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CASE REPORT

Primary Extramammary Paget's Disease Combined with Bowen's Disease in Vulva

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Extramammary Paget's disease (EMPD) is a uncommon neoplastic condition of apocrine gland-bearing skin and its occurrence in combination with Bowen's disease is very rare. The most common site of involvement is the vulva, although perineal, perianal, scrotal and penile skin may also be affected. EMPD is usually not combined with Bowen's disease. We report an interesting case of EMPD combined with Bowen's disease, which was confirmed by immunohistochemical stain. **(Ann Dermatol 23(S2) S222～S225, 2011)**

-Keywords-
Bowen's disease, Paget disease, extramammary, Vulva

INTRODUCTION

Extramammary Paget's disease (EMPD) is rare and affects individuals between the ages of 50 and 80 years[1]. The most frequently affected site is the vulva, followed by perineal, perianal, scrotal and penile skin regions[2]. Vulval EMPD represents 1% to 5% of all vulval malignancies, with a peak age incidence of 65 years[3,4]. The most common histologic type of squamous cell carcinoma *in situ* in the vulval area is Bowen's disease. If the lesion does not respond to topical therapy within 6 weeks, biopsy should be performed to exclude EMPD. But, concomittent expression of both diseases at the same lesion is very rare.

We present a case of primary EMPD arising in the vulva with histological findings ranging from a typical Paget cell morphology to cytological atypia resembling Bowen's disease, which were confirmed by the separate use of various immunohistochemical stains.

CASE REPORT

A 47-year-old woman presented with pruritic erythematous nodules on the vulva (Fig. 1A). The nodules had irregular shaped, slight eczematous surface with whitish to brown color. The patient had been treated using a topical steroid cream at a primary clinic for 5 years. On physical examination, an enlarged lymph node was palpable at the right groin. The first clinical diagnosis was EMPD. Three biopsy specimens were obtained from the right, middle, and left side of the vulva lesion.

The right side specimen showed acanthosis with full-thickness cellular atypia, focal hyperkeratosis and parakeratosis, which was consistent with Bowen's disease, but Pagetoid cells were not detected (Fig. 1B). The middle lesion showed scattered atypical cells with basal pagetoid cells (Fig. 1C). Interestingly, the left side lesion clearly showed focal areas of epithelium containing nests and singly-arranged large cells with pale-staining cytoplasm and occasional prominent nucleoli (Fig. 1D), suggesting Paget's disease.

Immunohistochemistry revealed focal and strong expression of cytokeratin 20 (CK20) and CK7 in basal layer of middle of the tumor, respectively (Fig. 2A). The pagetoid cells in the basal area were also positive for diastase-resistant periodic acid-Schiff (PAS) and were negative for carcinoembryonic antigen (CEA). These findings suggested Bowen's disease with basal pagetoid features.

