Uterine Fibroid Pseudocapsule: an Update of its Importance in Fibroid Management and Female Reproduction

Dr. Andrea Tinelli, MD, Prof

Abstract -- Uterine fibroids or myomas are the most common benign tumors of the female genital tracts, consisting mainly of smooth muscle cells with different amounts of fibrous tissue and are benign. During its growth, fibroid causes compressive phenomena on the surrounding myometrium, that for ischemic phenomena, produce a sort of pseudocapsule, constituted by a surrounding network of collagen fibers, neurofibers and blood vessels, as a separate fibroneurovascular tissue. Occasionally the pseudocapsule surface is interrupted by collagen fibers and vessels that anchor the fibroid to myometrium, well represented in microscopic sections. At the ultrastructural level, visualized by transmission electron microscopy, the pseudocapsule cells have the features of smooth muscle cells similar to the myometrium. So, the pseudocapsules are part of the myometrium which compresses the leiomyoma. Studies confirmed preliminary evidence that pseudocapsules is rich of neuropeptides together with their related fibers, as a neurovascular bundle, containing a vascular network rich in neurotransmitters, as a neurovascular bundle, with biological very important biological functions and a significant impact on the reproductive uterine functions. In this paper, after a review of all papers in such topic, I summarize the importance of this small structure in the context of the myometrium, for the purpose anatomical, pathophysiological and reproductive systems.

Keywords -- Uterine fibroids, myoma, myoma pseudocapsule, laparoscopic myomectomy, reproductive system, delivery.

International Translational Medicine and Biomodelling Research Group, Department of Applied Mathematics, Moscow Institute of Physics and Technology (State University) Moscow Region, Russia.
Department of Gynecology and Obstetrics, Division of Experimental Endoscopic Surgery, Imaging, Minimally Invasive Therapy and Technology, Vito Fazzi Hospital, Lecce, 73100, Italy.
Tel. +39/3392074078
Fax: +39/0832661511
E-mail: andreatinelli@gmail.com; andrea.tinelli@unisalento.it

1. INTRODUCTION

Uterine leiomyomas are the most common benign tumors of the genital organs of women of childbearing age, could have negative impact on reproductive system, can be single but are often multiple, causing significant female morbidity, with large interference on the quality of life. They typically referred as fibroids and arising from uterine smooth muscle cells, are the most frequent benign tumors of the female reproductive tract [1].

Literature data show that 5.4 to 77% of women have myomas, depending either on the study population or by diagnostic techniques applied to myoma detecting [2].

The first who described uterine myomas was Matthew Bailee in 1793: they consist mainly of smooth muscle cells with different amounts of fibrous tissue [3]. According to Blake, “leiomyomas may have single or multiple mutated smooth-muscle tumor nodules of varying size attached and/or within the myometrium that are encircled by varying amounts of extracellular fibrous connective tissue”. Histopathologically, they are well circumscribed, pseudoen capsulated, solid, and pearly white or lightly tanned round masses ranging from 1 mm to 30 cm in size. Microscopically, they have interlacing bundles of spindle-shaped or stellate smooth muscle cells with little cellular pleomorphism or mitotic activity [4].

Epidemiologic factors associated with the development of myomas are not yet fully understood, and they include many factors, as age race, heritage, reproductive factors, sex hormones, obesity, lifestyle (diet, caffeine and alcohol consumption, smoking, physical activity, stress and t alc use), environmental and other influences (hypertension, infection). Some of the epidemiological data are conflicting.

Clinically, fibroids are mostly asymptomatic and are often found incidentally on pelvic examination or by ultrasound (US); alternatively, they can present with menstrual irregularities, menorrhagia, and pelvic pain, which may vary depending on both locations and growth rate [5].

The initiation and growth pathways of fibroids have been studied extensively, but the exact initiation mechanism remains unknown. Recently, Wei et al demonstrated that in large uterine fibroids, the most
biologically active zone is the region next to the periphery with a higher level of gene expression, a higher density of blood vessels, a higher proliferative rate, and a lower level of hyaline degeneration [6]. During its growth, myoma determines compression phenomena on the surrounding structures (myometrial and connective tissue), that for ischemic phenomena involve the progressive formation of a sort of pseudocapsule, constituted by a surrounding network of collagen fibers, neurofibers and blood vessels, as fibroneurovascular tissue (Figure 1).

