FINDINGS OF DIFFERENT TISSUE FACTORS AND APOPTOSIS IN PRIMARY OBSTRUCTIVE MEGAURETER

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Objectives. Primary obstructive megaureter (POM) morphogenesis is not fully known. Some studies showed that there are increased amounts of connective tissue, hypertrophy of outer muscle layer, and atrophy of inner muscle layer in ureteral wall. Very few studies have investigated the immunohistochemical profile of POM. In this study, we evaluate several factors that participate in the regulation of ureters growth and development.

Materials and Methods. The study material was obtained from 11 children aged from one month to 15 years. Three control samples were obtained from children not associated with megaureters from their distal part of the ureter. Apoptosis was detected by terminal dUTP nick-end labeling (TUNEL) reaction. Protein gene product 9.5 (PGP 9.5), nerve growth factor receptor (NGFR), transforming growth factor beta 1 (TGFβ1), fibroblast growth factor receptor 1 (FGFR1), matrix metalloproteinase 2 (MMP-2), angiotensin 2 receptor type 2 (AT2R2), and sonic hedgehog (SHH) protein were detected using immunohistochemistry methods and their relative distribution was evaluated by means of the semiquantitative counting method.

Results. The megaureter material revealed transitional epithelium with scattered vacuolization, submucosa with inflammatory cells, chaotically organized and focally vacuolized muscle layers, and adventitia. Appearance of MMP-2, FGFR1, SHH, and apoptosis prevailed, but TGFβ1 positive cell number was lower in the patient group. Very strong positive correlations were observed between MMP-2 in epithelium and endothelium ($r_s = 0.867$; $p < 0.001$), FGFR1 and MMP-2 in epithelium ($r_s = 0.805$; $p = 0.005$), and TGFβ1 epitheliocytes and fibroblasts ($r_s = 0.942$; $p < 0.001$).

Conclusions. POM morphopathogenesis involves a dynamic apoptotic cell death as well as tissue degradation in epithelium, connective tissue, and blood vessels of the ureter wall. The decrease of tissue growth through diminished TGFβ expression and stimulation of FGFR1 and MMP-2 suggests a disbalance of tissue remodelation in the megaureter wall.