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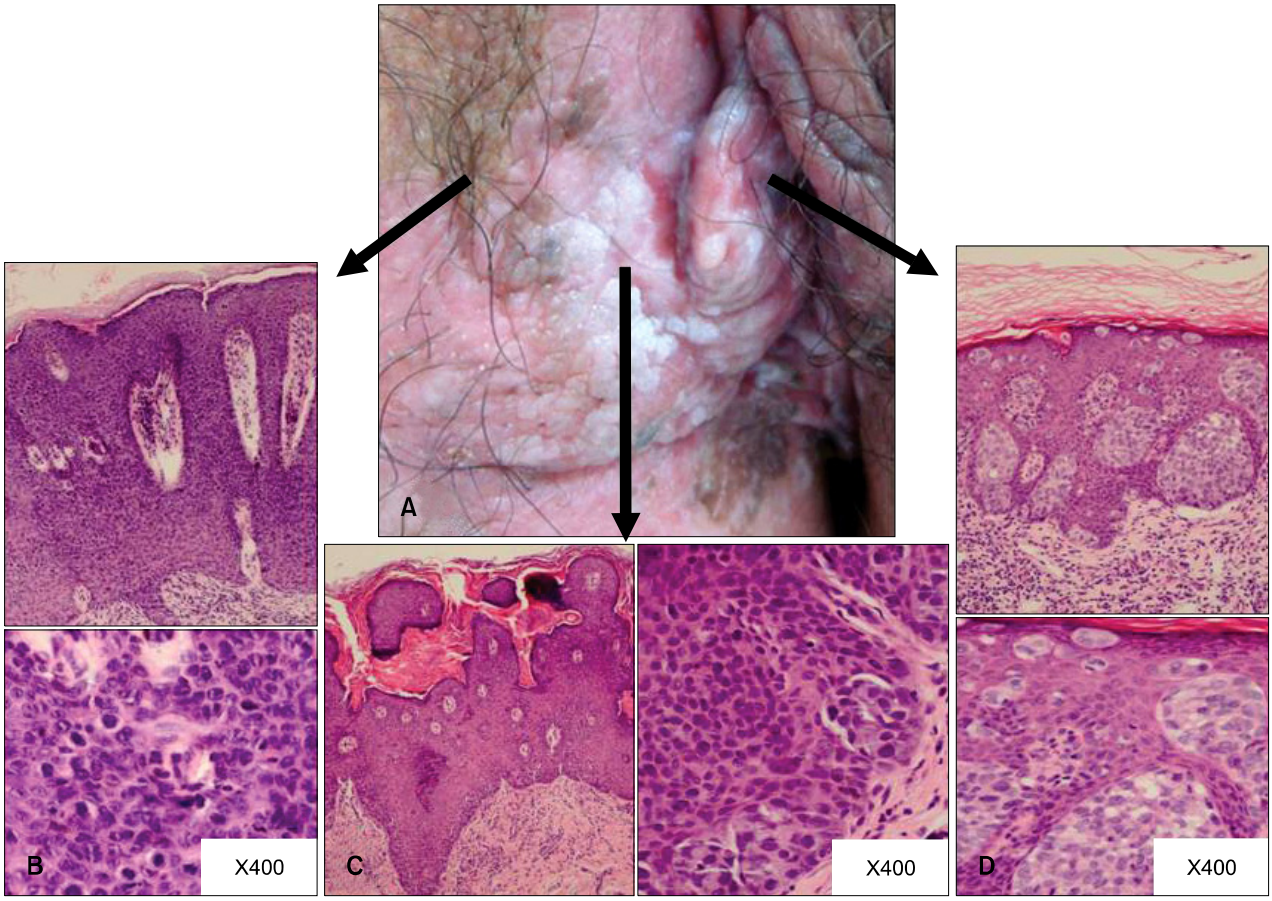

Fig. 1. Clinical appearance and histological findings of the biopsy specimen. Eczematoid nodules on the vulva was observed (A). Typical full thickness atypia (B), cellular atypia combined with basal Paget cells (C), and pagetoid distribution of Paget cells were observed (D) (H&E: ×100 and ×400).

In the left lesion of tumor, immunohistochemical staining for mucin core protein (MUC) 5-AC was strongly positive, but not for MUC-2 (Fig. 2B). In addition, CEA was also positive and S100 was negative (data not shown). Positron emission tomography-computed tomography (PET-CT) and the serum CEA levels did not show any abnormalities, except the signal uptake in inguinal lymph node of right side (SUV, 3.6; data not shown). Taken together, these data indicated that the primary EMPD revealing probable regional nodal metastasis was coincident with Bowen's disease in the same region of the vulva.

DISCUSSION

Presently, we report a patient with a nodule of vulva, which was a rare case of primary EMPD combined with Bowen's disease. The clinical appearance was EMPD, but the biopsy specimen showed Paget cells combined with squamous cell carcinoma *in situ*. Other authors have also reported the association of squamous cell carcinoma *in situ* with EMPD, occurring in the vulva and scrotum[5,6]. However, the exact mechanisms of these combinations are still unknown. Peralta et al.[7] described a tumor displaying histological features of Bowen disease admixed with EMPD. Malignant cells involved with the sweat glands and sweat ducts stained positive for CEA, while the atypical epidermal keratinocytes did not, suggesting the presence of a mixed carcinoma *in situ*. Other authors reported a case of vulval EMPD, in which Paget cells were positive for CEA, whereas atypical cells comprising the vulval intraepithelial neoplasia were negative for this molecule[8]. In contrast, Williamson et al.[9] described two cases of pagetoid Bowen disease in which neoplastic cells expressed CK7 but lacked other Paget cell markers. Recent reports indicated that the coexistence of EMPD with squamous cell carcinoma *in situ* occurs in the vulva, which means the lesions within the epidermis and its appendages have a multifocal origin[10].

