Estudio ecográfico de la unión mioendometrial

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Resumen

En los ultimos años ha surgido un nuevo concepto anatomico denominado la union mioendometrial. Dicha union es valorada por ecografia y se le ha relacionado directamente con la presencia de adenomiosis. Sin embargo, parece que se trata de dos entidades diferentes y su relacion con la fertilidad podria ser diferente.

Palabras clave: adenomiosis, infertilidad, ecografia, unión mioendometrial

Summary

Abnormal thickening of the Endometrial Subendometrial Myometrium Unit (ESEMy Unit, including basal endometrium and inner myometrium) has been detected on imaging and referred to as "diffuse adenomyosis" in infertile patients with proven endometriosis. However, no robust relationship exists between enlargement of the ESEMy Unit and adenomyosis proven on hysterectomy specimen examination; moreover, if any correlation exists, it lacks histological validation in women wishing to preserve fertility. While adenomyosis effects on fertility, if any, remain elusive, thickening of the ESEMy Unit have been consistently linked to fertility impairment in both experimental and clinical models. The hypothesis tested herein is that a novel condition exists, called "ESEMy Unit disruption disease"; it is epidemiologically different from adenomyosis, diagnosable on imaging and bears a clear impact on human fertility through various mechanisms. A new wave of good quality studies may be elicited by a clear distinction between adenomyosis and the "ESEMy Unit disruption disease".

Key words: adenomyosis; infertility; subendometrial myometrium; ultrasound.

Physiological non-gravid human uterus is composed by different tissue layers; in particular, the Endometrial Subendometrial Myometrium Unit (ESEMy Unit) includes basal endometrium (basal and initial glands branches surrounded by stromal components) and inner (subendometrial) myometrium[1], surrounded by outer myometrium. The ESEMy Unit is thought to play a pivotal role in several reproductive processes with potential profound influence on various reproductive functions[2]. Outer myometrium and ESEMy Unit have different embryological origin, cellular composition, receptor expression and functional activity. Outer myometrium is thought to derive from mesenchymal cells of non-paramesonephric origin, while ESEMy Unit originates from paramesonephric ducts[1]. In outer myometrium, smooth muscle cells are spatially organized either as a mesh of short fibers (stratum vasculare, inner part) or longitudinally (stratum supravasculare, subserosal part), while in subendometrial myometrium they are circularly oriented[3] and larger in size, richer in cell nuclei, and contain a lower water content compared to outer myometrium and endometrium[4]. In subendometrial myometrium, the expression of estrogen and progesteron receptors is similar to that displayed by the endometrium and is modulated throughout the menstrual cycle, a pattern that differs from that displayed by part of the outer myometrium or post-menopausal uterus where cyclic patterns are replaced by high constitutive expression[1]. Functionally, ESEMy Unit displays a wavy movement ("uterine peristalsis") mainly generated by the subendometrial myometrium whose occurrence and direction is variably reported in conflicting studies displaying either a peristaltic maximal activity[5] or suppression[6] during the periovulatory phase.

ESEMy Unit visualization has been attempted on ultrasound (US) and magnetic resonance imaging (MRI): "myometrial halo" and "junctional zone" are currently regarded as the imaging counterparts of the outer ESEMy Unit (the subendometrial myometrium) on US and MRI respectively[7,8]. The correlation between myometrial halo and junctional zone has been only object of hypotheses[9] and precise correlation studies between imaging and tissue composition are lacking; nevertheless, enlargement of the ESEMy Unit observed on MRI has been claimed has a major criterion for diagnosing diffuse adenomyosis in women bearing endometriosis[10] and a theory on a common origin of endometriosis and adenomyosis has been generated[11]. The diagnosis of adenomyosis on imaging has been repeatedly reported

by many groups on small numbers of patients, although the accuracy of either US or MRI is usually low outside a research context (reviewed in[12]).

