Risk Factors for Typical Endometrial Polypoid Adenomyoma

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Research Article

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Abstract

Objective: Typical endometrial polypoid adenomyoma (TPA) is a rare type of lesion in the uterine cavity or cervical canal. Although the clinical and pathologic features of TPA have been described extensively, reports on its pathogenesis and treatment remain inconclusive.

This study was conducted to investigate the risk factors for endometrial TPA and recurrence and to further define the pathogenesis and treatment.

Study design: This was a retrospective analysis of 488 cases of TPA and 500 cases of normal endometrium. Age, menopausal status, body mass index (BMI), reproductive history, and method of surgery were retrospectively analyzed. Among TPA cases, 360 were treated by conservative surgery. Risk factors for TPA and recurrence were assessed.

Results: There was a significant difference in age, menopausal status, BMI, gravidity, and parity between the two groups ($P<0.05$). Age >50 years, menopause, obesity, gravidity >3, and parity >2 were risk factors for TPA ($P<0.05$). The incidence rate of endometriosis and adenomyosis in the TPA group was significantly higher than that in the normal endometrium group ($P<0.05$). Follow-up data (22–77 months) were obtained for 360 patients, revealing gravidity >3, menopause, curettage, and polyp clamp as independent risk factors for the recurrence of TPA ($P<0.05$).

Conclusions: In addition to high estrogen levels, endometrial injury was the main contributor to TPA pathogenesis. Hysteroscopic electrotomy was the preferential treatment for TPA to avoid recurrence, especially for women with risk factors. Increasing the depth of ablation may prevent the recurrence of TPA more efficiently.

1. Introduction

Typical endometrial polypoid adenomyoma (TPA), also known as adenomyomatous polyp, is rarely detected. It is a benign neoplasm consisting of fibroid stroma and glands whose histological origin is unclear [1]. TPA accounts for 1.3% of endometrial polyps [2]. Histologically, endometrial polypoid adenomyomas can be divided into typical and atypical polypoid adenomyomas [3, 4]. The former is mainly composed of normal endometrial glands, with interwoven smooth muscle stroma [5, 6], whereas the latter is a lesion with unspecified malignant potential due to crowded, irregular, and complex glandular epithelium along with abundant, chaotic, and loose smooth muscle stroma, which can resemble atypical endometrial hyperplasia [7, 8].

TPA is easily confused with other uterine lesions. Few reports on TPA diagnosis and treatment, inadequate knowledge of the pathogenesis of TPA, and the lack of a systematic analysis of relevant clinical data justify the need for the present study. This study retrospectively analyzed the clinical data of 488 cases of TPA and 500 cases of normal endometrium. The risk factors for endometrial TPA and recurrence were investigated, and the pathogenesis and treatment were further defined.

2. Material And Methods

2.1. Clinical data

This study included 988 women who were admitted for the first time to undergo surgical treatment at Tianjin Central Obstetrics and Gynecology Hospital between January 2011 and December 2017. According to the pathological examination results, they were divided into two groups: 1) TPA group (n = 488; 49–69 [53.26 ± 10.46] years). 2) Normal group (women with a normal endometrium; n = 500; 50–68 [53.58 ± 10.45] years). Data on the patient's age, body mass index (BMI), reproductive history, and method of surgery were recorded. In the TPA group, 360 patients underwent conservative surgery, including hysteroscopic electrotomy, curettage, and polyp clamp. These 360 patients were followed up for 22–77 months (Fig. 1).

The data were collected through the institution's electronic medical records while preserving the patients' anonymity. The research ethics committee waived the requirement for ethical approval and informed consent because the study used previously stored data.

Patients with a normal endometrium were among inpatients undergoing diagnostic curettage due to other gynecological diseases.

