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## Research Article

# Intravascular Involvement in Adenomyosis: An Endometriosis Dissemination Pathway?

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### ABSTRACT

Intravascular adenomyosis is an entity described for years in the literature, but its clinical-pathologic correlation hasn't been studied in detail.

**Objective:** To study the prevalence of adenomyosis including intravascular involvement, as well as available literature review about this pathology.

**Material and Methods:** A retrospective observational study has been conducted in our hospital analysing hysterectomies specimens from January to December 2020.

**Results:** 447 hysterectomies specimens have been analysed, 68 with adenomyosis and just one with intravascular involvement.

**Conclusion:** Intravascular involvement adenomyosis is a rare entity but with potential etiopathogenic consequence.

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## Introduction

Adenomyosis is a benign uterus condition, defined as the presence of ectopic endometrial glands and stroma within the myometrium. Prevalence report is around 1 to 70%. This wide range show the lack of consensus on standard diagnostic criteria, both imaging studies and histopathology analysis [1]. Number of diagnostic strategies are being developed in the last few years, specially focus on imaging studies like two or three dimensional transvaginal ultrasound and magnetic resonance imaging. In the same way, it aims to set universal standards according to imaging studies findings.

It's an ordinary condition, but its etiology and natural history remains unknown now. There are four pathogenesis theories proposed: the first one (most widely accepted) explains a myometrial invasion from endometrial tissue. It remains unknown the motivation of this irruption, however it might be related to prior pregnancies (angiogenesis and trophoblast invasion), surgeries or immunological abnormal activity among endometrial-myometrial junction (endometrial tissue break-in myometrium during regeneration, healing process and re-epithelization)

[2]. Another second theory claims that adenomyosis is the result of embryonic pluripotent Müllerian remnants. This belief come from adenomyosis finding out of myometrial thickness (recto-vaginal septum) in a Rokitansky-Kuster-Hauser syndrome patient, thus, without functional endometrium [3].

An additional one hypothesis states that adenomyosis would be the consequence of endometrial basal invagination throughout intramyometrial linfatic system. Finally, there is the assumption that this pathology might be arise from bone marrow stem cells. It is not clear why adenomyosis appears in some women and not in others to date, though, it has been noted ultrastructural differences at smooth muscle cells level in adenomyosis uterus compared to normal [4].

Moreover, it has been recognized several risk factors that would increase the incidence, among which is hiperestrogenic environment (early menarche, body mass index, Tamoxifen previous treatment, oral contraceptives, ...). As well it has been associated with parity and previous uterine surgeries. On the other hand, it seems to be that women smoking would have lower risk [5]. As for the treatment, hysterectomy

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is the currently definitive management, although there are various alternatives that can mitigate the symptoms. We provide medical therapies on one side, non-steroidal anti-inflammatory drug, contraceptive oral pills, gestagenics, and even Danazol or Gonadotropin-releasing hormone agonist (GnRH). Similarly, there are several surgical techniques among which are endometrial ablation, hysteroscopy, uterine arterial embolization.

Settle on the best treatment in each case is complex, because of heterogeneous symptoms and others gynaecological conditions associated to adenomyosis, like endometriosis or myomas. From what, the decision will be based on factors like age, symptom severity, reproductive desire and comorbidities. Focusing on involvement intravascular in adenomyosis, there aren't many recent publications about it, for what the limited data is available. Intravascular involvement adenomyosis has been found in a series of hysterectomies in 12.4% of this adenomyosis uterus [6].

### Materials and Methods

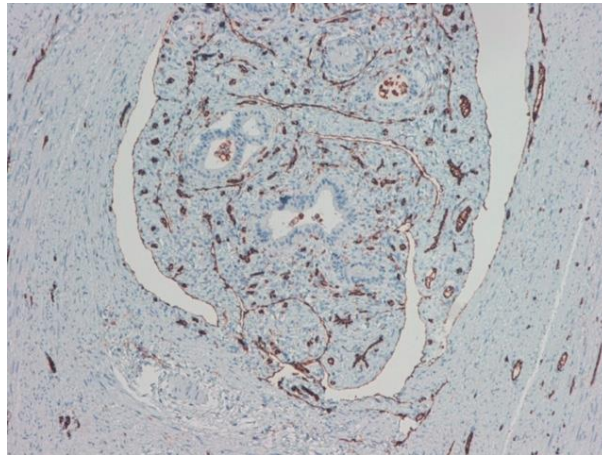
For this review, anatomopathological reports from every hysterectomies procedure at University Hospital Virgen Arrixaca were revised from January to December 2020. It is therefore a retrospective observational

study. The appearance or not of adenomyosis and, the presence or not of intravascular involvement in adenomyosis were the variables included. Within the adenomyosis group, the age, uterine weight and concomitant endometriosis and/or oncological diseases have been analysed too.

