

## A CASE OF ADENO-SQUAMOUS CELL CARCINOMA OF THE VAGINA

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**Synopsis** A 44 year-old woman with an adeno-squamous cell carcinoma of the vagina was presented. The patient didn't have a history of the intrauterine exposure to DES. This case might be a first published case report in the Japanese literature. The histogenesis of adeno-carcinoma components is discussed.

**Key words:** Adeno-squamous cell • Carcinoma • Vagina

### Introduction

In 1971, Kottmeier<sup>6)</sup> has established clear criteria for the diagnosis of the vaginal carcinoma. These are (1) the site of growth in the vagina, (2) an intact cervix and (3) no evidence of primary tumor in any other site. Primary malignancies of the vagina are rare. In addition, the primary adenocarcinoma is extremely rare and most of the case reports are of diethylstilbestrol related clear cell carcinoma, which was first described by Herbst et al.<sup>5)</sup> in 1971.

We recently treated a woman with an adeno-squamous cell carcinoma, which is presented in this report. In literature review, adeno-squamous cell carcinoma has been reported only by Frick et al.<sup>4)</sup>.

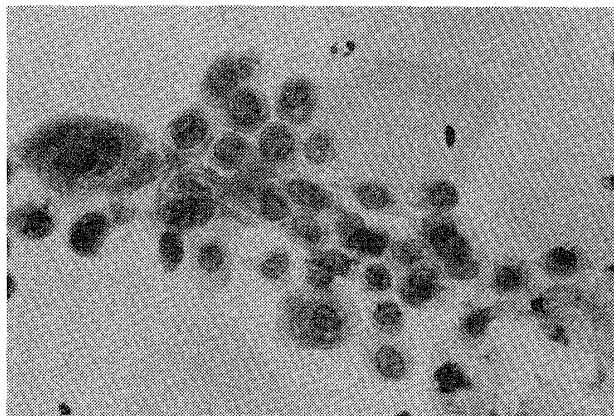
### Case Report

A 44-year-old gravida 4, para 3 woman was admitted to the department of Obstetrics and Gynecology of Osaka University Medical School on June 29, 1979 under the diagnosis of the squamous cell carcinoma in situ of the vagina.

Her menarche was 13 years old. Her periods have been 20 to 25 days' interval with the flow lasting 4 days. Her last menstrual period occurred on April 4, 1979. Her past and family history were unremarkable, without history of intrauterine exposure to DES.

The patient complained of dysmenorrhea and consulted with gynecologist who found the

Photo. 1. Pap. smear showing cells with hyperchromatic nuclei and high N/C ratio of the squamous cell origin.



cytological abnormalities by the vaginal pooling smear. The patient was referred to this hospital. Cytological tests were repeated and interpreted as showing the squamous cell carcinoma (Photo. 1).

By colposcopic examination, cervix was clear but on the vaginal wall near to the top of the posterior fornix, white and mosaic changes were found. The lesion was about 2 cm in diameter. Four quadrant punch biopsies were done with normal cervix. Colposcope directed punch biopsies of the vagina showed squamous cell carcinoma in situ (Photo. 2). Routine pre-operative laboratory studies were within normal limits. On July 3, the patient was operated with semi-radical hysterectomy, right adnectomy and lymphadenectomy. Post-

Photo. 2. Punch biopsy showing an area of in situ squamous cell carcinoma.

