Uterine Serous Papillary Carcinoma: A Retrospective Analysis of 22 Cases

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OBJECTIVE: The cases of 22 patients with uterine serous papillary carcinoma (USPC) were reviewed for this study.

STUDY DESIGN: The data of 22 patients diagnosed with USPC was examined. 18 patients underwent formal staging surgery including type I hysterectomy, bilateral salphingo-oophorectomy, para-aortic and bilateral pelvic lymphadenectomy, appendectomy and omentectomy in our clinic. Four patients were sent to our clinic from other hospitals after primary surgery. Staging of the disease was based on the FIGO 1998.

RESULTS: At the time of diagnosis the median age was 62.2 years. The most common clinic complaint was vaginal bleeding (86.3%). seven patients were stage I (31.8%), one was stage II (4.5%), eight were stage III (36.3%) and six were stage IV (27.3%). Median disease-free survival was 25 months. Recurrence was not influenced by the stage of disease, lymphatic metastasis, depth of myometrial invasion, adjuvant therapy and the type of adjuvant treatment. However, the recurrence was influenced by positive cytology and invasion of omentum.

CONCLUSIONS: Staging surgery should be performed on patients with USPC. Invasion of omentum and positive cytology were poor prognostic factors. The effect of adjuvant therapy on prognosis is not clear.

(Gynecol Obstet Reprod Med;14:1 30-35)

Key Words: Uterine serous papillary carcinoma, Prognosis

Introduction

Endometrial adenocarcinoma is the most common gynecologic malignancy in developed countries.[1] Uterine serous papillary carcinoma (USPC) is one of the aggressive subtypes of the endometrial carcinoma, which progresses with lymphovascular and deep myometrial invasion. The incidence of USPC is 1.6-10% in endometrial adenocarcinoma (2-5). In stage I and stage II, five-year survival is under 50%.[6]

In this study, clinical and pathological characteristics of USPC and the relation with the prognosis are evaluated.

Material and Methods

The medical files of 22 patients, who were diagnosed with USPC between 1998 and 2006, were reviewed. 18 patients have received their primary therapy in our clinic. These patients have had staging surgery (Optimal cytoreductive surgery: Type I hysterectomy [TAH] + bilateral salphingo-oofer-ectomy [BSO] + para-aortic and bilateral pelvic lymphadenectomy [PABPLND] + appendectomy + omentectomy). Four patients were transferred to our clinic after undergoing surgery in different hospitals (two of them have had TAH + BSO + PABPLND + omentectomy, one patient has had TAH + BSO and last patient has had Type II radical hysterectomy + BSO + PABPLND). The pathology specimens of these patients were re-examined in our hospital and adjuvant therapy was administered. The patients were staged according to FIGO 1998.

In the pathological examination of the specimens, only those with serous papillary tumor were designated as pure USPC, the specimens which included more than one of the histological type (serous papillary +/- clear cell +/- endometrioid tumor) were designated as mixed type tumors.

The period between the first surgery and recurrence is accepted as disease-free survival (DFS) whereas the period between the first surgery and exitus is accepted as overall survival (OS).

Descriptive statistics were calculated using the SPSS (Statistical Package for Social Sciences) 12.0 package program (SPSS Inc, Chicago IL, USA). The Annova Table Test and Chi-square test was used to evaluate proportions for statistical significance. The cut-off for statistical significance was set at $P < 0.05$.

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Submitted for Publication: *23.02.2008*
Accepted for Publication: *23.03.2008*

Results

22 of the 1369 (1.6 %) endometrial carcinoma patients who received treatment in our clinic had USPC. The median age of was 64.2 years (45-73), all of them being postmenopausal. The most common clinical symptom was vaginal bleeding (n=19, 86.3%) (Table 1).

