

Mucinous endometrial cancer: Clinical study of the eleven cases

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ABSTRACT

OBJECTIVE: In this study, we analyzed surgico-pathologic factors of mucinous type endometrial carcinoma and examined its frequency of recurrence.

METHODS: In this study, eleven cases, definitely diagnosed as pure mucinous type endometrium carcinoma between January 1993 and May 2013, were reviewed.

RESULTS: Of 1640 women with endometrium carcinoma, 11 (0.67%) of them had a mucinous cell type. Mean age of the study group was 55 years. According to the FIGO 2009, 10 (90.9%) cases were evaluated as stage I and 1 (9.1%) as stage IIIC1. The presence of lymph node metastasis was noticed in only one (12.5%) of eight patients who underwent lymphadenectomy. In this case, metastasis was detected in the pelvic lymph node. Four patients underwent adjuvant therapy as pelvic radiotherapy. Median follow-up time was 50 months (range, 5–84). Recurrence was observed in one (9.1%) patient with stage IIIC1 endometrial cancer in 30 months after primary surgery. The site of recurrence was only in the upper abdominal region.

CONCLUSION: Based on our study, mucinous endometrial carcinoma has good prognostic factors, and long term survival can be achieved surgically alone in patients with stage I.

Keywords: Endometrial carcinoma; mucinous type; survival.

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Estimates of the worldwide incidence and mortality from cancer of corpus uteri combined for 2012 are 320.000 new cases (4.8% of the cases in women) and 76.000 deaths (2.1% of the cancer death in women) [1]. Cancers of the uterine corpus substantially represented by endometrial cancers. Endometrial cancer (EC) has been firstly classified as type I (endometrioid) and type II (non-endometrioid) by Bokhman et al. in 1983 [2]. Type I EC is known as a lower grade, early detected and a better prognosis than type II.

Pure mucinous adenocarcinoma of the endometrium

is reported in the category of type II. The prevalence varies between 1% and 5%.³ To make the diagnosis of mucinous adenocarcinoma, more than half percent of the cell population should include periodic acid Schiff-positive diastasis-resistant intracytoplasmic mucin [3, 4]. The 5-year disease-free survival rate in patients with mucinous adenocarcinoma is 89% [5].

In this study, the determination of surgico-pathologic factors and recurrence patterns in patients with pure mucinous type EC is aimed.



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MATERIALS AND METHODS

In this study, eleven cases, definitely diagnosed as pure mucinous type EC between January 1993 and May 2013, were examined retrospectively. Surgical-pathological data of cases were collected from the electronic database of the Gynecologic Oncology Clinic. Exclusion criteria were as follows: (i) patient files which could not be obtained from the database, (ii) cases without the diagnosis of mucinous cell type, (iii) having a secondary type of component in addition to the mucinous tumor (mixed type) and (iv) tumors, including sarcoma components. Staging was made according to FIGO 2009.

Frozen/section is routinely applied intra-operatively in cases of EC in our clinic. Staging surgery is performed in cases of non-endometrioid adenocarcinoma tumor type, tumor grade 2 or 3, $\geq 1/2$ of depth of the myometrial invasion, the presence of cervical invasion, > 2 cm tumor size. In addition, staging surgery is directly applied if the preoperative pathological diagnosis is grade 3 endometrioid tumor or high-risk cell type. Staging surgery is performed as standard of total abdominal hysterectomy + bilateral salpingo-oophorectomy + systematic pelvic and para-aortic lymphadenectomy + cytological sampling + omentectomy. In the presence of intraoperative macroscopic pathology, additionally, cytoreductive surgery is applied.

Adjuvant treatment success was defined according to the World Health Organization criteria [6]. According to the assessment made in the first month after treatment, we defined clinical response as follows: (i) complete clinical response; disappearance of the macroscopic tumor, (ii) partial clinical response; shrinkage over 50% in the macroscopic tumor, (iii) stable disease; macroscopic tumor shrinkage less than 50% or not less than 25% growth, (iv) progressive disease; more than 25% growth in the macroscopic tumor or macroscopic appearance of new tumor foci.

The patients with complete clinical response were examined every three months in the first two years, every six months in the following three years and then once every year. This assessment included vaginal examination, abdominal ultrasonography, complete blood count and biochemistry. Chest X-ray was performed every year, and in case, there was clinical suspicion. When necessary, thoracic computerized tomography was used. Pap-smear and the CA-125 were not used routinely. The patients without a complete clinical re-

sponse were evaluated again, and their treatment was re-planned. The statistical analyses were performed using the Statistic Package for Social Sciences (ver. 11.0; SPSS Inc., Chicago, IL).