The diagnosis criteria of TPA were based on those described by Kenny et al. Polypoid adenomyoma of the uterus is an endometrial polyp in which the stromal component is made up of smooth muscle [1]. Only those patients with a definite pathological diagnosis of TPA were included; two experienced pathologists in our hospital rereviewed pathological specimens and adjudged the diagnosis. Patients with incomplete information or those lost to follow-up were excluded.

2.2. Statistical methods

SPSS21.0 software was used for statistical analysis (SPSS Inc, Chicago, IL, USA). The chi-square test was used for comparison. Multivariate analysis was performed using a logistic regression model. All tests were two-sided, and the level of significance was set at $P < 0.05$.

3. Results

3.1. Risk factors for TPA

Among the included 488 TPA patients (49–69 [53.26 ± 10.46] years), 156 patients were premenopausal women and the rest were postmenopausal women. The mean BMI of 156 premenopausal patients was 22.38 ± 3.21kg /m^2, and the mean BMI of 332 postmenopausal patients was 25.31 ± 4.17 kg /m^2. Three postmenopausal patients had a history of oral tamoxifen before surgery. Among the 488 patients, only 11 had no pregnancy history. Three patients never had sexual life, one patient's husband had infertility, and four patients used contraception methods. The other three patients did not use any contraception and were not pregnant after marriage. The average gravidity was 3.22, and the average parity was 1.74.

The height and weight were measured in all patients. BMI was calculated based on the classification criteria recommended by the Asian population experts of the World Health Organization and the Chamber of Commerce (WHO, 2004). Patients in both groups were divided into two or three levels, depending on age, menopausal status, BMI, gravidity, and parity.

There were significant differences in age, menopausal status, BMI, gravidity, and parity between the two groups ($P < 0.05$), and age > 50 years, menopause, obesity, gravidity > 3, and parity > 2 were risk factors for TPA ($P < 0.05$; Table 1).

Table 1
Univariate and multivariate analyses of the clinical characteristics of TPA

Parameter	TPA group (n = 488)	Normal group (n = 500)	Univariate analysis	Multivariate analysis	
			P-value	OR (95% CI)	P-value
Age (years)			0.021	1.41 (1.343–3.224)	0.031
≤ 50	189 (38.73)	266 (53.2)			
> 50	299 (61.27)	234 (46.8)			
Menopause			< 0.001	0.337 (0.260–0.438)	< 0.001
No	156 (31.97)	291 (58.2)			
Yes	332 (68.03)	209 (41.8)			
BMI			0.011	0.801 (0.370–0.955)	0.032
Normal	146 (29.92)	186 (37.2)			
Overweight	255 (52.25)	223 (44.6)			
Obese	87 (17.83)	91 (18.2)			
Gravidity			< 0.001	0.444 (0.344–0.573)	0.001
≤ 3	197 (40.39)	302 (60.4)			
> 3	291 (59.63)	198 (39.6)			
Parity			0.031	0.759 (0.590–0.976)	0.037
≤ 2	201 (41.18)	240 (48)			
> 2	287 (58.81)	60 (52)			

TPA, typical endometrial polypoid adenomyoma; BMI, body mass index

Table 2
Adenomyosis and endometriosis accompanied with TPA

Pathology	TPA group n (%)	Normal group n (%)	t-value	P-value
Endometriosis	47 (9.64)	12 (2.4)	4.987	< 0.001
Adenomyosis	73 (14.96)	43 (8.6)	5.630	< 0.001
TPA, typical endometrial polypoid adenomyoma				

3.2. Adenomyosis and endometriosis accompanied with TPA

The rate of adenomyosis and endometriosis was significantly different ($P < 0.01$) between the two groups (73 vs 12 cases of adenomyosis and 47 vs 43 cases of endometriosis in the TPA and normal groups; Table 3).