According to the FIGO 1988 staging system, seven patients (31.8%) were classified as stage I, one (4.5%) as stage II, eight (36.3%) as stage III, six (27.3%) as stage IV (Table 1). Seven patients (31.8%) had ascites. Twenty patients (90.9%) had pure USPC (Table1). 15 patients (68.2%) had deep myometrial invasion (>50%), 10 had (45.5%) lymphovascular space invasion (LVSI) and 11 had (50%) lymph node invasion (Table 2). Out of the 20 patients that underwent omentectomy, eight (36.4%) had metastasis. Seven patients (31.8%) had positive cytology (Table 2)

Sixteen patients (72.7%) received adjuvant therapy (Tabe1). Radiotherapy (RT) was administered to three (13.6%), chemotherapy (CT) was given in five (22.7%) and concurrent chemo-radiation (RT-CT) was ordered for eight (13.6 %) (Table 2). One of the patients could not receive adjuvant therapy due to postoperative renal failure. One patient who was stage IVB was planned to take adjuvant therapy, she wasn't accepted to the therapy and the clinical follow-up. The other four patients that did not receive adjuvant therapy were stages IA and IB.

The median follow-up time was 27.1 months (1-82). The patient with the follow-up time of one month did not appear for the clinical follow-up after surgery. Recurrence was detected in four of the patients (18.2%). For these patients disease-free survival was 25 months (8-50). Three of these patients were stage IV and one of them was stage III (Table 2). Myometrial invasion was positive in four patients, lymph node invasion in three and LVSI was in three. Three of four patients had omentectomy and omental invasion was positive. The patient who did not undergo omentectomy was operated on in the other clinic and later referred to our clinic for postoperative adjuvant therapy. Three of the four patients had ascites and all of them had positive peritoneal cytology. All of the patients with recurrence had received postoperative adjuvant therapy (Table 2).

Three of the patients who had recurrence were stage IVB and received six courses of paclitaxel-carboplatin for adjuvant therapy. In one of these patients recurrence was observed 14 months after the last chemotherapy and as the patient refused to undergo therapy in this period, there is no further data on the patients' last condition. In the second patient recurrence was observed 13 months after the last chemotherapy, in the upper abdomen. It was classified as platinum-sensitive and the start of the paclitaxel-carboplatin therapy as second-line chemotherapy was scheduled. However due to cardiac problems the patient was administered carboplatin in three week periods. After three courses of carboplatin, there was an isolated CA 125 elevation in this patient. For the next three

Table 1: Clinical features of patients

Characteristics		n	%
Age	<60	1	4.5
	≥ 60	21	95.5
Postmenapause		22	100
Weight	< 66	5	22.7
	≥ 66	17	77.3
Parity	< 4	6	27.3
	≥ 4	16	72.7
Clinical symptom	AUB	19	86.3
	AP	3	13.7
Stage	I-II	8	36.4
	III-IV	14	63.6
Ascites	Positive	7	31.8
	Negative	17	68.2
Histopathology	Pure type	20	90.9
	Mixt type	2	9.1
Adjuvant therapy	Positive	16	72.7
	Negative	6	27.3
LNM	Positive	11	50
	Negative	11	50
Recurrence	Positive	4	18.2
	Negative	18	81.8
Exitus	Positive	2	9.1
	Negative	20	90.9

LNM: *Lymph node metastasis,* ***AUB:*** *Abnormal uterine bleeding,* ***AP:*** *Abdominal pain*

months CA 125 was observed and due to a lack of decrease, a 50 mg/m^2 oral etoposide treatment was initiated. After five courses of etoposide, the patient was reexamined and after being designated as stabile, was taken into clinical observation. The vaginal, liver, pelvic and lung metastasis were discovered in this patient, after four months. Palliative therapy was administered to this patient and after five months the patient died (OS:55 months). In the third patient recurrence was observed in the lung four months after the last chemotherapy session. The patient was classified as platinum resistant and a 50 mg/m^2 liposomal doxorubicin treatment was initiated. After two courses progression was discovered. This patient refused further therapy and did not come in for controls. After four months, the patient died (OS: 18 months). The fourth patient with recurrence underwent surgery (TAH + BSO) and received a single course of adjuvant chemotherapy (cisplatin/endoxan) in another clinic and was then referred to our clinic. She was stage IIIA. Radiotherapy was given to this patient (5000 cGy external pelvic front-behind 16x14 cm area from 200 cGy/day doses and 3 cycle 1500 cGy intracavitary). Seven months later abdominopelvic recurrence was discovered and six courses of PF chemotherapy were applied. Three months later 6th course abdominal and cuff recurrence was discovered and 125mg/m^2 paclitaxel chemotherapy was administered. After two cycles of paclitaxel chemotherapy, the patient did not return for the clinical following.