RESULTS

Of 1640 women with EC, 11 (0.67%) of them had a mucinous cell type. Mean age of the study group was 55 years (range, 46-72). According to the FIGO 2009, 10 (90.9%) cases were evaluated as stage I disease and 1 (9.1%) case as stage IIIC1 disease. There was one case of primary carcinoid tumor of the appendix concurrently. Ten (90.9%) patients had a myometrial invasion. Eight (80%) patients had FIGO grade 1. Cervical invasion, adnexal involvement, omental involvement and lymphovascular invasion was not observed. Peritoneal cytology was negative in all patients. Macroscopic tumor was not present in any of the patients after surgery. Surgical pathologic data of the patients were described in detail in Table 1.

Pelvic and para-aortic lymphadenectomy was performed to eight patients. Depending on the choice of the surgeon, lymph node dissection was not performed to three patients who had tumor size less than 2 cm, myometrial invasion less than 50% and FIGO grade 1. We could not reach the data regarding the number of lymph nodes in one of eight patients underwent lymphadenectomy. Mean number of lymph nodes removed from the remaining seven patients was 38.4 (range, 10-69). The presence of lymph node metastasis was noticed in only one (12.5%) of eight patients who underwent lymphadenectomy. In this case, metastasis was detected in the pelvic region.

Depending on the choice of the gynecologic oncology council, only radiotherapy was administered as adjuvant treatment. Four of 11 patients underwent adjuvant pelvic radiotherapy (patient no#2, no#4, no#5, no#10 in Table 2). Adjuvant treatment was not applied to the remaining seven patients.

Median follow-up time was 50 months (range, 5-84). Only 1 (9.1%) patient was presented with recurrence. Recurrence detected in a patient with pelvic lymph node metastasis in the upper abdominal region 30 months after primary surgery (patient no # 2) (Table 2). This patient underwent only radiotherapy after recurrence, and we achieved partial clinical response. After 10 months from recurrence, the patient was alive with the disease.

TABLE 1. Surgical-pathological factors

Patient number	Age	FIGO 2009 stage	Grade	DMI	LVSI	Tumor size (mm)	Lymphadenectomy	Total removed lymph node number	Lymph node metastasis	Second primary tumor
1	56	IA	1	NI	Negative	NR	Performed	41	Negative	Negative
2	72	IIIC1	2	≥1/2	Negative	NR	Performed	NR	Pelvic	Negative
3	48	IA	1	<1/2	Negative	NR	Not performed	–	–	Negative
4	56	IA	1	<1/2	Negative	NR	Not performed	–	–	Positive ²
5	56	IB	2	≥1/2	NR	15	Performed	24	Negative	Negative
6	52	IA	1	<1/2	Negative	NR	Performed	27	Negative	Negative
7	46	IA	1	<1/2	Negative	NR	Not performed	–	–	Negative
8	56	IA	1	<1/2	Negative	NR	Performed	41	Negative	Negative
9	50	IA	1	<1/2	Negative	10	Performed	69	Negative	Negative
10	62	IB	NR	≥1/2	Negative	NR	Performed	10	Negative	Negative
11	51	IB	1	≥1/2	NR	90	Performed	57	Negative	Negative

DMI: Depth of myometrial invasion; LVSI: Lymphovascular space invasion; NR: Not reported; NI: No invasion; ²Appendicular carcinoid tumor.

TABLE 2. Clinical data of the patients

Patient number	Adjuvant therapy	Presence of recurrence	Recurrence location	Recurrence time (month)	Salvage treatment	Follow-up time (month)
1	Not received	Negative	–	–	–	36
2	Radiotherapy	Positive	Upper abdominal	30	Radiotherapy	40
3	Not received	Negative	–	–	–	48
4	Radiotherapy	Negative	–	–	–	84
5	Radiotherapy	Negative	–	–	–	78
6	Not received	Negative	–	–	–	60
7	Not received	Negative	–	–	–	84
8	Not received	Negative	–	–	–	72
9	Not received	Negative	–	–	–	16
10	Radiotherapy	Negative	–	–	–	12
11	Not received	Negative	–	–	–	5

DISCUSSION

Mucinous adenocarcinoma of the endometrium, with prevalence below 10%, is a rare variant of EC [2, 7]. At the end of 20 years of experience in our clinic, 0.67% of the treated EC cases were identified as pure mucinous type. Based on data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) registry from EC cases diagnosed between 1988 and 2009, patients with mucinous adenocarcinoma of the

endometrium comprised only 1.5% of the cases [8]. Ages of endometrial mucinous adenocarcinoma incidence in the literature is reported to vary between the late 50s and 60s [9–11]. In our study, in harmony with the literature, we have found to be a mean age of 55.

