ADENOMYOSIS. ETIOPHATOGENICAL, DIAGNOSTIC AND THERAPEUTICAL CONSIDERATIONS

ABSTRACT

SCIENTIFIC COORDINATOR:

PROF. DR. MIHAI B. BRĂILA, Ph.D.

Ph.D. Candidate:

DR. POPEȘCU CRISTIAN-IOAN

CRAIOVA 2011
INTRODUCTION

Adenomyosis is a frequent condition which is commonly expressed by menorrhagia in premenopausal women. Other conditions such as: benign endometrial hyperplasia, endometrial adenocarcinoma, intracavitary myomas, dysfunctional uterine bleedings present themselves with menorrhagia as the main symptom and, most frequently, at the same age as adenomyosis.

Usually, the diagnosis of adenomyosis is a histopathological one. Nevertheless, efforts should be made by all practitioners in order to establish the diagnosis as soon as possible because adenomyosis is a surgical condition.

GENERAL SECTION

Chapter 1. – Reproductive embryogenesis

The development of the ovary, genital ducts and vagina, as well as molecular regulation of this development are thoroughly presented.

Chapter 2. – Endometriosis. Etiopathology. Diagnostic. Therapeutic Strategy

Endometriosis is a condition characterized by the ectopic presence of endometrial tissue (glands and stroma).

John Sampson was the first author who suggested, in 1921, that pelvic endometriosis arises from seedings of ovarian endometriosis. He hypothesized that the retrograde flow of endometrial tissue is the probable
cause of the disease. The present theories concerning the etiopathogeny of endometriosis are the following:

1. The theory of endometrial tissue transplantation
2. The theory of coelomic metaplasia
3. The theory of induction

The clinical findings, the imaging, the role of CA-125, laparoscopy, classification and staging, as well as the therapeutic strategy are fully discussed.

Chapter 3. – Dysfunctional uterine bleedings

The physiopathology and the diagnosis of dysfunctional uterine bleedings, especially in premenopausal women are presented.

SPECIAL SECTION

Chapter 4. – Adenomyosis. Genetic or acquired pathology?
The importance of adenomyosis in current practice

Adenomyosis was described for the first time by Rokitansky in 1860 and more clearly defined by von Recklinghausen in 1896 under the term of “adenomyomata and cystadenomata” of the uterus and the fallopian tube wall. The name of adenomyosis was used first by Frankl in 1925.

Adenomyosis is characterized by the presence of multiple intramyometrial small ducts lined by endometrial mucosa (glands and stroma) and communicating with the uterine cavity.

Cullen, in 1908, stated that adenomyosis represents the migration step by step of normal endometrium into the myometrium.
Traditionally, the histologic diagnosis of adenomyosis is established when endometrial glands and stroma are seen at least at one small power microscopic field under the endometrial junction.

Hoang – Ngoc Minh et al, in 1992, gave another explanation to the intramyometrial ducts: glandular tubes which are originating in the mullerian blastem and migrate from the myometrium towards the uterine cavity. The proliferative potential of the mullerian blastem cells could be activated in the adult life by the presence of some inductors, such as fragments of endometrial tissue carried during menses into the vascular return system of the uterus, catamenial products of degradation transported into the transition zone: proteins, enzymes, freed from the lysosomes of the endometrial disintegrated cells; different other substances which can modify the subcellular receptors, the intercellular matrix or the activity of some growth factors.

Adenomyosis should usually be considered in a woman of 40 to 50 years presenting dysmenorrhea and menorrhagia of progressive intensity, with a generally enlarged, firm and sensible uterus. The preoperative diagnosis is sometimes difficult because the dysfunctional uterine bleedings and the small, multiple leiomyoma could present themselves in a similar way. The HSG, the ultrasound examination and the MRI are useful tools in establishing the diagnosis.

The uterine curettage does not help in establishing the diagnosis and is not an efficient method of treatment, even though is a frequently practiced due to the presence of heavy metrorrhagia.

The small amount of the estrogen receptors and the total absence in up to 40% of the progesterone receptors explain why all the attempts of progestative or estro-progestative treatments are doomed to failure. The GnRH agonistics therapy shrinks the uterus and abolishes the menorrhagia and dysmenorrhea, but the symptomatology reappears after the treatment. That is why the surgical treatment remains the only logical issue for adenomyosis.
Chapter 5. – Material and Methods

My study is a retrospective study and covers a period of ten years (2001 – 2010). The study group included all the patients admitted between 2001 – 2010 in which the diagnosis of adenomyosis was histopathologically confirmed. We therefore analyzed all the cases in which a hysterectomy was performed and a final histopathologic examination was obtained. From a total of 2570 hysterectomies performed during this period, the diagnosis of adenomyosis was histopathologically confirmed in 779 cases, that is in 31% of the hysterectomies.

Chapter 6. Results and Discussions

The general incidence of adenomyosis is 31% of all hysterectomies, whatever the preoperative indication.

The C-section or the myometrectomy do not appear to be risk factors for adenomyosis in our study, as was formally stated by Harris et al.

75.35% of cases with adenomyosis belonged to the 41 to 50 years age group. 82% were parous women and 89% had at least one abortion in their medical history. In 83.54% of cases the main symptom was menorrhagia, while dysmenorrhea was the main complaint in 37.97%.

The association between fibromyoma and endometrial hyperplasia with adenomyosis was present in 65%, while the association between fibromyoma or endometrial hyperplasia alone with adenomyosis was 20% and 10% respectively. 15% of all the patients in our study followed different regimens of preoperative hormonal treatments.