The third patient who died was stage IIIC, a postoperative adjuvant radiotherapy was scheduled however due to bilaterally hydronephrosis and renal failure, adjuvant therapy could not be administered and the patient died (OS: 4 months).

Age, weight, parity, lymph node invasion, deep myometrial invasion, the administration of adjuvant therapy and the kind of adjuvant therapy did not have any effect on recurrences. However omental metastasis, ascites and positive cytology increased the recurrence ratio (Table 3).

Table 2: The clinical and histopathologic features and survival of 22 patients with USPC

No	Age	Stg	LNM	DMI	LVSI	Ascite	Cytology	Adjuvant Therapy	Omental Metstasis	Recurrence	DFS (month)	Last situation
1	60	IVB	+	+	-	s	+	CT	+	+	14	Give up the clinical following
2	60	IB	-	-	-	+	-	RT+CT	-	-		LNED
3	70	IVB	+	+	+	+	+	CT	+	+	50	Exitus
4	61	IA	-	-	-	+	-	-	-	-		LNED
5	64	IC	-	+	+	-	-	-	-	-		Give up the clinical following
6	70	IVB	-	+	-	-	#	RT+CT	+	-		LNED
7	72	IIIC	+	+	+	-	-	RT	-	-		Give up the clinical following
8	72	IIB	-	+	+	-	-	RT	-	-		LNED
9	73	IB	-	-	-	-	-	RT	-	-		Give up the clinical following
10	58	IIIC	+	+	+	-	-	-	-	-		Exitus
11	65	IVB	-	+	+	+	+	CT	+	+	8	Exitus
12	70	IVB	+	+	+	-	#	-	+	-		Give up the clinical following
13	70	IIIA	+	+	+	-	+	RT+CT	¶	+	11	Give up the clinical following
14	65	IIIC	+	+	-	+	+	CT	+	-		LNED
15	64	IIIC	+	+	-	-	#	RT+CT	-	-		LNED
16	60	IB	-	-	-	-	-	RT+CT	-	-		LNED
17	64	IIIC	+	+	+	-	-	RT+CT	-	-		Give up the clinical following
18	62	IIIC	-	+	+	+	+	CT	+	-		LNED
19	60	IB	-	-	-	-	-	-	-	-		LNED
20	60	IVB	+	-	-	+	+	RT+CT	+	-		LNED
21	45	IA	-	-	-	-	#	-	¶	-		LNED
22	68	IIIC	+		+	-	#	RT+CT	+	-		LNED

***#:** no cytology, **LVSI:** lymphovascular space invasion, **RT:** Radiotherapy, **¶ :** no omentectomy, **DFS:** Disease free survival, **CT:** Chemotherapy*
***Stg:** Stage, **LNM:** Lymph node Metastasis, **LNED:** Live with no evidence of disease*

Table 3: Prognostic factors for recurrence

Prognostic factor		Recurrence		p
		Negative	Positive	
Age	≤60	6 (85.7)	1 (14.3)	0.694
	>60	11 (78.6)	3 (21.4)	
Weight	≤66	4 (100)	-	0.091
	>66	3 (50)	3 (50)	
Parity	≤4	10 (83.3)	2 (16.7)	0.748
	>4	7 (77.8)	2 (22.2)	
Stage	I-II	8 (100)	-	0.081
	III-IV	9 (69.2)	4 (30.8)	
Lymph node metastasis	Negative	10 (90.9)	1 (9.1)	0.223
	Positive	7 (70)	3 (30)	
LVSI	Negative	8 (100)	-	0.072
	Positive	6 (66.7)	3 (33.3)	
DMI	≤50	7 (100)	0 (0)	0.116
	>50	10 (71.4)	4 (28.6)	
Omental metastasis	Negative	12 (100)	-	0.013
	Positive	4 (57.1)	3 (42.9)	
Ascites	Negative	13(92.9)	1 (7.1)	0.049
	Positive	4 (57.1)	3 (42.9)	
Cytology	Negative	10(100)	-	0.006
	Positive	3 (42.9)	4 (57.1)	
Adjuvant therapy	Negative	5 (100)	-	0.214
	Positive	12 (75)	4 (25)	

LVSI: *Lymphovascular Space Invasion,* ***DMI:*** *Deep Myometrial Invasion (>50%),*

Discussion

USPC is a rare and aggressive tumor among endometrial adenocarcinomas. It has a poorer survival rate than the other subtypes.[5,7] In studies its frequency is stated to be 1.6-10% .[2,8-14] In this study the frequency was almost the same as observed within the other studies (1.6%).