Occasionally the continuous surface of the pseudocapsule is interrupted by bridges of collagen fibers and vessels that anchor the myoma to myometrium. It allows a constitution of a clear cleavage plane between myoma and the pseudocapsule, and between the pseudocapsule and the surrounding myometrium. The pseudocapsule allows to myoma only a displacement action (but not destructive) on myometrium, retaining the integrity and contractility of uterine structure [7].

This structure was recently largely analyzed in literature, showing increasing interest to researchers, since many investigations has looked into the functional and structural characteristics of uterine fibroid pseudocapsules. This structure was analyzed in its thickness [8] by a study involving ultrasound and histology data matching on: subserosal fibroids (SSF); intramural fibroids (IMF) and fibroids near the endometrial cavity (FEC). FEC’s pseudocapsules were considerably thicker than those of IMF and SSF measured by US and histology (P = 0.001). A clear cut-off existed between FEC pseudocapsule thickness and all other pseudocapsules, with significant differences observed at 2 mm (P = 0.001). Similarity between histological and US measurements was observed only with IMF pseudocapsules, whereas FEC or SSF showed significant differences. The pseudocapsule of fibroids is considerably thicker near the endometrial cavity when compared those of both intramural and subserosal fibroids.

Since fibroids closest to the endometrial cavity are the most involved in fertility and infertility [9,10] and fibroid pseudocapsule is considerably thicker near the endometrial cavity, it is possible to hypothesize an involvement of fibroid pseudocapsule near on endometrium, since pseudocapsule contains many neuropeptides and neurotransmitters that are physiologically active. In fact, pseudocapsules contain many neuropeptides and neurotransmitters that are physiologically active in many physiological neuro-vascular-muscular actions: enkephalin (ENK) and oxytocin (OXT), neotensin (NT) and protein gene product 9.5 (PGP9.5) and neuropeptide tyrosine (NPY), vasoactive intestinal polypeptide (VIP) and substance P (SP) [11-14]. These substances play a significant role in wound healing [15-17] and innervation of repairing tissues [18,19], and are essential for reproductive [20,21] and sexual function [22,23]. Indeed, the lower urinary tract neuropeptide-receptor system may represent a potential target also for therapeutic interventions [24,25]. These neurotransmitters in uterine tissue vary considerably depending on the sampling site, being substantively increased in the region of the uterine isthmus [12-14,26,27].
Structurally, the fibroid pseudocapsule is the portion of the myometrium in closer contact with the myoma [28], enriched of blood vessels and neurotransmitters, as a neurovascular bundle with a distinct endocrine peculiarity [7,11-15]. The uterine fibroid pseudocapsules has specific biological properties and peculiarities. The gene expression profiles display a specific angiogenic profile [29] and a geometrical analysis revealed an highly complex vasculature network of myoma pseudocapsule, with geometrical characteristics similar to those in malignant neoplasms [30]. Thus, the pseudocapsule angiogenic profile would suggest a sort of system-intrinsic muscular reparative system, as a biological microchip ready to repair damage caused by myoma growth, due to its highly complex auto-angiogenic vasculature network. Therefore, the fibroid removal absolutely must preserve this delicate structure of a few millimeters, independently both by laparoscopic or open approach, by a sort of pseudocapsule sparing. Certainly, the surgical technique of pseudocapsule sparing is easier to perform by laparoscopic or robotic surgery, since it works on a structure of a few millimeters with better magnification of the image [31,32]. This procedure to preserve the pseudocapsule neurovascular fibers reduces myometrial damage and the surgical blood loss [33], with favorable impact on fertility outcomes, especially if applied when the fibroid is under 6 cm of diameter [34]. Since fibroids may give rise to specific obstetrical complications such as pain due to degeneration, fetal malpresentation, or placenta previa, even during delivery of a patients with uterine fibroids it is possible to enucleate fibroids by pseudocapsule preserving, with favourable outcome [27]. There are still many aspects of fibroids that have not yet been analyzed, but certainly this structure surrounding fibroid showed many peculiarities of the utmost importance in the management and in the reproductive outcomes after myomectomy.

REFERENCES


