Adenocarcinoma, adenoacanthoma, and mixed adenosquamous carcinoma of the endometrium

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Summary

Purpose: To determine the frequency of endometrial adenocarcinoma (AC) with squamous cell differentiation and to compare the histopathologic and clinical characteristics of patients with adenoacanthoma (AA) and adenosquamous carcinoma (AS) to evaluate possible prognostic differences.

Materials and Methods: Two hundred forty patients with endometrial carcinoma (72.2% AC, 21.25% AA, 6.25% AS) treated at the Department of Gynecologic Oncology of Marmara University Hospital, between January 1986 and December 1997, were reviewed. The diagnoses of the diseases were made with fractional D&C, and the definitive therapy for all patients was carried out at the same hospital. Extrafascial hysterectomy + BSO with or without pelvic and para-aortic lymph node dissection, and omentectomy according to the FIGO staging and grading system were performed.

Results: AC and AS had median ages around 60 years with a similar percent distribution of postmenopausal patients (around 74%). AA had an earlier median age of 51 years which reflects an incidence of only 50% postmenopausal patients. There was a tendency for AA to be of low-grade malignancy (72%), 51% of AC were of low-grade, while only 20% of AS were low-grade tumors. There was no difference for any of the three pathological entities in survival by FIGO stages. Over 80% of the tumors were Stage I and about 10% were Stage II, with less than 10% in Stages III and IV.

Conclusion: Considering the more modern and uniform approaches in therapy for these tumors, there seems to be no differences in prognosis for adenocarcinoma with or without squamous elements. The neoplasms AC, AA and AS should be regarded, and consequently approached, as any low-grade adenocarcinoma of the endometrium.

Key words: Adenocarcinoma; Adenoacanthoma; Adenosquamous carcinoma.

Introduction

Endometrial carcinoma occurs most often in the sixth and seventh decades of life with an average age at onset of 60 years. It is estimated that 75% of the cases occur in patients 50 years and older, and 95% occur in patients over 40 years. Many endometrioid carcinomas contain squamous epithelium. In a well-sampled neoplasm, the squamous element should constitute at least 10% of the tumor to qualify as an adenocarcinoma with squamous differentiation [1]. Adenocarcinomas with squamous elements were divided into those with benign-appearing squamous differentiation and designated adenoacanthoma (AA) whereas those with malignant-appearing squamous epithelium were termed adenosquamous carcinoma (AS) [2]. These neoplasms differ markedly in their behavior; the 5-year survival for AA is 70-87% compared with 19-40% for AS [3, 4]. The biological behavior of adenocarcinomas with squamous elements is similar to endometrioid carcinoma without squamous epithelium. Categorization of carcinomas with squamous epithelium according to the depth of myometrial invasion and the grade of the glandular component provides more useful prognostic information than the division into AA or AS [5, 6].

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Materials and Methods

The records of the Gynecologic Oncology Unit of the University Hospital Marmara, Istanbul from January 1986 to December 1987 yielded 240 patients with endometrial carcinomas. The diagnoses of the diseases were made with fractional D&C, and the definitive therapy for all patients was carried out at the same hospital by performing extrafascial hysterectomy + BSO with or without pelvic and para-aortic lymph node dissection and omentectomy according to the FIGO staging and grading system. The pathological specimens were investigated by the Department of Pathology of the same hospital. A total of 240 endometrial carcinomas were divided into three distinct pathologic entities following the criteria of Ng and Reagan [2, 7]. 1) Adenocarcinoma (AC) consisting of only malignant glandular tissue; (Figure 1) 2) Adenoacanthoma (AA) consisting of a mixture of malignant glandular components and benign-appearing squamous components; (Figure 2) 3) Adenosquamous carcinoma (AS) consisting of a mixture of malignant and malignant-appearing squamous components (Figure 3).

Results

The age, menopausal status, clinical history, symptoms and per survival category for all three tumors are presented in Table 1. Both AC and AS had median ages around 60 years with a similar percent distribution of postmenopausal patients (around 74%). AA in this series had an earlier median age of 51 years which reflects an inci-

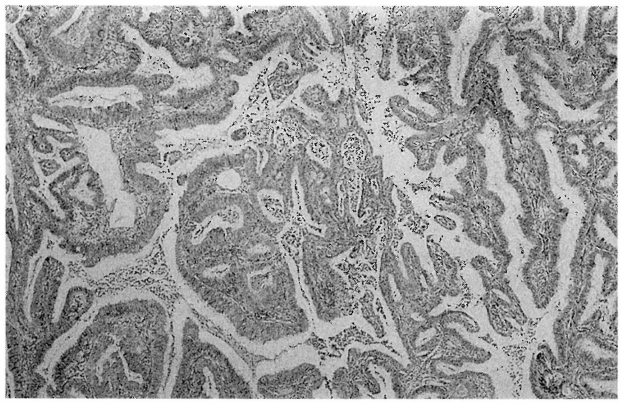

Figure 1. — Endometrioid adenocarcinoma. The tumor is composed of well formed glands and papillae (H&E x 40).