Table 3
Univariate and multivariate analyses for risk factors of recurrence (n = 32)

Variable	Recurrence rate (%)	Univariate analysis	Multivariate analysis	
		P-value	OR (95% CI)	P-value
Age (years)		0.021	1.41 (1.343–3.224)	0.031
≤ 50	10.10 (20/198)	0.418	Variable removed	
> 50	7.41 (12/162)			
Menopause		< 0.001	3.143 (1.986–5.113)	< 0.001
No	2.83 (3/106)			
Yes	11.41 (29/254)			
BMI		0.886	Variable removed	
Normal	9.43 (10/106)			
Overweight	8.78 (18/205)			
Obese	8.16 (4/49)			
Gravidity		0.020	1.483 (1.345–3.226)	0.029
≤ 3	3.40 (5/147)			
> 3	12.68 (27/213)			
Parity		0.517	Variable removed	
≤ 2	7.64 (12/157)			
> 2	9.85 (20/203)			
Method of surgery		0.026	1.429 (1.056–2.968)	0.037
Hysteroscopic electrotomy	2.41 (8/332)			
Curettage	80.95 (17/21)			
Polyp clamp	100 (7/7)			

BMI, body mass index

3.3. Risk factors for recurrence of TPA

Among 360 TPA patients who underwent conservative surgery, including hysteroscopic electrotomy, curettage, and polyp clamp, there were 32 cases (8.89%) of relapse. Parity, menopausal status, and surgery method were related to TPA recurrence, and gravidity > 3, menopause, curettage, and polyp clamp were independent risk factors for the recurrence of TPA ($P < 0.05$; Table 5).

4. Discussion

TPA is a rare lesion occupying the uterine cavity or the cervical canal consisting of fibroid stroma and glands [1]. It is easily confused with other uterine lesions, making its clinical diagnosis difficult. The pathogenesis of TPA is still not clear. Some scholars [9, 10] believed that adenomyomatous polyps originate from stromal progenitor cells in the endometrium, which can differentiate into smooth muscle and may be the product of long-term estrogen stimulation. Lin et al. reported a case in which a gonadotropin-releasing hormone agonist effectively reduced the size of the lesion, suggesting that the growth is dependent on the estrogen level [11]. In this study, the average age of onset of the patients was 53.26 years, and the incidence rate was significantly higher in women > 50 years old than in women < 50 years old, which may be related to the long-term or continuous estrogen stimulation with little or no progesterone antagonism in this age group. Moreover, tamoxifen has been reported to exhibit a weak estrogen-like effect in postmenopausal women that increases the occurrence and recurrence rate of TPA [12, 13]. On the contrary, in this study, there was no significant difference in the recurrence rate between the different age groups after conservative surgery of TPA, and age was not a risk factor for the recurrence of TPA. This may be related to the short follow-up duration and the small sample size of the present study.

However, our findings reveal that chances of TPA occurrence and relapse are greater in postmenopausal women. The decreased estrogen level in postmenopausal women elevates follicle stimulating hormone level, leading to increased estrogen receptor expression in utero [14]. Longacre et al. also reported that in addition to the high estrogen level in patients, the abnormal expression of estrogen receptors in the local endometrium is also associated with TPA occurrence [15]. Postmenopausal women had a significantly higher BMI than premenopausal women in the present study. Overweight and obesity rates were also significantly greater. The BMI of postmenopausal women has been reported to be positively correlated with the estrogen level over an extended period [16]. Weight gain and obesity result in insulin resistance and hypertension, and insulin resistance is closely linked to abnormally high estrogen levels. Therefore, obese individuals are more likely to develop TPA. In this study, 255 patients (52.25%) were overweight, and 87 patients (17.83%) were obese, supporting the above views on TPA occurrence.

