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POSSIBLE REGULATORY MECHANISMS IN THE OVARIAN DISORDERS

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INTRODUCTION

Long-term investigation of prevalence of antiovarian antibodies in serum of girls and adolescent women confirm their significantly higher incidence in patients with primary amenorhea (PA), oligomenorhea and secondary amenorhea (OSA). Simultaneously, in association with ovarian disorders, significantly increased levels of gonadotropins, particularly FSH, LH and their ratio (FSH/LH) declare an actual state of the ovary[1]. Because of the result of above-mentioned diseases is a substantial depletion of follicular apparatus; the aim of this study was to analyze morphological and functional design of the human ovary.

MATERIAL END METHODS

Bioptic samples of 33 ovaries, obtained by diagnostic laparoscopy, were investigated at the light and electron microscopical level. Simultaneously, serum levels of some gonatropins (FSH, LH, 17-β estradiol and progesterone) and autoantibodies against ooplasm, zona pellucida and granulosa, theca and lutein cells and were examined. Apoptic markers were detected as an expression of fragmentation of DNA (TUNEL), activated caspase 3 (using M30 CytoDeath) on ovarian sections as well as incidence of steroid receptors (estradiol). Immunohistochemical evaluation of endothelial nitric oxide synthase (e-NOS), as a source of nitric oxide (NO) that can be effective as a proapoptotic and/or proliferative signal molecule, was performed.

RESULTS AND DISCUSSION

Biochemical findings confirmed a dissociation of hormonal levels of FSH and LH in patients with PA and OSA. Significantly higher levels of both hormones were accompanied with the syndrome of non-responding ovary

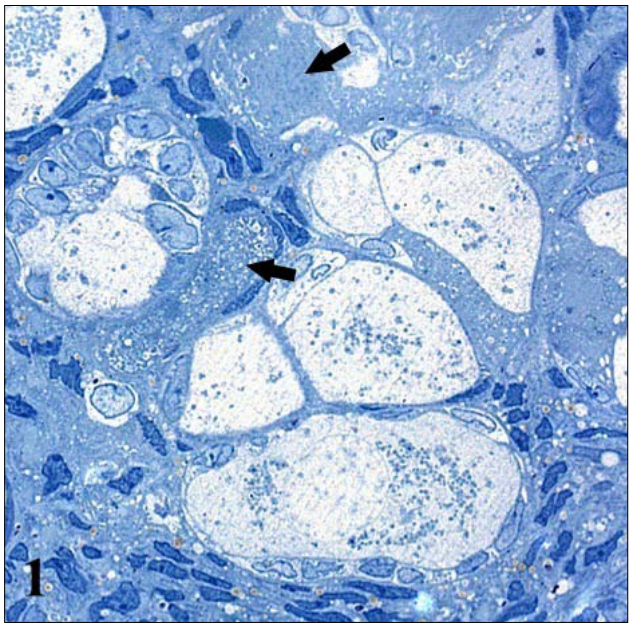

Fig. 1. A group of primary and secondary follicles. Arrows depict atretic changes. Semithin section, toludine blue. 850 x.

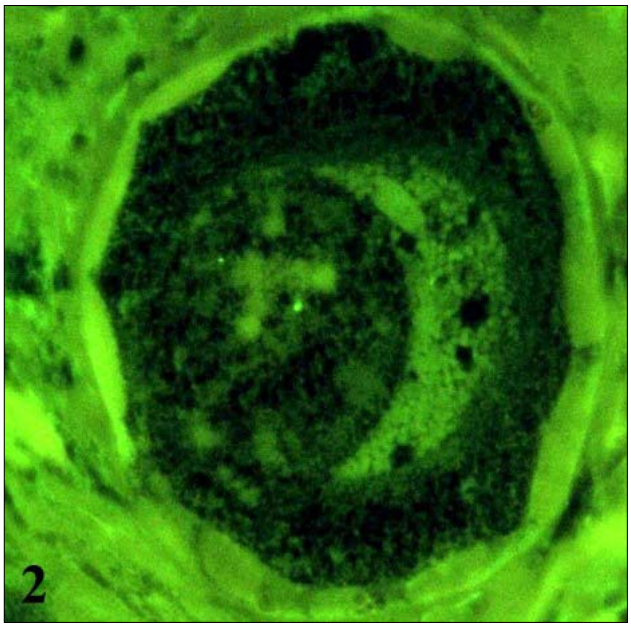

Fig. 2. M30 CytoDeath demonstrates cleaved cytokeratine 18 as a marker of activated caspase 3. 1200 x.

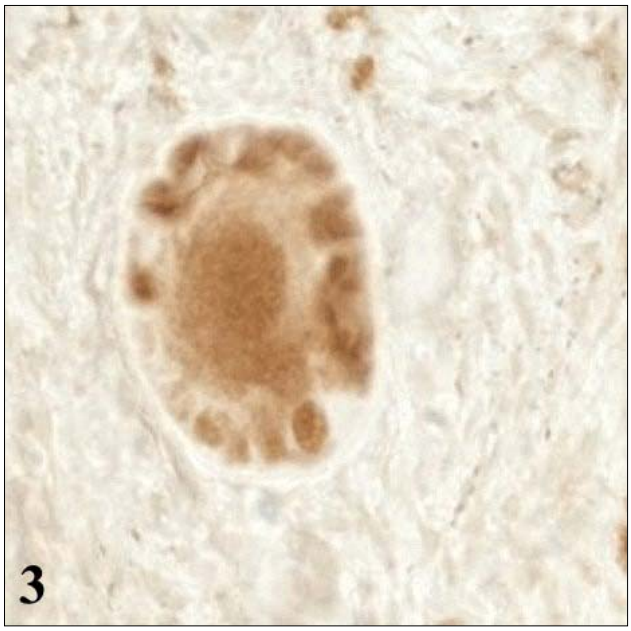

Fig. 3. Positive findings of TUNEL method confirm a fragmentation of nuclear DNA in granulosa cells and oocyte. De-eponized semithin section, 800 x.