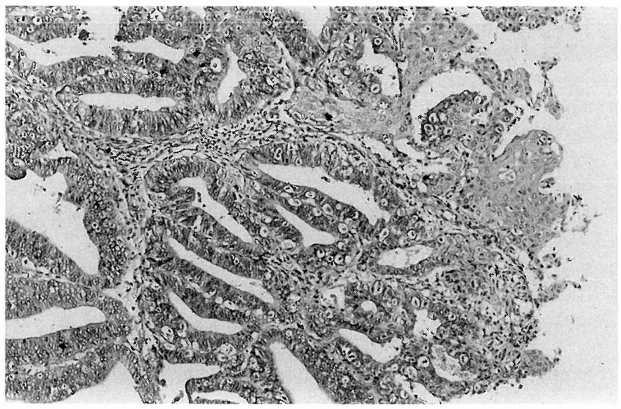

Figure 2. — Endometrioid adenocarcinoma with grade 1 squamous differentiation (adenoacanthoma). The tumor is composed of well-differentiated glandular and squamous elements (H&E x 100).

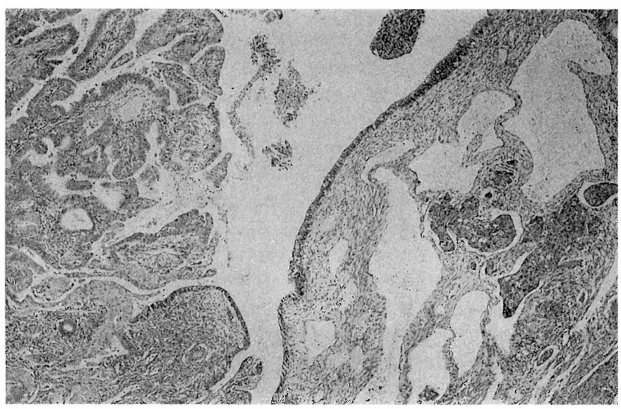

Figure 3. — Endometrioid adenocarcinoma with grade 2 squamous differentiation (adenosquamous carcinoma). Besides areas of adenocarcinoma the tumor is composed of malignant squamous elements infiltrating the myometrium and lymphatics (H&E x 40).

dence of only 50% of postmenopausal patients. There was no statistically higher incidence for any of the symptoms or clinical history in any of the three tumors. Vaginal bleeding was the most common presenting symptom and was present over 80% of the cases. The follow-up was completed for 240 cases. The life-table (actuarial) method was utilized for survival (distribution per survival category) [8]. This presents the percent age of patients with and without disease per survival category. Whenever a patient died and there was not sufficient evidence to suspect the contrary, it was assumed that the patient died with disease. The actuarial life-table technique with Greenwood's approximation to the variance was employed to establish statistical significance of multiple comparisons done in this study [8].

The incidence and 5-year survival by FIGO stage, grade, and myometrial invasion for all three tumors appear in Table 2. There was no difference for any of the

Table 1. — *Age and menopausal status (% of patients).*

	AC	AA	AS
Age			
Mean	59	54	64
Median	53.3	53	60
Range	35-82	37-78	46-86
Status			
Menopausal	32	49	18
Postmenopausal	68	51	82
Clinical history			
HRT	23	7	0
Vag. bleeding	87	81	86
Obesity	62	56	47
Nulliparity	43	37	34
Late menopause	56	61	54
Per survival category			
Alive, NED	72	88	57
Dead, NED	11	8	16
Total, NED	83	96	73
Alive with disease	2	0	0
Dead with disease	15	4	27
Total with disease	17	4	27

Abbr.: AC = Adenocarcinoma, 174 patients; AA = Adenoacanthoma, 51 patients; AS = Adenosquamous carcinoma, 15 patients; NED = No evidence of disease.