Pathologically, TPA resembles adenomyosis, i.e., both conditions are characterized by abundant smooth muscle stroma and endometrial glands. TPA is reported to occur when an adenomyoma breaks into the endometrial cavity, which is why TPA may be considered under the category of uterine adenomyosis [17]. Although a link between TPA and adenomyosis has been established, there are some differences between the two pathologies. In adenomyosis specimens, the endometrial glands and stroma are divided into islands by the smooth muscle within the myometrium. Moreover, the uterine smooth muscle tissue in

adenomyosis is morphologically different from that in TPA. However, polypoid adenomyomas are often accompanied by adenomyosis, and the two pathologies may be similar in histogenesis [7]. In this study, we found that most patients had a history of pregnancy. Patients with gravidity > 3 and parity > 2 were more likely to develop TPA, and gravidity > 3 and parity > 2 were independent risk factors for TPA. Chances of relapse were greater in patients with gravidity > 3. Besides, the rate of adenomyosis and endometriosis in the TPA group was higher than that in the normal group. All these results suggest that surgery of the uterine cavity and endometrial injury may be related to the occurrence of TPA [5].

Among the 360 TPA patients who underwent conservative surgery,hysteroscopic electrotomy, curettage, and polyp clamp, there were 32 cases (8.89%) of relapse. Parity, menopausal status, and surgery method were related to TPA recurrence, and gravidity > 3, menopause, curettage, and polyp clamp were independent risk factors for TPA recurrence. This supports the link between elevated levels of estrogen and its receptors and endometrial damage. When planning the surgery, it is important to consider the unique pathogenesis and pathological characteristics of TPA. Because the lesion cannot be directly targeted by curettage and polyp clamp and because the texture of adenomyomatous polyps is arduous and the base is broad, the postoperative residual rate of lesions is high. Hysteroscopy can altogether remove the directly visible lesion, and other suspected endometrial lesions can be biopsied simultaneously, with minimal trauma.

In this study, 332 patients who underwent hysteroscopic electrotomy were followed up successfully; only eight patients exhibited recurrence without any malignant change, indicating that hysteroscopic electrotomy is a safe and effective treatment method. Hysteroscopic resection of directly visible lesion tissues could reduce trauma and preserve fertility, yielding a definite curative effect [18]. Therefore, a four-step hysteroscopic resection of the lesion is preferred: (1) complete resection of the lesion from the root pedicle; (2) removal of 0.2–0.5 cm of the endometrial tissue around the root pedicle; (3) ensuring that the myometrium below the root pedicle is about 0.3 cm deep; (4) multi-point biopsy of the endometrium at other locations of the uterine cavity [19].

5. Conclusions

The main strength of this study is that a large number of patients with TPA and normal endometrium were included. Moreover, 360 cases of TPA were followed up for 22–77 months. Besides, patients who underwent conservative surgery were from the same sample group, reducing bias and yielding more accurate results.

However, this study also has some unavoidable limitations due to its retrospective design. First, we could not assess all variables potentially associated with the occurrence and recurrence of TPA in this single study. Furthermore, the inclusion of cases involving only one hospital might have reduced the external validity of the results, and further prospective studies with a larger sample size in a broader context are needed.

In conclusion, endometrial TPA is a particular type of lesion occupying the uterine cavity. Although the pathogenesis of the disease is not clear, elevated estrogen levels and its receptors and endometrial damage are risk factors for the occurrence and recurrence of TPA; however, the relationship between these risk factors and the occurrence of the disease still needs further experimental study. Hysteroscopic electrotomy is the preferred treatment for endometrial TPA, especially for women with risk factors. The unique pathogenesis and pathology of TPA suggest that increasing the depth of ablation may prevent the recurrence of TPA.

Declarations

This study has been performed according to the Declaration of Helsinki. Institutional review board approval was obtained. Informed consent was not required for our study. This study had no funding support.

Conflict of interest

The authors declare no conflict of interest.

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Author contribution

Xinmei Wang: Project development, data collection, manuscript writing.

Hongyuan Zhang: Data collection and data analysis.

Juan Xu: Data collection and data analysis.

Pengpeng Qu: Project development.

