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• **ORIGINAL PAPER** •

Expression of Survivin Gene among Human Normal Endometrium, Atypical Hyperplasia of Endometrium and Endometrial Carcinoma

Jian-ying XU[1], Shu-fang WANG[2], Zhong-yan WAN[2], Wei-jie ZHU[1]

1. Institute of Reproductive Immunology, Jinan University, Guangzhou 510632, China

2. Department of Obstetrics and Gynecology, the Second People Hospital of Zhuhai, Zhuhai 519000, China

Objective *To investigate the expression of survivin gene among human normal endometrium, atypical hyperplasia of endometrium, and endometrial carcinoma.*

Methods *Tissue samples of human normal endometrium during proliferative phase (NE, n=20), atypical hyperplasia of endometrium (AHE, n=11), and endometrial carcinoma (EC, n=9) were collected. Besides, Paraffin embedded sections of NE (n=20), AHE (n=20), and EC (n=20) were used. The expression of survivin gene was determined by immunohistochemistry and the real-time reverse transcription polymerase chain reaction.*

Results *Survivin immunostaining appeared in the cytoplasm of endometrial epithelial cells. Both survivin staining and mRNA had higher levels in AHE or EC than those in NE ($P<0.01$). No difference was found on survivin staining and mRNA between AHE and EC ($P>0.05$).*

Conclusion *High expression of survivin gene in human endometrium is associated with the risk of atypical hyperplasia progressing to endometrial carcinoma. The high level of survivin expression is useful as a predictive indicator for endometrial carcinoma.*

Key words: survivin; endometrium; atypical hyperplasia of endometrium; endometrial carcinoma

Survivin gene has been designated as a member of the inhibitor of apoptosis (IAP) gene family since 1997[1]. This gene contains a single baculovirus IAP repeat and lacks a carboxyl-terminal ring finger. Survivin gene encoded a structurally unique IAP is a powerful

Corresponding author: Wei-jie ZHU; Tel: +86-20-85225718; E-mail: tzhuwj@jnu.edu.cn

inhibitor of apoptosis gene, and is implicated in mitosis regulation and preservation of cell viability[2]. It is required for suppression of apoptosis as a direct inhibitor of caspase-3 and caspase-7, and ensures cell division in the G_2/M phase of the cell cycle[3]. Survivin gene has been found to be expressed during development and in proliferating cells, and has been undetectable in the most differentiated tissues. On the other hand, survivin gene is highly expressed in most human malignancies such as hepatocellular carcinoma, breast carcinoma, epithelial ovarian carcinoma and cervical carcinoma[4-7].

Despite advance on the diagnosis and treatment of gynecological cancer, endometrial carcinoma associated mortality rate seems to increase in relation with the gradually rising annual incidence[8]. If asymptomatic women at early-stage of endometrial carcinoma were efficiently diagnosed, the majority of them would be healing well after hysterectomy. Atypical hyperplasia of endometrium is considered a precancerous lesion for estrogen-driven endometrial carcinoma, and has been most strongly associated with progression to endometrial carcinoma[9]. The present study was carried out to investigate the expression of survivin gene among human normal endometrium, atypical hyperplasia of endometrium and endometrial carcinoma, and to elucidate whether survivin expression level would be useful as a predictive indicator for endometrial carcinoma.

Materials & Methods

Tissue samples

Tissue samples of human atypical hyperplasia of endometrium (AHE, *n*=11) and endometrial carcinoma (EC, *n*=9) were obtained at hysterectomy or diagnostic curettage, and the patients were 51.3 ± 4.7 (34–59) and 56.1 ± 5.4 (41–68) years old, respectively. Samples of human normal endometrium during proliferative phase (NE, *n*=20) were collected from benign uterine disease that unrelated to endometrial dysfunction (e.g., leiomyoma, cervical dysplasia, uterine prolaps), and the patients were 48.4 ± 3.9 (31–54) years old. Inclusion criteria were that histology of all malignant samples was endometrioid adenocarcinoma. Exclusion criteria were that patients received exogenous hormone treatment and chemotherapy within the last 3 months before surgery. All patients signed informed consent letters and the study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University and the Second People Hospital of Zhuhai.

One part of each sample was immediately frozen in liquid nitrogen and subsequently stored at −70℃ until further process for real-time reverse transcription polymerase chain reaction (RT-PCR). The other part was fixed in 10% formalin and embedded in paraffin for the histopathological examination and immunohistochemistry.