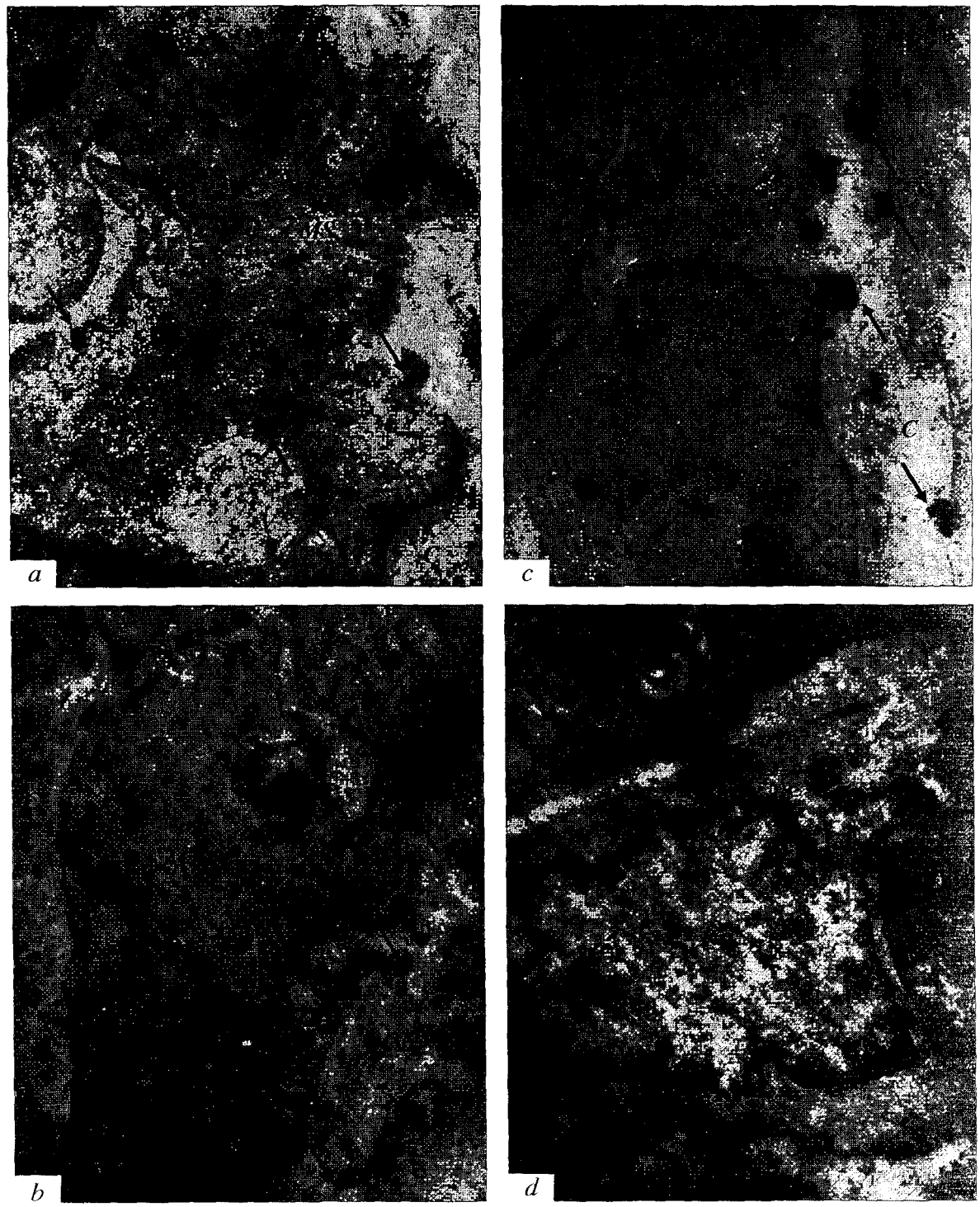

Fig. 1. Cathepsin B in rat uterus during postpartum involution. *a*) postpartum day 2. Vacuoles (V) with collagen in smooth muscle cell (SMC) cytoplasm. Arrows indicate collagen degradation products in vacuoles and on cytolemma. N: nucleus; C: collagen. ×30,000. *b*) postpartum day 3. Intense catepsin B-positive staining. Collagen degradation product (indicated by arrows) lies extracellularly on SMC cytolemma and collagen fibrils (C). One SMC vacuole (V) also contains collagen degradation product. ×15,000. *c*) postpartum day 2. Exptracellular collagen degradation product (indicated by arrows) on SMC cytolemma and adjacent collagen fibrils (C). ×30,000. *d*) control sample. No collagen degradation products. ×10,000.

degraded by SMC intracellularly via phagocytosis and hydrolysis in phagolysosomes.

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