Early-stage disease, low-grade tumors, low incidence of lymphovascular space invasion are found in the majority of patients with endometrial mucinous adenocarcinoma [12]. In our study, 90.9% of the patients

were diagnosed at stage I, and there was no evidence of lymphovascular space invasion. Myometrial invasion was found in the majority of our patients (10 patients, 90.9%), while it was less than 50% in six (54.5%) cases. Additionally, we have not observed a lymphovascular invasion. In the study of Melhem and Tobon, the myometrial invasion was found in 66% and lymphovascular space invasion was found in 5.5% of the patients in a series of 18 cases [12]. In the study of Ross et al., the myometrial invasion was found in 50% of the tumors [3].

In most studies, cases were defined as stage I in accordance with our study [12, 13] However, most of these studies are old and the proportion of patients treated with radiotherapy in the preoperative period is quite high in these series. More recently, Jalloul et al. defined 16.1% of patients as stage III disease in their series of 31 cases [14]. In our study, 9.1% of the patient was defined in stage III disease. In this case, the tumor had spread to pelvic lymph nodes. Lymph node metastasis is a poor prognostic sign in EC [15]. EC of mucinous histology has been reported as an independent risk factor for lymph node metastasis in the study from Musa et al. [16]. In series of Jalloul et al., recurrence was observed in four of five patients with lymph node metastasis [14]. In our study, recurrence was developed in a patient with lymph node metastasis only in the upper abdominal region 30 months after primary surgery. Partial clinical response was obtained after recurrence by radiotherapy treatment. After 40 months from recurrence, the patient was alive with the disease.

Several studies show that mucinous adenocarcinoma of the endometrium has a better prognosis than endometrioid adenocarcinoma [10, 12]. In the study of Ross et al., the two histological types (mucinous and endometrioid) with the same grade and stages have been reported to have similar clinical behavior and prognosis [3]. Another study reported that there was no difference in recurrence-free and overall survival between patients with endometrioid and mucinous adenocarcinoma [16]. The findings of the studies indicate that there are different opinions about the prognosis of mucinous EC.

Mucinous EC is managed in a similar fashion to low-grade EC [17]. The most common adjuvant treatment considered for endometrial carcinoma has been radiation therapy. Chemotherapy has traditionally been deemed ineffective [18, 19]. Several prospective trials (PORTEC-1 and 2, GOG#99) have shown that the use of adjuvant RT in the intermediate-risk and the high- intermediate-

risk groups decreases locoregional recurrence but has no effect on overall survival [20]. The median follow-up time in our study was 50 months. Four of 11 patients underwent adjuvant pelvic radiotherapy with stages of IIIC1, IB, IA, IB. One patient with stage IIIC1 has recurred in the upper abdominal region outside the radiation field, after 30 months of the pelvic radiotherapy.

Retrospective nature and the limited number of patients are important limitations. In addition, our study was from a single-center, the pathology materials have been evaluated by gynecopathologists and the patients have been followed by a gynecologist oncologist.

As a result, the present study showed that endometrial mucinous adenocarcinoma, concerning surgical-pathologic factors, was found to have a good prognostic factor. The median follow-up time was 50 months in the presented study. Patients have good prognostic factors in this series. The findings suggest that high survival can be achieved with good prognostic factors in pure mucinous EC. On the other hand, this study shows the necessity of adjuvant therapy in advanced stage tumors. However, the available data do not support the need for staging each of the population. To obtain clear results about recurrence pattern of mucinous cell type and overall survival rates, further prospective studies in larger series and longer follow-up periods are needed to confirm or refute these data.

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Authorship Contributions: Concept – SD; Design – OT; Supervision – TTu; Materials – GK; Data collection and/or processing – IND, TTa; Analysis and/or interpretation – AK, DB; Writing – SD, OT; Critical review – IU, TTu.

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