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Risk factors for adenomyosis in patients with symptomatic uterine leiomyomas

Czynniki ryzyka występowania adenomiozy u pacjentek z mięśniakami trzonu macicy

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Summary

Objective: *The aim of the study was to evaluate the potential risk factors for adenomyosis in patients with symptomatic uterine leiomyomas.*

Material and methods: *The medical charts and histopathology reports of 1499 women who underwent hysterectomy between 2003-2007 were retrospectively reviewed. The study group was composed of 135 patients with coexisting uterine leiomyoma and adenomyosis. The control group comprised 176 patients with uterine leiomyoma without adenomyosis.*

Results: *Among 233 patients with adenomyosis 135 (57.9%) had associated uterine fibroids. Women who delivered twice or more were at increased risk for adenomyosis in relation to nulliparuos women: RR (95% CI) 2.44 (1.04-5.72), p=0.040. No relationship was found between adenomyosis and cesarean section rate, abortions, menorrhagia or dysmenorrhea.*

Conclusion: *Results of our study indicate that multiparity is a risk factor for adenomyosis in women with symptomatic leiomyomas.*

Key words: **adenomyosis** / **uterine leiomyoma** / **hysterectomy** / **parity** /

Streszczenie

Cel pracy: *Celem badania była ocena potencjalnych czynników ryzyka występowania adenomiozy u pacjentek operowanych z powodu mięśniaków macicy.*

Materiał i metody: *Retrospektywnej analizie poddano historie chorób oraz wyniki pooperacyjnych badań histopatologicznych 1499 pacjentek, u których wykonano histerektomię w latach 2003-2007. Badana grupa obejmowała 135 pacjentki, u których zdiagnozowano mięśniaki macicy oraz adenomiozę. Do grupy kontrolnej zakwalifikowywano pacjentki z rozpoznaną mięśniakowatością macicy, bez adenomiozy.*

Wyniki: *Wśród 233 pacjentek ze zdiagnozowaną adenomiozą, u 135 (57,9%) zdiagnozowano mięśniaki macicy. Kobiety rodzące dwa bądź więcej razy były w grupie zwiększonego ryzyka występowania adenomiozy w porównaniu z nieródkami: RR (95% CI) 2.44 (1,04-5,72), p=0,040. Nie wykazano zależności pomiędzy występowaniem adenomiozy i ilością cięć cesarskich, poronieniami, nieprawidłowymi krwawieniami i bolesnym miesiączkowaniem.*

Wnioski: *Wyniki naszego badania wskazują, że wielorództwo u kobiet z mięśniakami macicy jest czynnikiem ryzyka występowania adenomiozy.*

Słowa kluczowe: **adenomioza** / **mięśniaki macicy** / **histerektomia** / **rodność** /

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Introduction

Adenomyosis is a benign condition defined as a growth of the endometrial glands and stroma deep into the myometrium [1]. Despite its high prevalence, etiology of adenomyosis has been not completely explained. Epidemiological data indicate that parity, caesarean section, induced abortion, dilatation and curettage, use of tamoxifen, uterine malformation and late age at menarche may be the risk factors for adenomyosis development [2, 3, 4, 5, 6, 7, 8].

However, due to the fact that adenomyosis is rarely diagnosed prior to hysterectomy and usually concurs with other pelvic pathologies, a significant selection bias in studied populations makes results of epidemiological studies contradictory. Most frequently adenomyosis coexist with leiomyomas. It is diagnosed in approximately 20% of uterine specimens removed due to fibroids and 35-55% of all cases of adnomyosis is found together with leiomyomas [3, 4, 5, 8].

Preoperative identification of adenomyosis coexisting with fibroids is difficult, however it may be of great importance for patients scheduled for uterine artery embolisation, as presence of adenomyosis may be the reason for failure of the procedure [9].

The aim of this study was to evaluate the potential risk factors for adenomyosis in patients with symptomatic uterine leiomyomas.

Material and methods

This retrospective study comprised 1499 women who underwent hysterectomy at 2nd Department of Gynecology Medical University of Lublin, Poland between 2003-2007.

The patients' charts and histopathology reports were systematically reviewed and demographic, obstetric and clinical data were obtained.

Adenomyosis was diagnosed when the distance between the lower border of the endometrium and the affected myometrial area was 2.5mm or more. The study group included 135 patients with coexisting uterine leiomyoma and adenomyosis. The control group comprised 176 patients with uterine leiomyoma without adenomyosis. First fifty consecutive hysterectomies from each year were selected and patients with uterine leiomyomas qualified for the control group.

Statistical analysis was performed with StatisticaStatsoft vrs 8 software ((Statsoft Inc,. Tulusa, OK, USA)). T-test, χ^2, and logistic regression analysis were used as appropriate. A p value less than 0.05 was considered statistically significant.

