

Mixed endometrial carcinoma: histology and survival, a 10-year retrospective cohort study

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Abstract

Mixed epithelial carcinoma of the uterus are a rare subtype of endometrial cancer, representing less than 1% of all patients. Due to the rarity of this condition, its characteristics, including its epidemiology, histology and survival, are not well understood yet.

In this retrospective cohort case series, we describe the characteristics and the survival of all patients that underwent surgery for mixed endometrial cancer in our Trust in the last 10 years (from 2009 to 2019), focusing on the epidemiology and the survival rates of this cancer, depending on their histological components.

34 patients were identified, all postmenopausal, and they all underwent total hysterectomy and bilateral salpingo-oophorectomy for endometrial cancer. Most patients underwent laparoscopy, while 30% of patient had laparotomy. All patients had a preoperative biopsy (either a pipelle or an endometrial biopsy) that was consistent with endometrial cancer, however only 26% of them correctly identified all the components of the mixed endometrial carcinoma, while most of them only detected one of the single components. Postoperative histology showed that the most common combination was represented by endometrioid and serous components (71%), followed by serous and clear cell components (17%), mixed serous carcinoma and sarcoma components (5.7%) and a mixture of endometrioid, serous and clear cell components (5.7%).

Overall, the 5-year survival was 67%, although different components showed different survival rates. Even if mixed endometrioid and serous carcinoma was more commonly diagnosed later, its prognosis tended to be better than the other histological mixed types, with a 5-year survival rate of 76%.

Since the prognosis seems strongly related to the histological types, it is strongly recommended to carefully identify all the components of this endometrial cancer after performing primary surgery, in order to correctly counsel patients.

Introduction

Mixed epithelial carcinoma are defined as tumors composed of “two or more different histological types of endometrial carcinoma, at least one of which is of the type II category” (non-endometrioid, non-mucinous type). Since they are a rare subtype of endometrial cancer, accounting for less than 1% of all patients, there are limited studies on the literature that describe the behaviour of this cancer. Our aim in this retrospective cohort case series is to review the epidemiology, histology and survival of patients with mixed endometrial carcinoma.

Methodology

We identified all patients that underwent surgery for mixed endometrial cancer at Oxford University Hospitals NHS Foundation Trust in a 10-year interval, between 2009–2019, and their data was collected retrospectively. Statistical analysis was performed using the MedCalc software.

34 patients were identified, representing <4% uterine malignancies treated in our unit. 22 of these patients were referred to OUH from district hospitals in the Thames Valley area, where they were then followed up after surgery.

The average age at the time of the diagnosis was 70 (interval 52–84) and they were all postmenopausal.

The most common associated comorbidity was hypertension (61%); 37% of patients were obese (BMI>30). There wasn't a strong association with diabetes mellitus, PCOS, use of HRT or smoking. 14% of patients also had breast cancer. CT scan was the most commonly used imaging modality preoperatively (58.8%). Average time interval from the first MDT meeting to the day of the surgery was 55 days.

All patients underwent primary surgery (hysterectomy and bilateral salpingo-oophorectomy): the majority of patients (70%) were treated with laparoscopy, while the remaining 30% underwent laparotomy. 82% of patients (28/34) also underwent bilateral pelvic lymphadenectomy and the average number of removed lymph nodes was 13. Lymph nodes histology was positive for disease invasion in 7 patients. 70% of patients (24/34) also had omentectomy. 23% of patients (8/34) sustained operative postoperative complications, mostly represented by infection (50% of complications), followed by nerve injury, postoperative ileus and one episode of acute coronary syndrome which required ITU admission. 62% of complications occurred in laparotomies, while only 3 of the 8 complications occurred in laparoscopies.

We then considered their histological findings (histological components, FIGO staging, myometrial/cervical/adnexal involvement, serosal breach and LVSI) and survival rates and these data were analyzed using MedCalc software.

Results

Consistently with the literature, the most common combination was represented by endometrioid and serous components (25/34, 71%), followed by serous and clear cell components (5/34, 17%), mixed serous carcinoma and sarcoma components (2/34, 5.7%) and a mixture of endometrioid, serous and clear cell components (2/34, 5.7%).

Preoperative histology (pipelle or endometrial biopsies) was consistent with the final diagnosis only in 26% of the cases (9/34), while the remaining preoperative histological findings only detected one of the mixed components.

Even if the majority of patients underwent laparoscopy (70%), complications occurred more commonly in laparotomies.

Overall, the 5-year survival was 67%, although different components showed different survival rates.

Post-operative staging was documented in all cases and showed that both mixed serous carcinoma and sarcoma combination as well as mixed endometrioid, serous and clear cell carcinoma were more likely diagnosed early (all stage 1), while mixed endometrioid and serous carcinoma, as well as serous and clear cell carcinoma were diagnosed later in the disease (28% and 50% respectively were stage 3 at the time of diagnosis). Despite this, the prognosis mostly reflected the histological types, rather than the staging: mixed serous carcinoma and sarcoma combination was the most aggressive with a 5-year survival of 0% (0/2), followed by mixed serous with clear cell components (33%, 2/5) and mixed endometrioid, serous and clear cell carcinoma [50%, 1/2], while mixed endometrioid and serous carcinoma was the least aggressive, with a 5-year survival of 76%.

Due to the limited number of cases owing to the rarity of the combination of mixed serous carcinoma and sarcoma components (2 cases), as well as of the combination of three histological subtypes (2 cases), the comparison of survival curves did not reach statistical significance. However, when comparing the remaining groups (mixed endometrioid and serous carcinoma; serous and clear cell carcinoma) the survival difference was statistically significant (Logrank test, p-value 0.024), confirming the hypothesis that the single histological components of the mixed epithelial carcinoma mostly define the prognosis.

Conclusion

Mixed epithelial carcinoma of the uterus are rare, but clinically significant subtypes of endometrial cancers, which do not seem related to obesity, diabetes mellitus or use of HRT. Most patients can be treated with a laparoscopic approach, with less complication rates and shorter hospital stay.

The overall 5-year survival rate was 67%, which is consistent with the literature, however the prognosis mostly reflected the individual components. Mixed endometrioid and serous components are the most common and least aggressive combination among mixed epithelial carcinoma of the uterus, followed by the combination of serous and clear cell components.

The prognosis seems more strongly related to the histological types, rather than the staging. Indeed, endometrioid and serous mixed carcinomas are more commonly diagnosed later in the disease (stage 3), but their survival curves are better than the other histological subtypes, even if the other combinations are diagnosed earlier (mostly stage 1).

Preoperative pipelle or endometrial biopsies correctly identified the mixed epithelial carcinoma only in a minority of cases, while in 74% of cases only identified one of the components. It is therefore imperative to perform histological analysis of all samples after primary surgery and to clearly identify all the histological types at the time of the diagnosis, in order to correctly counsel patients.

Further studies will be useful in order to further compare the management of mixed endometrial carcinomas with their corresponding individual components.