Thickening of subendometrial myometrium and adenomyosis have different epidemiological profiles: large "myometrial halo" or "junctional zone" prevail in young infertile women (mean age 33 years) bearing pelvic endometriosis and correlate with previous use of intrauterine devices, dysmenorrhea, exposure to diethylstilbestrol or clomiphene citrate and the use of assisted reproduction techniques, while fibroids, uterine malformations, abnormal uterine bleeding, previous caesarean section, dilatation and curettage or history of miscarriage have been excluded in women displaying large junctional zones[12]. Conversely, adenomyosis proven on hysterectomy specimen examination has been consistently associated to older multiparous patients in their 40s-early 60s and linked to previous caesarean section, dilatation and curettage, miscarriage, uterine malformation, use of tamoxifen, abnormal uterine bleeding, late age at menarche or endometrial hyperplasia, while no association has been found with dysmenorrhea, chronic pelvic pain, termination of pregnancy, use of oral contraceptive, dyspareunia, or use of intrauterine device[12]. Interestingly, epidemiological profiles of women with a surgical diagnosis of adenomyosis also differ from those of women with a surgical diagnosis of endometriosis[13].

In women undergoing US or MRI, the highest thickness of the uterine zones obtained at perpendicular cross section of the uterine body has been measured[9]: in normal controls, US thickness of the ESEMy Unit has been reported as hypoechoic halo (myometrial halo) surrounding the endometrium and variably measured as one third of the total myometrium[14], 3.5 + 1.1 mm (15), or 2.2 + 0.00 mm[9], or the thickness of the combined endometrium and subendometrial myometrium[9] with no differences between the follicular and luteal phase or patient age. In healthy women undergoing MRI, the ESEMy Unit has been also variably reported as subendometrial myometrium (junctional zone) with a thickness of 2-8 mm[8] or as thickness of the combined endometrium and subendometrial myometrium[9, 16] measuring 15.9 + 3.9 mm in one study[9]. Criteria for assessing abnormal thickening of ESEMy Unit are not established: in a small study on women with proven endometriosis, an age-dependent 5.2-6.8 mm mean thickness has been reported on US, significantly different from that of healthy women, while on MRI the junctional zone thickness was found at 9.4 + 3.1 mm in endometriosis-bearing patients, significantly different from that of healthy subjects[15]. For measurement of ESEMy Unit thickness, MRI have been privileged in recent years; however, MRI is expensive and require specific training and technical adjustment, therefore is unpractical in routine clinical settings; in addition, the best accuracies reported in literature lack robust validation in women who wish to preserve fertility, and physiological contractions of the subendometrial myometrium may impair correct measurement[17-19]. Although new US markers for the diagnosis of adenomyosis in infertile women have been recently published[20], consensus criteria for US diagnosis of adenomyosis are still lacking. US measurement is safe, cheap and more widely applicable in routine practice.

Although the precise cell composition and tissue architecture of the myometrial halo or junctional zone have not been firmly elucidated, "abnormal" thickening of part of the ESEMy Unit has been repeatedly reported to impair several reproductive function in both animals, non human primates and humans (reviewed in depth in[12]). Research has recently focused on a single mechanism to explain the reproductive function impairment, i.e. changes in the direction and extent of uterine peristalsis causing disturbed sperm transportation[21]; however, many additional mechanism have been indicated as causative factors for reproductive impairment, including smaller uterine volume, impaired implantation and loss of nerve fibres at the endometrial-myometrial interface causing high prevalence of pre-eclampsia[12]. Some of these mechanisms are neither justified nor caused by perturbation of uterine peristalsis. The endometrial counterpart of the ESEMy Unit has been usually excluded from studies, largely focusing on the subendometrial myometrium. Also, the cervical area has not been considered in most studies.

Preliminary data from our group confirm that ESEMy Unit can be reliably measured in early follicular phase[22] on both transabdominal and transvaginal ultrasound in healthy young nulliparae patients not taking medications, with no fibroids or endometrial problems, not undergoing treatments for infertility, with no previous use of intrauterine devices or presence of uterine malformations detectable on US. Reproducibility is higher when the entire ESEMy Unit including both basal endometrium and subendometrial halo is measured as an area, thus reducing the possible pitfalls arising from transient uterine contractions[17]. Cervical area should also be included, when visible. Preliminary observations show that, in assisted reproduction cycles with controlled ovarian hyperstimulation, ESEMy Unit measurement is difficult or impossible starting from day 5, possibly due to histological changes occurring in this area.

In conclusion, the "ESEMy Unit disruption disease" is proposed as a novel nosological entity, distinguished from adenomyosis and assessable on US with a broad potential to explain impairment in spontaneous fertility, implantation failure, recurrent miscarriage and failed assisted reproduction.

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