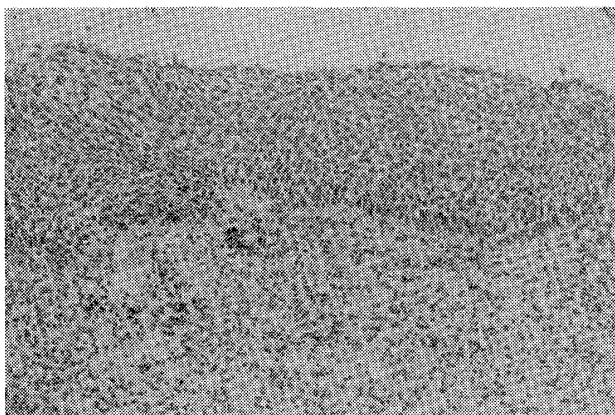
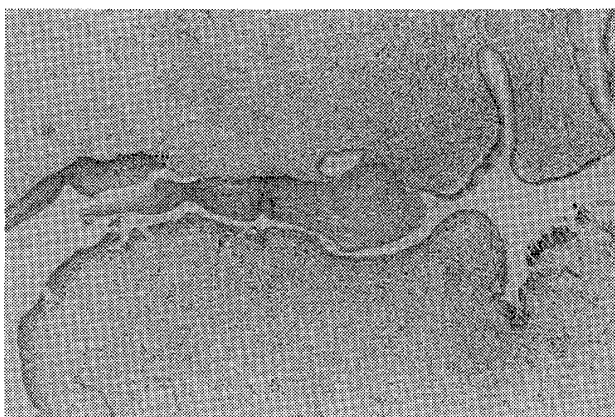


Photo. 3. Normal squamous epithelium was found between the columnar epithelium of the cervix and the atypical squamous lesion of the vagina.



operative course was uneventful. The patient was discharged on July 23 and have been followed up in the out-patient ward, without any evidence of recurrence.

#### Pathological Findings

Grossly, uterus and vagina were unremarkable except for iodine negative area measuring 2 cm in diameter on the posterior vaginal wall. Uterine cervix was divided radially into 12 blocks with negative results.

Histological examination of the vagina revealed in situ squamous cell carcinoma in addition to adeno-squamous cell carcinoma. The cervical columnar epithelium covered the

posterior lip of the cervix near to the posterior fornix (Photo. 3). On the vagina near to the top of posterior fornix, atypical squamous epithelium was found (Photo. 4). In typical adenocarcinoma, the glands were crowded together with little intervening stroma and replaced by stratified atypical columnar cells containing hyperchromatic nuclei (Photo. 5). In mixed area, the in situ squamous cell carcinoma came into with the adenocarcinoma in one portion (Photo. 6) and two types were intermingled with each other in the other portion (Photo. 7).

There was a reserve cell hyperplasia with parakeratosis which covered the adenocarcinoma area (Photo. 8).

Photo. 4. High power view of the post-operative vaginal lesion showing atypical squamous epithelium.

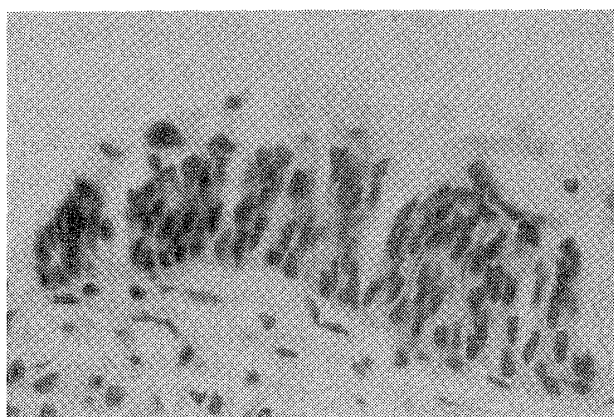


Photo. 5. Adenocarcinoma in which glands were crowded with little intervening stroma and composed of stratified atypical columnar cells.

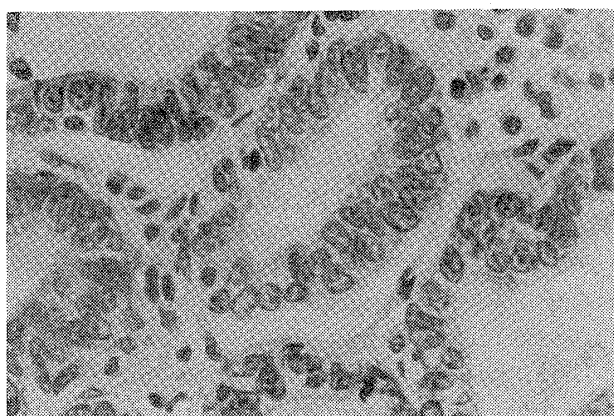


Photo. 6. Microinvasive adenocarcinoma and in situ squamous cell carcinoma were found in the left and in the right, respectively.

