Correlation between preoperative endometrial sampling and final endometrial cancer histology

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Summary

Objective: We conducted a study to evaluate the correlation between pre-operative endometrial sampling to the final endometrial cancer histology, in particular the non-endometrioid subtypes. *Methods:* This involved 191 hysterectomy specimens of patients undergoing treatment at the Pan-Birmingham Gynaecological Regional Cancer Centre (BGCC) over a two-year period (2006-2007). *Results:* The majority of the patients in this study were found to have endometrioid histology subtype (140/191, 73%). However, the non-endometrioid histologic subtypes were well presented in our population (51/191, 27%). We found good correlation for endometriod histology subtype (78%) and certain types of the non-endometrioid cell types (carcinosarcoma 90%, uterine papillary serous carcinoma 67%, clear cell carcinoma 67%) but poor in sarcomas (40%). Our results also demonstrated that both pre-operative endometrial sampling methods (curettage and pipelle biopsy) were reliable in identifying endometrioid and non-endometrioid cancer cell types, with sensitivities of 96.5% and 86.5%, respectively. *Conclusion:* We concluded that preoperative endometrial sampling had good overall histological correlation to hysterectomised corpus specimen. This is especially so for the endometrioid and certain subtypes of the non-endometrioid endometrial cancer cells.

Key words: Complex atypical hyperplasia; Endometrial carcinoma; Endometrial sampling; Post menopausal bleeding.

Introduction

Endometrial assessments by means of pipelle biopsy or curettage are useful procedures in the assessment of patients with suspected endometrial cancer. Very few studies in the literature have evaluated the accuracy of histological tissue obtained by these techniques to the final endometrial cancer histology. These studies were limited by small numbers of patients and most of the studies do not make reference to patients with non-endometrioid histology, which generally carries a much poorer prognosis.

Material and Methods

One hundred and ninety-one hysterectomy specimens of patients undergoing treatment at the Pan-Birmingham Gynaecological Cancer Centre (BGCC) were analysed and reported for the final histology subtypes. Such patients were included in the study.

Preoperative endometrial sampling histology was retrospectively obtained from each respective referring hospitals where the patients had initially presented. These were classified into complex atypical hyperplasia (CAH) endometrioid adenocarcinoma (EA), clear cell carcinoma (CCC), uterine papillary serous carcinoma (UPSC), carcinosarcoma (CS), sarcoma and unclassified. Post-operative hysterectomy specimens were categorized as EA, CCC, UPSC, CS and sarcoma. The non-endometrioid group included CCC, UPSC, CS and sarcoma.

The concordance rate for each histological subtype was calculated. The sensitivity and positive predictive value (PPV) for preoperative sampling for both endometrioid and non-endometrioid histology were also determined.

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Results

The majority of the patients in this study were found to have endometrioid histology subtype (140/191, 73%). However, the non-endometrioid histologic subtypes were well presented in this population (51/191, 27%). This group can be further divided into the following respectively: CS in 31 patients (16%), UPSC in nine patients (5%), CCC in six patients (3%) and five patients had sarcoma (2%) (Table 1).

The overall concordance rate between the initial preoperative endometrial sampling and the final hysterectomy histology was 78% (149/191). Of these, EA accounted for 109 patients (57%), CS in 28 patients (15%), UPSC in six patients (3%), CCC in four patients (2%), and sarcoma in two patients (1%) (Table 2).

When the concordance rate for each respective histology subtype was analysed, the results were as follows: 78% in EA (109/140), 90% in CS (28/31), 67% in UPSC (6/9), 67% in CCC (4/6) and 40% in sarcomas (2/5) (Table 1).

The overall non-concordance rate between the initial pre-operative endometrial sampling and the final hysterectomy histology was 22% (42/191). Of these, CAH accounted for the majority with 22 patients (11.5%), followed by non-endometrioid type in 12 patients (6.3%), endometrioid type in four patients (2.1%) and the remaining were unclassified (2.1%) (Table 3).

The sensitivity for pre-operative endometrial sampling to accurately detect endometrioid or non-endometrioid subtypes were 96.5% and 86.5%, respectively (Table 4). The corresponding PPVs were 93.9 and 91.8, respectively.

Table 1. — *Correlation of preoperative sampling subtypes to final specimen histology*.

Final Sampling	EA	CS	UPSC	CCC	Sa
EA	109	2	0	0	2
UPSC	1	1	6	1	0
CCC	5	0	0	4	0
CS	1	28	2	0	1
Sa	0	0	0	0	2
CAH	22	0	0	0	0
Unclassified	2	0	1	1	0
Total (n)	140	31	9	6	5
Correlation (%)	77.8	90.0	66.7	66.7	40.0

EA: Endometrioid adenocarcinoma; UPSC: Uterine papillary serous carcinoma; CCC: Clear cell carcinoma; CS: Carcinosarcoma; Sa: Sarcoma.

