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From Leiomyoma to Leiomyosarcoma: Role of Obesity

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Abstract

Leiomyoma and leiomyosarcome (LMS) appear as two stages of tumor progression process of a transformed smooth muscle cell. Obesity is a well-established risk factor of leiomyoma. The connection between both of them are not well understood. The involvement of obesity in this transformation needs more investigation to be highlighted. Here, we discussed from a tumor immunology perspective, by focusing on the microenvironment immunosuppression that, probably, allows LMS to escape the antitumor immune response.

Editorial

Leiomyoma are benign monoclonal tumor arising from the smooth muscle cell of the myometrium. Leiomyoma are the most common indication for gynecologic surgery in the U.S. and accounts for around 350,000 hysterectomies and 30,000 myomectomies per year [1]. Common symptoms of leiomyoma are heavy and prolonged menstrual bleeding, pelvic pain, dysmenorrheal, urinary incontinence, sexual dysfunction, lower back pain, and sub fertility as well as pregnancy complications [2]. Cumulative exposure to estrogen and progesterone is believed to be a major etiologic factor [3], and may influence the hormonal milieu. Leiomyosarcoma (LMS) is a rare tumor that represents 1% of described uterine tumors. However, at the diagnosis LMS mimics the phenotype of leiomyoma. At the pathological level, the difference between leiomyoma and LMS are resumed in the presence of infiltrative borders, coagulative necrosis and nuclear atypia [4-5].

Obesity is a major established risk factor of malignancies promotion and growth increase that can lead to metastasis. The fat tissue produces and releases adipokines and hormones like a lymphatic organ, which increases the risk of leiomyoma and certainly LMS [6]. The question is, why doesn't leiomyoma progress to LMS? Are there biomarkers able to establish the possible connection between both entities? The answers to those questions will help the development of clinical management for both diseases. The connection between leiomyoma and LMS is not clear [7-8]. Studies of the transformation process from benign tumor, such as leiomyoma, to full tumorigenic phenotype exhibited by LMS are needed. Based on our cumulated experiences in the field of tumor immunology, immunosuppression is the key of tumor progression and metastasis. We know that inflammation is promoted in leiomyoma, but not enough to lead to the LMS stage, maybe due to the involvement of steroid hormones: Estrogen

and/or Progesterone signaling alteration. To highlight this area, the characterization of the immune signature in leiomyoma and LMS needs more investigation to establish possible links that will explain their connection.

A growing body of studies are supporting the inflammatory status of leiomyoma but not yet the immunosuppression characteristics reported from regular immunogenic tumors. Leiomyoma expresses and releases several pro-inflammatory cytokines such as, TNF-α, IFN-Y, IL-6 [9-10]. The microenvironment milieu of either leiomyoma or LMS are supposed to be mixtures of infiltrating immune cells (T-cells, B-cells, NK cells, macrophages, dendritic cells). Usually, these immune cells assure the immunosurveillance of the normal myometrium. Their role is to clear through inflammatory response, the resultant damage from stress assault on myometrium tissue. We know that tumor cells release pro-inflammatory cytokines and up-regulate ligands to induce the immunosuppression and evade the tumor immune response. The tumor pro-inflammatory cytokines are able to polarize effecter CD4 T-cells to regulatory T-cells that suppress cytotoxic CD8 T-cells [11-13]. We believe that the immune system could be able to block the progression of leiomyoma to LMS. Based on that, LMS will be the result of Leiomyoma that escape the tumor immune response generated by the local immune system. Also, we recommend that the involvement of adipose tissue expansion, related to obesity, needs to be compared between both groups, in animal model settings. Finally, this matter to solve the issue of LMS clinical management impact and risk on the health of concerned women patients, is our priority.

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