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Risk of coexisting endometrial carcinoma in case of atypical endometrial hyperplasia diagnosed on total hysteroscopic resection

Audrey Pivano [a], Patrice Crochet [a], Xavier Carcopino [b], Ludovic Cravello [a], Léon Boubli [b], Aubert Agostini [a,*]

[a] Obstetrics and Gynecology Unit, Assistance Publique-Hôpitaux de Marseille, Hôpital La Conception, Marseille, France
[b] Obstetrics and Gynecology Unit, Assistance Publique-Hôpitaux de Marseille, Hôpital Nord, Marseille, France

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ABSTRACT

Objective: To evaluate the rate of coexisting endometrial carcinoma or atypical endometrial hyperplasia (AEH) residue in patients who had a total hysteroscopic resection with diagnosis of AEH and without suspicious lesions detected during hysteroscopy.
Study design: This retrospective bicentric study included patients diagnosed with AEH on hysteroscopic resection products, and who subsequently underwent secondary hysterectomy. Cases of hysteroscopic appearance suggesting an endometrial carcinoma were excluded. Histopathological results of hysterectomy specimen determined the persistence or absence of AEH and the possible presence of coexisting endometrial carcinoma.
Results: Thirty-two patients were selected. Histopathological analysis of hysterectomy specimens diagnosed an absence of AEH in 24/32 (75%) subjects, an AEH residue in 6/32 (18.8%) subjects and a coexisting endometrial carcinoma in 2/32 (6.2%) subjects.
Conclusion: The risk of missing an endometrial carcinoma in patients diagnosed with AEH based on total hysterocopic resection is low when there is no suspicious hysteroscopic aspect, but this risk cannot be entirely excluded. Total hysteroscopic resection may be a possible alternative to hysterectomy in patients with AEH who refuse hysterectomy or are a high surgical risk. These patients require a close and long term follow-up due to the risks of residual lesion.

Introduction

Endometrial carcinoma is the most common gynecological cancer in the western world, with an incidence ranging from 15 to 25 cases per 100,000 women [1]. Atypical endometrial hyperplasia (AEH) is a precursor lesion, whose diagnosis implies a risk of concurrent or future endometrial carcinoma. The rate of AEH progressing to endometrial carcinoma within 20 years is estimated around 25–30% [2]. Diagnosis methods include blind sampling or hysteroscopy. Diagnostic or operative hysteroscopy is considered a safe procedure allowed even in case of suspicion for endometrial cancer [3]. There is a risk of coexisting endometrial carcinoma in patients diagnosed with AEH, especially in case of diagnosis obtained using blind sampling [4–6]. This risk tends to decrease when the diagnosis of AEH is performed on hysteroscopic resection products with no suspected malignant pattern visualized during hysteroscopy. However the risk of missing an endometrial carcinoma in these circumstances is not well documented [7–10].

The aim of this study was to estimate the rate of coexisting endometrial carcinoma or AEH residue in patients with AEH diagnosed by total hysteroscopic resection of the endometrium.

Materials and methods

Population

This was a retrospective bicentric study conducted in the Obstetrics and Gynecology Department of two academic hospitals (Hôpital La Conception and Hôpital Nord) in Marseille, France. It involved patients treated for AEH during 1996–2014. Inclusion criteria were a diagnosis of AEH from products of total hysteroscopic resection and a subsequent hysterectomy for

* Corresponding author at: Department of Gynecology and Obstetrics, la Conception Hospital, 147 boulevard Baille, 13005 Marseille, France.
Tel.: +33 491383785; fax: +33 491381673; mobile: +33 610568052.
E-mail address: aubert.agostini@ap-hm.fr (A. Agostini).

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treatment of AEH. Exclusion criteria were tamoxifen therapy and abnormal features suggesting an endometrial carcinoma observed during hysteroscopic inspection. Institutional Review Board approval was obtained for this study (no. CEROG-2014-GYN-0905).

Clinical and pathological data

Patients were selected using a standard hospital coding system. Information regarding patient characteristic, treatment and subsequent follow-up was collected from the medical records. Patients age, body mass index (BMI), gravidity, parity, menopausal status, hormonal replacement therapy (HRT), indication for hysteroscopy, preoperative ultrasound examination, hysteroscopic inspection of the uterine cavity, pathology reports were collected. Histological diagnoses of AEH and endometrial carcinoma were made according to the criteria of the World Health Organization (WHO) Classification System [11] in the department of pathological anatomy of the two hospitals. Final histology on hysterectomy specimens was analyzed to determine the persistence of AEH or the possible presence of coexisting endometrial carcinoma.

