A case of breast carcinoma-like vulvar adenocarcinoma
—Cytological and immunocytochemical study—

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A case of vulvar adenocarcinoma in a 76-year-old woman is reported. The tumor has cribriform and “Comedo” like pattern in histology, polyhedral aggregate and prominent nucleoli in cytology, which are similar to those in breast carcinoma. Tumor cells revealed, expression not only of epithelial membrane antigen, keratin and carcinoembryonic antigen, but also of human papilloma virus antigen and estrogen receptor. Further, many tumor cells showed a strong staining of proliferating cell nuclear antigen. In this report, possible origin and biological behavior of the tumor are discussed.

Key words: Vulvar carcinoma—Cytology—Ectopic breast tissue

I. Introduction

Vulvar adenocarcinoma is an extremely rare tumor. It usually arises from the cells of sweat gland and Bartholin's gland. In a few cases, occurrence of the tumor has been reported in mammary ectopic tissues. Here we report a case of vulvar adenocarcinoma, which is similar to those in breast carcinoma.

II. Case Report

A 76-year-old woman was admitted to the Department of Obstetrics and Gynecology at Ogachi Central Hospital because of an increasing size of the vulvar nodule with contact bleeding and without pain. She referred that the nodule was present for several years. Past history was unremarkable. Physical examination showed a well-nourished, afebrile woman. The ulcerated nodule with a stalk was present at the lateral side of left labium majus. Around the nodule, three small tumors were observed. Inguinal lymph nodes were not enlarged. The other including gastro-intestinal tract and mammary gland were normal. Routine X-ray films and CT scanning were all within normal...
Fig. 1  Tumor cells had large irregular nuclei, prominent irregular nucleoli, thick nuclear margin and coarse chromatin (Papanicolaou stain, ×40)

Fig. 2  Histological staining showed an adenocarcinoma composed of solid, ductal and cribriform pattern with central tumor necrosis (comedo change) (Hematoxylin-eosin stain, ×4)

limits. The tumor had no communication with urethra and Bartholin's glands. Since pathological evaluation of biopsied specimen showed the presence of adenocarcinoma cells, vulvectomy with inguinal lymphadenectomy was performed. Clinical stage of the patient was classified as FIGO-Stage II (T₂N₀M₀). The patient made a recovery and is alive well 11 months after surgery.

Cytological examination was carried out on smears scraped from tumor mass. The sections were fixed in 95% alcohol and stained with Papanicolaou technique. With necrotic background, numerous polyhedral aggregates of atypical cells were observed. The tumor cells had large irregular nuclei, prominent irregular nucleoli, thick nuclear margin and coarse chromatin (Fig. 1).

Gross examination of the surgical specimen, which was measured 3.5 × 2.0 × 2.0 cm in largest dimensions, revealed a firm mass from the right labium majus. The color of the mass was yellowish red, and the surface was ulcerated. In the skin around the tumor, approximately 5.0 × 5.0 mm-sized, several tumors were found.

Histological examination from formalin-fixed tissue sections showed a moderately differentiated adenocarcinoma composed of solid, ductal and cribriform pattern with central tumor necrosis (comedo change) (Fig. 2). The microscopic appearances had close resemblance to those in breast carcinoma. Epidermis of the tumor was ulcerated, the tumor cells infiltrated the hypodermal fat tissues. No metastasis was seen in the inguinal lymph nodes.

Immunocytochemical examination was performed with antibodies raised against the following antigens: keratin, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), CA 125, CA 19-9, human papilloma virus antigen (HPV), proliferating cell nuclear antigen (PCNA), estrogen receptor (ER). All the antibodies were purchased from Dako Corporation (Santa Barbara, CA, USA). The antigen-antibody reaction was then visualized employing the avidin biotin complex method using a kit (Vectastain; Mountain View, CA, USA), and diaminobenzidine as chromogen. A sample of appropriate control, stained in a parallel fashion with the tumor tissues, was used to assess quality of the immunoperoxidase staining.

Strong cytoplasmic reactivity in the tumor cells was detected for EMA, CEA and ER, and to a lesser extent, for keratin and HPV. A nuclear positivity in tumor cells was found PCNA and ER (Fig. 3). No reactivity was seen against CA 125 and CA 19-9.

**III. Discussion**

Vulvar adenocarcinoma is a very rare disease. The tumor usually arises from the cells of sweat
Fig. 3 Strong nuclear reactivity in the tumor cells was detected for estrogen receptor (ABC method, × 20)

In a few cases, primary adenocarcinoma of the vulva appears from embryonic rest or ectopic tissues. To our knowledge, only 8 cases of adenocarcinoma arose from ectopic breast have been reported so far. This tumor had close resemblance to breast carcinoma in that both diseases have similar histological structures, consisting of solid, ductal and cribriform pattern with central tumor necrosis (comedo change). In the cytological appearance, the tumor is again similar to breast carcinoma, as having necrotic background, numerous polyhedral aggregates of tumor cells, large irregular nuclei, prominent irregular nucleoli, thick nuclear margin and coarse chromatin. Moreover, this tumor showed a positive staining for not only EMA and CEA, but also for ER immunocytochemically. Therefore, we believe that the tumor may have an origin of ectopic breast tissue.

In the previous reports, vulvar breast carcinomas occur in peri- and postmenopausal women. Their ages ranged from 42 to 70 years (mean 57.3 years). The tumor is often long-standing and painless, has lymphatic spread and has poor prognosis.

Biological behavior of the tumor is not fully understood. It is very interesting to speculate that what mechanism could affect carcinogenesis in the ectopic breast tissue. From our study, human papilloma virus that is observed in cervical carcinoma and vulvar squamous cell carcinoma may be involved in the tumor as oncogenic stimuli. Positive staining for PCNA suggests that the tumor has tendency toward aggressiveness of this tumor. Also, several chemotherapy agents that had activity in S stage in cell cycle may be effective. On the other hand, existence of ER in this tumor may propose the evidence to rationality of anti-estrogenic therapy.

Detection of vulvar carcinoma in early stage is difficult, which requires frequent cytological screening with suspicion. In conclusion, cytological and immunocytochemical analyses were useful for the improvement of its prognosis.

要約

76歳の女性にみられた外陰腺癌の1例を報告する。この癌は、組織学的にはcribriform patternやcomedo patternを呈し、細胞診では八つ頭状集塊、著明な核小体がみられ、これらの像は乳癌に類似していた。腺癌細胞は、epithelial membrane antigen、keratin、carcinoembryonic antigenのみならずhuman papilloma virus antigenとestrogen receptorを発現していた。また、多くの腺癌細胞がproliferating cell nuclear antigen強陽性であった。本癌の起因とbiological behaviorについて考察する。

References