Table 2. — *Concordance rate*.

	n =	%
Concordance overall:		
Final histology to preoperative sampling	149	78.0
Concordance by preoperative histology:		
Endometrioid adenocarcinoma	109	57.0
Carcinosarcoma	28	14.7
Uterine papillary serous carcinoma	6	3.1
Clear cell carcinoma	4	2.1
Sarcoma	2	1.0

Table 3. — *Non concordance rate*.

	n =	%
Non-concordance overall:		
Final histology to preoperative sampling	42	22.0
Non-concordance by preoperative histology:		
Complex atypical hyperplasia	22	11.5
Non-endometrioid	12	6.3
Endometrioid adenocarcinoma	4	2.1
Unclassified	4	2.1

Table 4. — *Preoperative sampling method*.

	%
Sensitivity of:	
detecting endometrioid subtype	96.5
detecting non-endometrioid subtype	86.5
Positive predictive value of:	
detecting endometrioid subtype	93.9
detecting non endometrioid subtype	91.8

Discussion

The BGCC is the largest of four regional centres that cover the whole of the West Midlands area. These include the Birmingham Women's Healthcare NHS Trust (Central and South Birmingham), Good Hope Hospital (North Birmingham) Heartlands Hospital (East Birmingham) and Walsall Manor Hospital (Walsall). The approximate catchment population of the BGCC is two million although it has been difficult to accurately establish this because of extensive cross-border flow. In addition the centre also receives tertiary referral from outwith the network.

To our knowledge, there has not been a study that evaluated the correlation between histological tissues obtained pre-operatively to the final endometrial cancer specimen histology. Most of the studies in the literature do not make reference to patients with non-endometrioid either, which generally carries a much poorer prognosis [1].

For many years, endometrial curettage and pipelle biopsy have been the methods of choice in assessing abnormal uterine bleeding, the latter being a minimally invasive method which is believed to reduce the costs of a diagnostic work up.

Our results demonstrated that both preoperative endometrial sampling methods (curettage and pipelle biopsy) were sensitive in detecting endometrial cancers. This was particularly so in identifying the endometrioid (96.5%) and to a lesser extent, the non-endometrioid histology subtypes (86.5%). This is in line with a meta-analysis which reports the accuracy of the pipelle biopsy in detecting cancer to be between 91% and 99% [2].

When we analysed each histology subtypes in turn, our study showed that the overall correlation between the initial preoperative endometrial sampling and the final hysterectomy histology to be 78%. The majority of this correlation was of the EA cell type, which showed a correlation rate of 78%. These are cells composed of malignant glandular epithelial elements [3].

Our results also showed that certain types of the non-endometrioid cell types showed good correlation (CS 90%, UPSC 67%, CCC 67%, respectively) but poor in sarcomas (40%). We do acknowledge that in our study, the numbers of patients with these non-endometrioid cell types were smaller than the endometrioid subtypes. Therefore care should be taken when interpretating these results. In addition, non-endometrioid cells are more difficult to ascertain histologically as they do often overlap in their cell characteristics.

Non-endometroid type endometrial cancers also collectively carry poorer prognosis and have greater propensity for extrapelvic metastases. For example, UPSC is an aggressive variant of endometrial cancer, and is found in 5% of cases. Even with surgical Stage I cancer, the 5-year survival rate is 60%. UPSC resembles papillary serous carcinoma of the ovary and the fallopian tube histologically. Although adjuvant chemotherapy is helpful, UPSC does not have the same duration of response to cytotoxic agents (e.g., paclitaxel, carboplatin) as its ovarian counterpart [4].

Clear cell carcinoma is another variant of endometrial carcinoma characterised by its aggressive behaviour. It makes up about 3-6% of all endometrial carcinomas. The 5-year survival rate associated with these tumours is 45-60% [5]. Often, elements of clear cell carcinoma are associated with UPSC [4].

Carcinosarcomas or homologous mixed müllerian tumors typically have an endometrioid carcinoma, usually a higher grade, and an undifferentiated spindle cell sarcoma. These tumours can have a recurrence rate of up to 50% but demonstrate indolent growth and late recurrences. Likewise, sarcomas have a high metastatic poten-

tial and the histopathologic diagnosis can be unclear until time of definitive surgery [6].

With respect to the non-concordance results, our study showed that 52% (22/42) of those with an endometrioid type as a final histology had complex atypical hyperplasia at pre-operative sampling. This is in line with the original study by Kurman *et al*. that found when left untreated, complex atypical hyperplasia had a 29% rate of progression to cancer [7]. Numerous studies had also found concurrent carcinoma with these biopsies, at rates ranging from 17-52% [8, 9]. For these reasons, it is best practice to clinically treat patients with complex atypical hyperplasia similarly as per those with endometrioid adenocarcinoma histology.

Conclusions

Our findings have shown that both endometrial curretage and pipelle biopsy are sensitive methods in identifying both endometrioid and non-endometrioid cancer cell types.

The data suggests that our preoperative endometrial sampling had a good overall correlation to the histological subtype of endometrial cancer in the hysterectomised corpus specimen. This is especially so for the endometrioid and certain subtypes of the non-endometrioid endometrial cancer cells.

As more than a quarter of patients were found to have non-endometrioid cancer subtypes, which generally have a propensity for extrapelvic metastases, such findings would substantiate the concept of extended surgical staging, and involvement of a gynaecology oncologist in these patients' management.

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