We were able to establish the preoperative diagnosis of adenomyosis in only 21 cases using HSG, 3D/4D ultrasonography or MRI.
Chapter 7. – Conclusions

1. Adenomyosis is a disembryoplastic condition characterized by the presence of intramyometrial ducts lined by endometrial cells and stroma whose main feature is the weak expression of estrogen receptors and the almost total absence of progesterone receptors. The practical issue of this facts is that the adenomyosis lesions do not respond to estro-progestative regimens and respond, only during the treatment, to GnRH agonists. In our study group, 15% of the patients with the final diagnosis of adenomyosis have followed preoperative progestative treatment with in fact meant a loss of time and money.

2. As shown in the literature, neither the C-section nor the myometrectomy are risk factors for adenomyosis. This in an indirect argument in favor of the disembryoplastic hypothesis.

3. The same explanation is found for the fact that in our study group the maximum incidence of adenomyosis was among adult women, over 85% of our cases were identified in women past 41 years old.

4. We have noticed an association of adenomyosis with endometrial hyperplasia in 75% and with fibromyoma in 85% of the cases. Both the fibromyoma and the endometrial hyperplasia have the same etiopathogenesis: the hyperestrogenic micro and macro climate, which is not the case for the adenomyosis.

5. In a paciente in her forties with a uterus slightly enlarged and menorrhagia, in which a biopsy reveals an endometrial hyperplasia, it is difficult to establish if the menorrhagia is the
consequence of the hyperplasia associated with fibromyoma or/and of a simultaneous adenomyosis.

6. Like other practitioners, I have noticed that the only efficient therapeutic path in adenomyosis is the surgical treatment, mostly total hysterectomy with or without adnexectomy. It seems obvious to avoid useless conservatory treatment and this can only be done by establishing the preoperative diagnosis of adenomyosis as soon as possible.

7. Unfortunately there are no available reliable biochemical, immunological or genetic markers to point out the predisposition of some women for developing adenomyosis. The discovery, in the future, of such markers is likely to facilitate an early highlighting of the intramyometrial lesions and the establishing of a quick diagnosis.

8. Adenomyosis remains an underdiagnosed condition, on one side due to the common symptomatology shared with fibromyoma associated with endometrial hyperplasia and the on the other hand due to the fact that although adenomyosis is frequently suspected, the preoperative diagnosis is difficult to sustain because of the lack of usual accessibility to advanced investigations (MRI).

9. As any gynecologist should think that endometriosis is present in one out of ten examined patients, he should also think that almost one third of the performed hysterectomies could have as a unique or associated indication the adenomyosis.
# Curriculum Vitae

## Personal information

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<tr>
<th>First name(s) / Surname(s)</th>
<th>Cristian-loan, Popescu</th>
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<tbody>
<tr>
<td>Address(es)</td>
<td>No 9, Street Iacob Negruzzi, Bucharest, Romania</td>
</tr>
<tr>
<td>Telephone(s)</td>
<td>+40 21 2234630</td>
</tr>
<tr>
<td>E-mail</td>
<td><a href="mailto:cristianpopescu53@gmail.com">cristianpopescu53@gmail.com</a></td>
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<tr>
<td>Nationality</td>
<td>Romanian</td>
</tr>
<tr>
<td>Date of birth</td>
<td>7th of August 1953</td>
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<td>Gender</td>
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## Occupational field

Obstetrics-Gynecology

## Work experience

8000 attended or supervised births

2000 C-sections

Advanced surgical proficiency in abdominal and vaginal approach

Practice Resident Instructor in Clinical Hospital Caritas since 2001

Member of the Coordination Group for the Romanian Clinical Guides in Obstetrics and Gynecology – RoNeonat Project

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<th>Occupation or position held</th>
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<tr>
<td>Chief Of Department of Obstetrics and Gynecology III – Clinical Hospital Caritas “Acad. N. Cajal”</td>
<td>01/05/2010 – 31/03/2011</td>
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<tr>
<td>Senior Practitioner in Obstetrics and Gynecology Clinical Hospital Caritas “Acad. N. Cajal”</td>
<td>2001 – 2009</td>
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<tr>
<td>Chief Of Department of Obstetrics and Gynecology Municipal Hospital Oltenita</td>
<td>1988 – 2001</td>
</tr>
<tr>
<td>Specialist in Obstetrics and Gynecology County Hospital Calarasi</td>
<td>1985 – 1988</td>
</tr>
<tr>
<td>Rezident in Obstetrics and Gynecology Emergency University Hospital of Bucharest</td>
<td>1982 – 1985</td>
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<tr>
<td>Intern Emergency University Hospital of Bucharest</td>
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Education and training

- 2004 Doctoral Studies
- 1990 Senior Practitioner in Obstetrics and Gynecology
- 1985 Specialist in Obstetrics and Gynecology
- 1982 Rezidency Addmision Exam
- 1978 Graduated from Faculty of Medicine-University of Medicine and Pharmacy “Carol Davila” Bucharest
- 1972-1978 Student of the Faculty of Medicine-University of Medicine and Pharmacy “Carol Davila” Bucharest
- 1968-1972 “Mihai Viteazu” Lyceum Bucharest

Personal skills and competences

Native language
Romanian

Other language(s)
- English: C2
- French: C2

Self-assessment

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(*) Common European Framework of Reference for Languages

Social skills and competences
- Team spirit
- Ability to adapt to multicultural environments
- Good communication skills

Technical skills and competences
- Acquired surgical abilities

Driving licence
- Full, clean, driving license since 1973

Additional information

Hobbies:
- Literature
- Sports
- Traveling

Date: 13.06.2011
Signature: Cristian Ioan Popescu