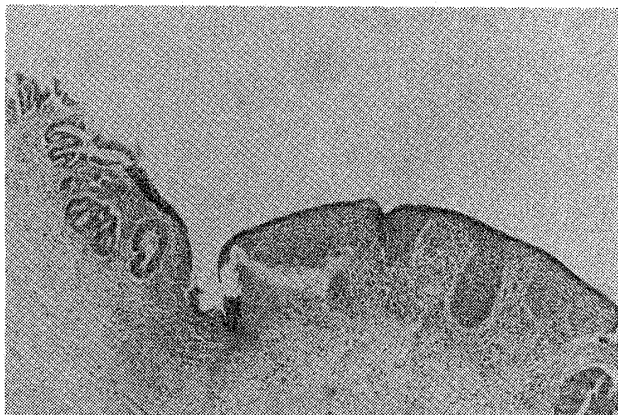


Photo. 7. Low power view of the vaginal lesion showing adeno-squamous cell carcinoma. Two components were intermingled with each other.

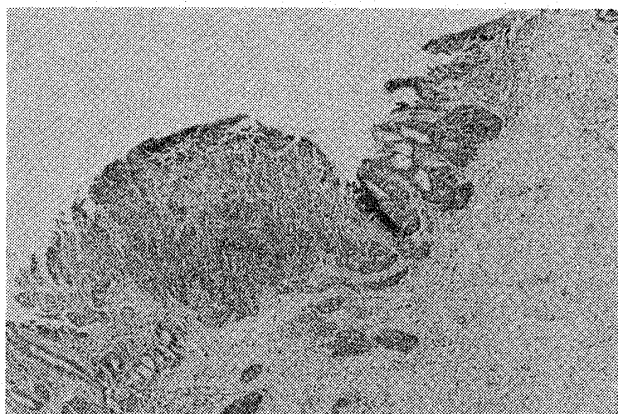
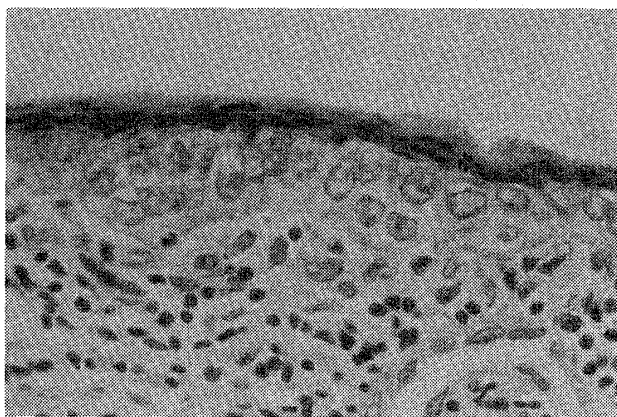


Photo. 8. High power view of the vaginal surface epithelium overlying adenocarcinoma area showing the reserve cell hyperplasia with parakeratosis.



## Discussion

The primary vaginal carcinoma is rare tumor, and it represents about 1-2% of all gynecologic malignancies<sup>2)4)10)12)16)</sup>. Adenocarcinoma of the vagina accounts for 2.5-6% of primary carcinoma of the vagina. The reported cases of adenocarcinoma has generally been classified in 2 categories; adenocarcinoma and mesonephroma (clear cell carcinoma). The latter includes embryonal forms and clear cell carcinomas related to intrauterine exposure to DES. These tumors are not cases which are discussed in this present paper.