Results

Adenomyosis was diagnosed in 233 (15.5%) patients. One hundred and thirty-five of them (57.9%) had associated uterine fibroids. Indications for surgery in other patients with adenomyosis were: uterine prolapse, metrorrhagia, cervical carcinoma, benign ovarian tumour, ovarian carcinoma, endometrial hyperplasia with atypia and endometrial carcinoma. Adenomyosis has been suspected prior to surgery only in 4 cases (1.73 %).

Patients from study and control groups did not differ significantly in terms of age, BMI and parity. (Table I).

Multiparity appeared to be the only risk factor associated with presence of adenomyosis. No relationship was found between adenomyosis and cesarean section rate, abortions, menorrhagia or dysmenorrhea. (Table I).

Comment

Despite prevalent coexistence of leiomyomas and adenomyosis, it is rather unlikely that these conditions share common pathogenetic features. Although both are estrogen dependent, gene expression profile differs significantly between leiomyomas and adenomyosis [10].

Table I. Univariate analysis of risk factors for adenomyosis in women with symptomatic uterine leiomoymas.

	Uterine leiomyoma with adenomyosis (n=135)	Uterine leiomyoma without adenomyosis (n=176)	RR (95% CI)
Age (years)	50.6±6.2	49.5±8.3	
BMI (m^2/kg)	27.2±5.2	27.7±5.3	
Mean parity	2.1±1.0	2.2±1.4	
Parity 0 1 or more	 8 (5.9%) 127 (94.1%)	 22 (12.5%) 154 (87.5%)	2.27 (0.97-5.28), p=0.058
Parity 0 1 2 or more	 8 (5.9%) 17 (12.6%) 110 (81.5%)*	 22 (12.5%) 30 (17.1%) 124 (70.5%)	1 1.33 (0.47-3.79), p=0.539 2.44 (1.04-5.72), p=0.040
Cesarean section (among parous)	23 (18.1%)	40 (26.0%)	0.63 (0.35-1.13), p=0.118
Spontaneous abortions	25 (18.5%)	23 (13.1%)	1.50 (0.81-2.80), p=0.199
Metrorrhagia	74 (54.8%)	84 (47.7%)	1.31 (0.83-2.06), p=0.240
Dysmenorrhea	50 (37.0%)	50 (28.4%)	1.53 (0.95-2.46) p=0.079

* Higher incidence adenomyosis in multiparous compared with nulliparous women (χ^2=4.45, p=0.035)

Risk factors for development of both diseases seem to be different as well. Risk of leiomyomas is up to four time higher in nulliparous than in multiparous women [11], whereas development of adenomyosis is attributed to such reproductive factors as multiparity, cesarean section or induced abortion [3, 4, 5, 6, 7, 8]. Most probably, the fact that both disorders are widespread and that uterine leiomyomas are the most frequent indication for hysterectomy may account for high rate of coincidence in posthysterectomy specimens.

In this study we evaluated obstetric and clinical factors potentially influencing the presence of adenomyosis in patients hysterectomized due to symptomatic uterine lyiomomas. Multiparity appeared to be the only significant factor increasing the incidence of adenomyosis. Relative risk of adenomyosis was more than twice higher in multiparous compared with nulliparous women. Other reproductive factors such as spontaneous abortion and cesarean section had no significant effect. Association between multiparity and adenomyosis has been recognized earlier for the populations of hysterectomized women regardless of the indications for surgery [1].

Our study showed that birth trauma may also play important pathogenectic role in development of adenomyosis in patients who underwent surgery due to fibroids. Role of cesarean section is less clear. Some reports indicated that abdominal delivery increases the rate of adenomyosis [2, 4, 12], but other, in line with our findings, did not find such association [3, 7, 8, 13].

Diagnosis of adenomyosis may be of great importance for patients with symptomatic leiomyomas selected for uterine-sparing procedures such as uterine artery embolization (UAE). Smith et al. [9] showed that patients after UAE who were scheduled for hysterectomy due to persistent abnormal bleeding and pelvic pain had viable adenomyotic lesions. In other reports concomitant adenomyosis was found in 36% [14] and 25% [15] of patients who underwent hysterectomy because of UAE failure. Although adenomyosis is not regarded as a contraindication for UAE [16, 17], results, especially long term ones, are worse then with leiomyomas. Approximately 45% of women with adenomyosis have treatment relapse after 2-3 years after UAE [18, 19, 20]. Overall, patients with concomitant adenomyosis are at greater risk for procedure failure.

It is obvious that presence of fibroids makes identification of adenomyosis more difficult. History, clinical examination and imaging studies may be not conclusive. Transvaginal ultrasound has good accuracy in diagnosis of adenomoysis but its specifity decreases significantly in the presence of leiomyomas [21]. It is unclear if symptoms such as metrorrhagia or dysmenorrhea are related to adenomyosis per se or to associated pathologies [22]. In our population incidence of dysmenorrhoea was slightly, but not significantly, higher in patients with adenomyosis. Data from other reports are contradictory.

In conclusion, results of our study indicate that women with leiomyomas who delivered twice or more are at greater risk for concomitant adenomyosis. This determinant should be taken into account in patients planned for uterine artery embolization.

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