In USPC, the median age is higher than the other subtypes of endometrial carcinoma.[2,8,10,11] In studies it is stated that the patients are in their 6th-10th decades.[5] In this study, the median age of patients was 64.2 and all of them were post-menopausal. However in endometrial adenocarcinoma, 25% of the patients are in pre-menopausal period and 5% of these patients are under age of 40.[5] Like the other subtypes of endometrial carcinomas, vaginal bleeding is most common symptom in USPC.

Unlike endometrioid adenocarcinoma, the patients with USPC are admitted with an advanced stage malignancy (21-56%) (2,5,15). It is correlated with an aggressive progression of USPC. In this study 63.6% of the patients were in advanced stages.

Deep myometrial invasion ratio is 25% in endometrioid adenocarcinoma. In USPC deep myometrial invasion rates is between 36-45% [10,11,16-18] and it is correlated with poor prognosis. In this study deep myometrial invasion ratio was 68% however it did not have any influence on recurrence.

In recent studies omental metastasis ratio is about 20%.[18-20] In this study omental metastasis was 36.4% and cytology was positive in 31.8 % of the patients. Omental metastasis and positive cytology increase the risk of recurrence.

Advanced stage, the degree of myometrial invasion, LVSI, lymph node metastasis did not effect the recurrence risk in this study but in some studies, these parameters are correlated with poor prognosis.[3-5,11,21,22]

There is no common opinion on adjuvant therapy and type of therapy and the outcomes of prognosis. In this study adjuvant therapy and type of therapy did not affect the outcome of prognosis, either. There are similar results recorded in other studies.[7,23] Huh et al. found no difference in their study on prognosis in stage I USPC patients who were only included in follow-ups or received radiotherapy.[23] On the other hand, better results were recorded in the chemotherapy group. Thomas et al reported that observation could be a suitable alternative management in stage IA.[24] However they also reported

chemotherapy and brachitherapy can decrease recurrence in stage IB and IC. In another study Thomas et al figured out chemotherapy increases survival rates in stage IIIC and IV cancer.[25] There is further need for prospective studies on this subject

Uterin Seröz Papiller Karsinoma : 22 Hastanin Retrospktif Incelemesi

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22 uterin seröz papiller karsinomalı (USPC) hastanın verileri bu çalışma için incelendi.
USPC tanısı olan 22 hastanın verileri incelendi. 18 hastaya kliniğimizde tip 1 histerektomi, bilateral salpingoooforektomi ,paraaortik ve bilateral pelvik lenfadenektomi, appendektomi ve omentektomiyi içeren evrelendirici cerrahi yapıldı. 4 hasta primer cerrahileri yapıldıktan sonra kliniğimize sevk edilmişti. Hastalar FIGO 1998 evreleme sistemine gore evrelendirildi.
Tanı sırasında ortalama yaş 62.2 idi. En sık klinik şikayet vajinal kanama idi (86.3%). 7 hasta evre 1 (31.8%),1 hasta evre 2 (4.5%), 8 hasta evre 3 (36.3%) ve 6 hasta evre 4 (27.3 %) idi. Ortalama hastalıksız yaşam süresi 25 aydı. Nüks varlığı ile hastalığın evresi, lenfatik metastaz, myometrial invazyon derinliği, adjuvan tedavi verilmesi ve adjuvan tedavinin tipi arasında ilişki yoktu. Öte yandan pozitif sitoloji ve omentum invazyonu nüksü etkilemekteydi.
USPC tanılı hastalarda evrelendirici cerrahi uygulanmalıdır. Omentum invazyonu ve pozitif sitoloji kötü prognostik faktörlerdir. Adjuvan tedavinin prognoza etkisi net değildir.

Anahtar Kelimeler: Uterin seröz papiller karsinoma, Prognoz

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