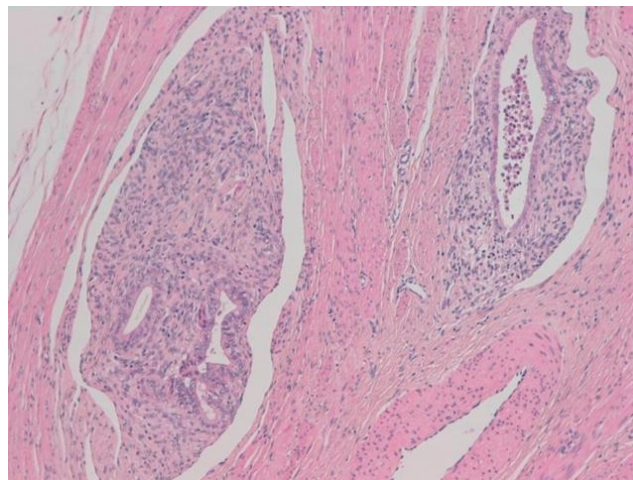
### Results

447 hysterectomies procedures in our center. 68 (15.1%) have been diagnosed like adenomyosis by pathologists. The mean age of these women was 51.57 years, and the mean uterine weight was 200.77 grams. Endometriosis was present in 29.41% (20) of adenomyosis, and 25 hysterectomies cases had been made in an oncological context (16 of whom have been for endometrial adenocarcinoma, which represents the 23.53% of adenomyosis).

In only one surgical specimen was detected intravascular involvement, inform like "perivascular / intravascular zones placement with growth towards vascular lumen, always been endotelized in their surfaces (immunohistochemical techniques confirmed)" (Figure 1). "In other ways, active endometrial mucosa had been identified within intramyometrial veins, surrounded by red blood cells and plasma" (Figure 2).



**Figure 1:** Adenomyosis with intravascular involvement. Focus covered by endometrium. (CD31 marker).



**Figure 2:** Adenomyosis with intravascular involvement. Hematoxylin-eosin stain.

## Discussion

In 447 hysterectomies reviewed, we recognize 15.21% of adenomyotic uterus. Lower prevalence compared other reported series, since average frequency was over 20 and 30% [1]. Adenomyosis and endometriosis were considered part of the same entity until 1920s, but after define them like different pathologies, several studies have enquired about the relationship between them [7]. 29.41 % of adenomyosis have endometriosis associated (adenomyosis intravascular involvement included), higher percentage compared with other studies reported, as that of Di Donato *et al.*, which discuss a 21.28% of correlation among these two entities [7].

Vascular involvement can lead to a malign misdiagnosed, this is why pathologist knowledge of this entity is required. It might be mistaken for endometrial stromal sarcoma, which is distinguished by absence of a macroscopic mass (unless an adenomyoma), as well as typical uterine adenomyosis appearance. In addition, stromal cells look atrophic in adenomyosis, in contrast to sarcoma expansive growth pattern which could spreads outside uterus [6]. Conversely, there is another entity, intravascular leiomyomatosis, which is smooth muscle tumoral cells mass growing into uterine venous system. It comes along with a leiomyoma and, sometimes with adenomyosis. Smooth muscle cells presence would be the key of differential diagnosis with adenomyosis with intravascular involvement [8].

Despite of have just diagnosed only an adenomyosis with intravascular involvement, it should be considered. It may not have clinical significance, but it might be speculated that intravascular tissue could shatter from vessel wall giving the meaning of brain and lung endometriosis, places where the two common histopathological endometriosis theories (retrograde menstruation theory and coelomic metaplasia theory) cannot justify the endometrial tissue presence [6]. Intravascular growth could involve a potential way of disease dissemination.

## Conflicts of Interest

None.

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