In our literature review, we have examined the published reports of the vaginal carcinoma which were not related to intrauterine exposure to DES and have shown the incidence of adenocarcinoma in comparison with the squamous cell carcinoma (Table 1). In 1979, Clement and Benedet<sup>1)</sup> reported firstly a case of adenocarcinoma in situ of the vagina. The lesion was diagnosed 15 months following hysterectomy for in situ squamous cell and in situ adenocarcinoma of the cervix. They made a speculation concerning to the origin of the vaginal adenocarcinoma in situ as follows: (1) downward extension of the cervical adenocarcinoma in situ, because normal ectocervical squamous epithelium was not demonstrated microscopically in the hysterectomy specimen separating the cervical adenocarcinoma in situ from the vagina. (2) malignant transformation of a small focus of pre-existent vaginal adenoma which occur, almost rarely, in females without a history of intrauterine exposure to DES.

In concerning to the gland in the vagina, Sandberg et al.<sup>13)</sup> reviewed the reported cases of benign adenosis vaginae. They offered speculations regarding histogenesis as follows: (1) embryologic development and subsequent persistence of fully developed Müllerian glands in the vaginal subepithelium. (2) postembryonic persistence of individual undifferentiated, Müllerian cells in the subepithelium which, under certain stimuli later in life, differ-

Table 1. Incidence of primary vaginal carcinoma

Authors	Years observed	Primary carcinoma (Number of cases)	Adenocarcinoma (Number of cases)	Adenocarcinoma and Squamous cell ca. (Number of cases)
Palmer & Biback <sup>9)</sup>	1919-1952	112	0	0
Whelton & Kottmeier <sup>17)</sup>	1930-1955	117	3	0
Edward <sup>3)</sup>	1945-1970	51	2	0
Dunn & Napier <sup>2)</sup>	1938-1960	46	1	0
Frick et al. <sup>4)</sup>	1930-1961	45	4	1
Underwood & Smith <sup>16)</sup>	1954-1969	35	2	0
Perez et al. <sup>10)</sup>	1948-1968	118	3	0
Pride et al. <sup>11)</sup>	1956-1971	48	1	0
			(clear cell ca.)	
Rutledge <sup>12)</sup>	20 years	101	5	0
Kusanagi et al. <sup>7)</sup>	1960-1976	9	0	0
Suzumura et al. <sup>14)</sup>	1950-1975	65	0	0
Ushimaru et al. <sup>15)</sup>	1947-1977	30	2	0

entiate and form endocervical-like glands. (3) metaplasia of subepithelial, mesodermal, non-Müllerian connective tissue cells or metaplasia of basal squamous epithelial cells to cylindrical cells which produce mucus and form glands. In considering our case of adenosquamous cell carcinoma, we can neglect the possibility of the downward extension of the cervical lesion, because of the absence of malignant changes in the cervix and the presence of normal squamous epithelium between the normal cervix and the atypical lesion of the vagina. Also, the possibility of its arising from endometriosis can be neglected because of absence of endometriosis in the ovary, uterus and vagina. Finally, it is generally accepted that colposcopic examination is a useful technique for the diagnosis of suspected vaginal carcinoma as well as cervical carcinoma.

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**概要** 腫瘍原発の癌は少なく、中でも腺癌及び線維癌の発生は極めて少ない。我々は腔壁原発の adenosquamous cell carcinoma を経験したので報告する。症例は44歳の4回経妊3回経産婦人で、家族歴・既往歴には特記すべきことなし。

コルポスコピー検査にて子宮腔部は外子口周囲にわずかにみられたが、後者では広く認められた。後腔壁に mosaic と punctation がみられ生検にて扁平上皮内癌と診断された。細胞診では N/C 比大でクロマチンは微細・粗顆粒状、異型細胞は集団又は孤立散在していた。拡大単純性子宮全摘術及びリンパ節廓清を行なった。摘出標本では、子宮腔部の12分画に異常なく、腔壁は adeno-squamous, cell carcinoma であつた。文献上、Frick et al. の1例の報告があるのみで、我が国では同様の報告をみない。