Operative hysteroscopy

Operative hysteroscopy began with an inspection of the uterine cavity. In absence of suspicious aspect of the endometrium, a total hysteroscopic resection was performed using a 8- or 9-mm resectoscope. This endometrial resection of the uterine cavity was performed using a monopolar loop, including in the fundus and peri-ostial areas. A complementary resection using the rollerball was performed only in case of residual endometrium. Glycine was the distention medium and a coagulation supplement was performed if necessary. Suspicious features of the endometrium suggesting an endometrial carcinoma were defined by at least one of these criteria: irregular or papillary surface contour, evidence of necrosis, irregular vessels pattern [12,13]. In premenopausal women the procedure was performed during the proliferative phase of the menstrual cycle. All operative hysteroscopy were conducted by qualified and experienced surgeons.

Results

Thirty-two eligible patients were included in this study. Four patients treated during the 1996–2001 period were already included in a previous study [7]. The demographic characteristics are reported in Table 1. Indication for operative hysteroscopy was uterine bleeding in all cases. Hysteroscopic inspection revealed endometrial hypertrophy in 20 cases (62.5%), focal endometrial hypertrophy in 2/32 cases (6.2%) and hypertrophy associated with endometrial polyps in 10/32 cases (31.2%). All 32 patients underwent subsequent total hysterectomy. Hysterectomy was performed at a median time of 60 days (range 13–150) after the diagnosis of AEH. Histopathological analysis of hysterectomy specimens diagnosed no remaining AEH in 24/32 cases (75%), an AEH residue in 6/32 cases (18.8%) and 2/32 cases of coexisting endometrial carcinoma (6.2%).

The two cases of endometrial carcinoma diagnosed were grade 1, FIGO stage 1A (FIGO classification 2009) and subsequently received complementary treatment with high-dose brachytherapy. No recurrence was found in these patients in a five-year follow-up.

Table 1
Characteristics of women with atypical endometrial hyperplasia.

	n (%)	Mean (±SD)
Age (years)	–	52.6 (±8.5)
Gravidity		2.1 (±1.6)
Parity		1.6 (±1.2)
BMI (kg/m^2)		27.3 (7.5)
Obesity (BMI ≥ 30 kg/m^2)	6 (18.7)	–
Postmenopausal status	16 (50)	–
Hormone replacement therapy	5 (15.6)	–
Ultrasound examination		
Endometrial thickness > 10 mm	12 (37.5)	–
Polyps	6 (18.7)	

Variables were expressed as means ± standard deviations (SD), or number with percentage (%).
BMI, body mass index.

Comment

This study assessed the risk of remained abnormal findings in patients initially diagnosed with AEH after a total hysteroscopic ablation. Histopathologic analysis of hysterectomy specimens proved that in such cases, there is a small proportion of coexisting endometrial carcinoma (6.2%), and a more substantial proportion of AEH residue (18.8%).

According to the World Health Organization (WHO) classification, the presence of nuclear atypia defines atypical hyperplasia, which is classified in two sub-categories: simple atypical hyperplasia (SAH) and complex atypical hyperplasia (CAH) [11]. However, the diagnosis of SAH is so rare that atypical hyperplasia is often used to denote any hyperplasia with atypia. Furthermore, the original WHO classification revealed a low reproductibility [14]. This reproductibility is enhanced when the WHO classification is redefined as two categories: non-atypical endometrial hyperplasia and atypical endometrial hyperplasia, as in the present study [15].

The risk of a spontaneous evolution of an AEH into an endometrial carcinoma is high, estimated between 25 and 30% [16,17]. In a case-control study nested in a cohort of 7947 patient diagnosed with endometrial hyperplasia, Lacey et al. estimated the 20-year cumulative progression risk for AEH patients at 28% [2]. This risk was not influenced by patient age at diagnosis.

AEH diagnosis can be obtained through different methods that influence the risk of ignoring a cohexisting endometrial carcinoma. Trimble et al. investigated diagnostic performances of endometrial biopsy specimens: they prospectively included 289 patients with a diagnosis of AEH and reported a 43% rate of coexisting endometrial carcinoma on subsequent hysterectomy specimen [6]. Touboul et al. analyzed in a retrospective cohort of 79 patients the predictive factors of endometrial cancer in patients diagnosed with AEH. In multivariable analysis, the only predictive factors of endometrial cancer were older age and the suspicion of cancer on hysteroscopy [9]. Garuti et al. [10] also evaluated the diagnostic value of hysteroscopic aspect of the endometrium in patients with diagnosis of AEH. Endometrial carcinoma was diagnosed in 2/16 patients (12.5%) without suspicion lesions during hysteroscopic inspection. Thus, a non-suspicious appearance of the endometrium lower the risk of coexisting endometrial carcinoma in patients diagnosed with AEH. This risk risk cannot be entirely excluded, but it is limited.

Few studies evaluated the role of total hysteroscopic resection in management of the AEH. In a retrospective study of 25 patients diagnosed with AEH by total hysteroscopic resection between 2008 and 2012, Litta et al. [18] reported a AEH residue in 2/25 (8%) of cases on hysterectomy specimen and no case of coexisting endometrial carcinoma. Our findings revealed a slightly higher risk of residual disease. Ploteau et al. found a AEH residue in 19/43 (44%) of cases and a rate of 3/43 (7%) of coexisting endometrial