Table 2. — *Incidence and 5-year survival by FIGO Stage.*

	Adenocarcinoma		Adenoacanthoma		Adenosquamous ca	
Stage	No. pts. (%)	% 5-yr. surv. (SE)	No. pts. (%)	% 5-yr. surv. (SE)	No. pts. (%)	% 5-yr. surv. (SE)
I	144 (82)	84 (± 3)	43 (84)	98 (± 4)	12 (81)	82 (± 4)
II	21 (12)	64 (± 3)	6 (12)	94 (± 4)	2 (13)	100 (± 5)
III	6 (4)	19 (± 6)	2 (4)	100	1 (6)	0 (NE)
IV	3 (2)	0 (NE)	0 (0)	–	0 (0)	–
Grade						
1	89 (51)	92 (± 4)	36 (72)	98 (± 4)	3 (20)	94 (± 6)
2	73 (42)	87 (± 4)	13 (27)	90 (± 4)	7 (47)	81 (± 5)
3	12 (7)	59 (± 8)	2 (1)	50 (± 8)	5 (33)	60 (± 4)
Myometrial invasion						
None	52 (30)	89 (± 5)	16 (31)	100 (NE)	5 (33)	100 (NE)
<50%	110 (63)	80 (± 4)	31 (61)	96 (± 5)	7 (47)	71 (± 7)
>50%	12 (7)	61 (± 9)	4 (8)	59 (± 6)	3 (20)	33 (± 3)

Adenocarcinoma, 174 patients; Adenoacanthoma, 51 patients; Adenosquamous carcinoma, 15 patients; SE = standard error; NE = non-available. Stages IA and IB considered together. Survival for Stages IA and IB were statistically the same.

three pathological entities. Over 80% of the tumors were Stage I, and about 10% were Stage II, with less than 10% in Stages III and IV. There was no difference in survival for FIGO Stages IA and IB. Therefore, they were grouped into Stage I. There was no statistical difference in survival of Stages I and II, or between the AA and AS tumors; but in AS it was appreciably lower. However this observation was based on only one patient with AS Stage III and must be taken as not being statistically valid.

There was a tendency for AA to be of low-grade malignancy (72%), approximately 51% of AC were of low-grade malignancy, while only 20% of AS were low-grade tumors. For any given grade, there was no statistically significant difference in the 5-year survival for any of the three pathological entities. Curiously there was no difference in survival for FIGO grades 1 and 2 with a 5-year survival of almost 90%; FIGO grade 3 had a significantly lower 5-year survival of around 56%. There was a greater tendency for myometrial invasion in the AS group. There was no major difference in 5-year survival for any of the three tumors with the sole exception of AS invading more than 50% of the myometrium which was found to be 33%. This low survival was obtained in three patients among whom two deaths has occurred and one patient alive and free of disease more than five years after the primary treatment. However, this observation was based only on three patients and may not be significant.

Discussion

Squamous metaplasia of the basal cells located beneath the columnar cells of the endometrial glands can give rise to squamous epithelium within the uterus [9]. There are two types of endometrial carcinomas which share in common the presence of squamous epithelium: adenoacanthoma and mixed adenosquamous carcinoma. These two neoplasms differ from the pure endometrial carcinomas solely by the presence of squamous elements. Factors which are important in the determination of prognosis include the age of the patient [4, 10, 11], the stage of the tumor [3, 10], the depth of myometrial invasion [2, 3, 11], and the histologic grade [2, 3, 10]. In the present series, the patients with AS tended to be slightly older than those with AC and AA (64 years vs 59 for AC and 54 for AA) (Table 1).

There were no basic differences in stage distribution for any of the three entities in five-year survival by stage for AC, AA, or AS (Table 2). In fact, it can be stated that endometrial cancer, regardless of type, is seen at very early stages; over 80% of the patients are Stage I and over 90% Stages I and II.

Deep myometrial invasion repeatedly was found to be strongly associated with an increased probability of lymph node metastasis and death from tumor. We found no significant difference in the frequency of lymph node metastasis when AC was compared with AA and AS at each level of invasion. AA usually occurred in the younger group (mean age 54 years), and were seen 9% to involve more than half the length of the myometrium, with 5-year survival relatively good (59%). AS was correlated with higher age (mean age was 64 years), a poorly differentiated glandular component and more deeply infiltrating tumors (20%); it also had a relatively bad prognosis (33%) (Table 2).

In conclusion, considering more modern and uniform approaches in therapy for these tumors, there seems to be no difference in prognosis for adenocarcinoma with or without squamous elements. The neoplasms AC, AA, AS should be regarded, and consequently approached, as any low-grade adenocarcinoma of the endometrium. The grading of the adenomatous component to a greater extent, and the stage of the lesion with the depth of the myometrial invasion to a minor extent, dictate the overall prognosis for all these endometrial tumors [5]. Since endometrial cancer is overwhelmingly detected in over 90% of the cases at an early stage (Stage I and II), they constitute perhaps one of the few malignant tumors in humans with a good and predictable prognosis.

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