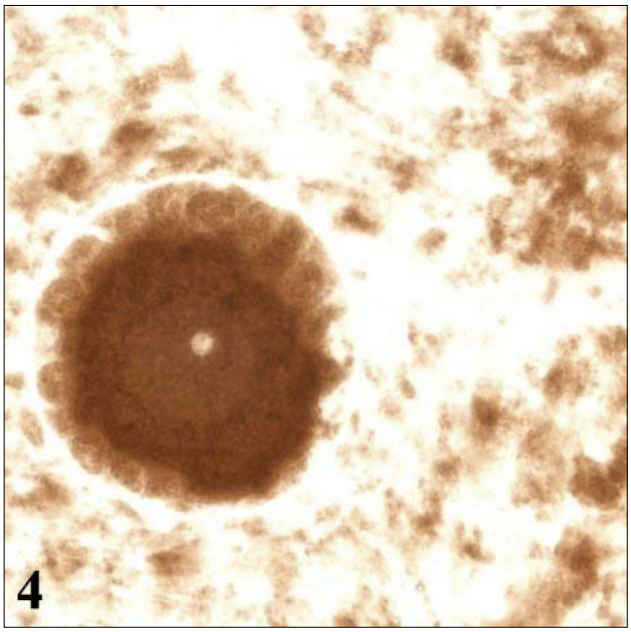

Fig. 4. Immunohistochemical expression of e-NOS in granulosa cells as well as in the ooplasm of early stimulated follicle. Paraffin section, peroxidase labeling. 720 x.

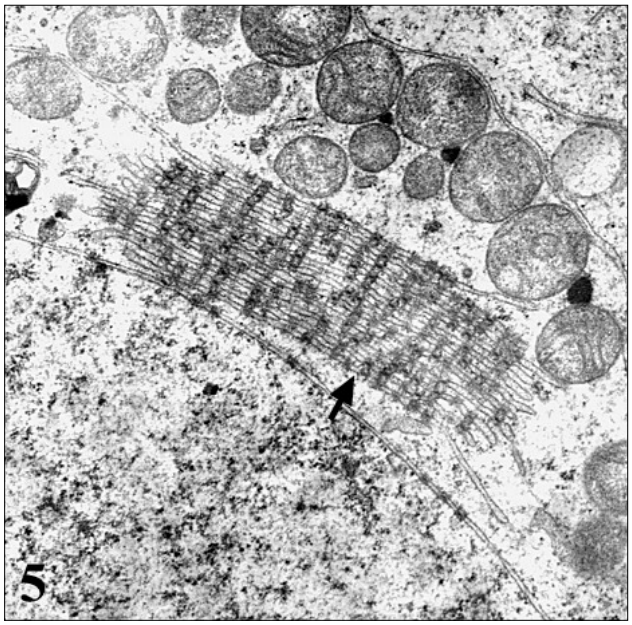

Fig. 5. Anulate lamellae in the paranuclear ooplasm agree with starting process of programmed cell death. Electron micrograph, double stained, x 6,500.

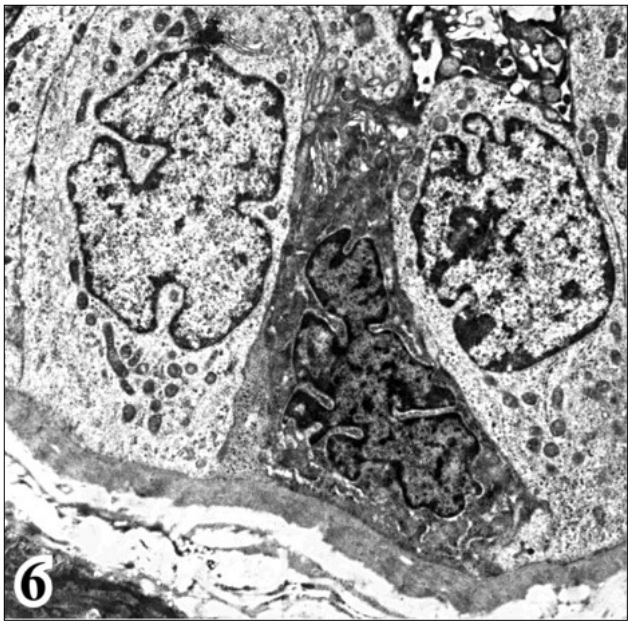

Fig. 6. Peripheral region of secondary follicle demonstrates a marked thickening of basement membrane and apoptosis of some granulosa cells. Double stained epon section, x 4,800.

in PA group and also chromosomal abnormalities were more frequent in these patients[2]. Disorders in hypothalamus-hypophysis-ovary axis can be expressed in ratio of FSH/LH. Morphological and immunohistochemical investigations of ovary confirmed distinct depletion of follicular apparatus due to stimulated and accelerated apoptotic processes (Fig. 1–3) at both (granulosa cells and oocytes). This atresia folliculi can terminate in some PA patients as complete absence of primary follicles. Residua of corpora lutea and tertiary follicles can be found in OSA patients. Expression of apoptotic markers confirmed apoptotic nature of that programmed cell death (Fig. 5,

6). A multi-factorial role in this process is supported by literature data for c-AMP[3] as well as by findings of hormonal disorders, prevalence of antiovarian autoantibodies and signal molecules as NO (Fig. 4). Therefore some non-invasive methods (hormonal levels, autoantibodies) can serve as important factors for final clinical diagnose.

ACKNOWLEDGEMENTS

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