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Figures

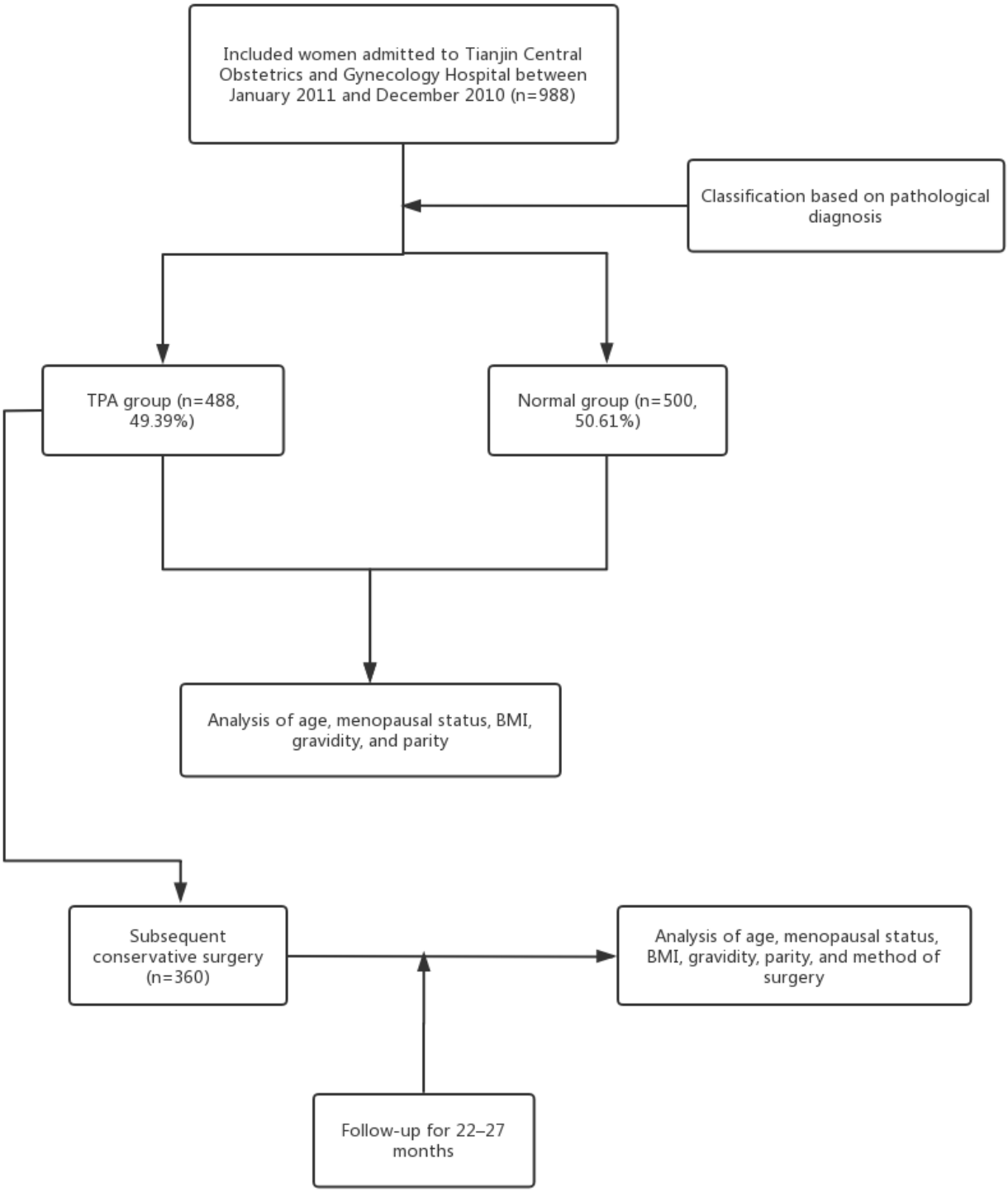

Figure 1

Study flowchart