Paget's cells typically stain for markers of apocrine and eccrine derivation including low molecular weight CK,

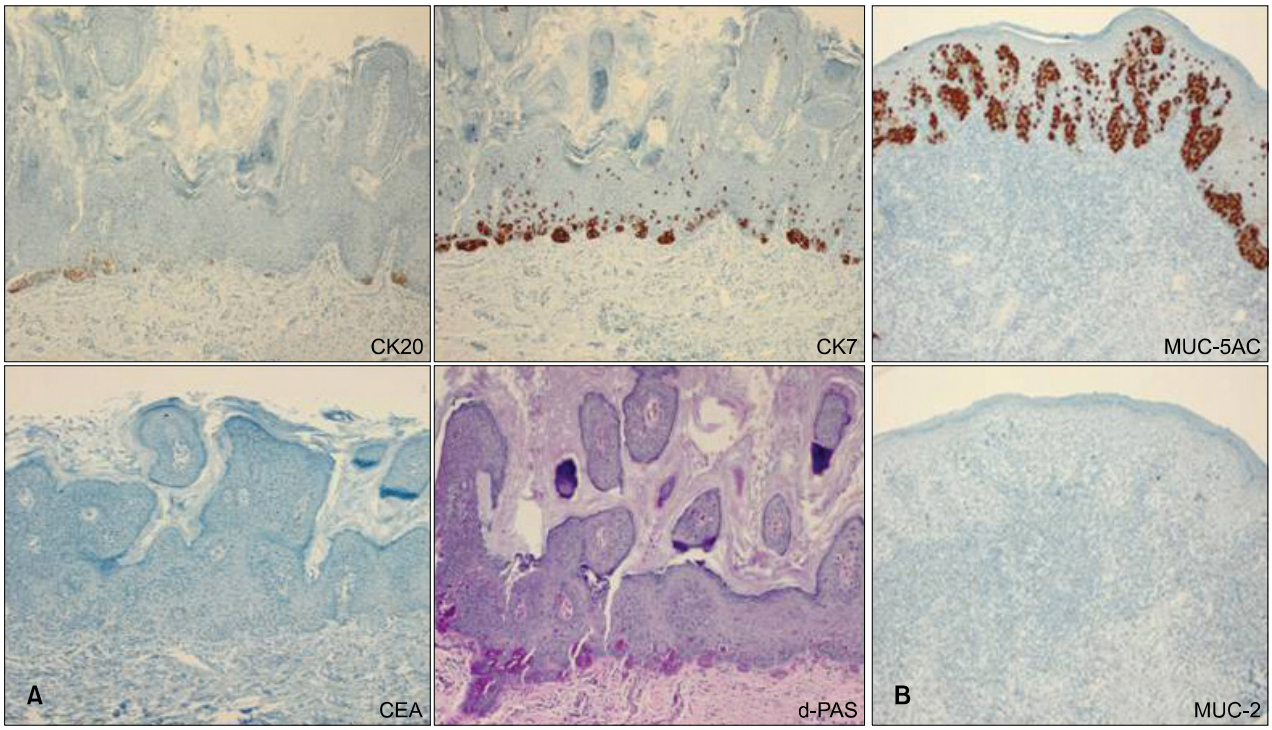

Fig. 2. Immunohistochemistry examinations of the biopsy specimen. (A) In the middle lesion of tumor, immunohistochemical staining of cytokeratin 20 (CK20), CK7, carcinoembryonic antigen (CEA), diastase-resistant periodic acid-Schiff (PAS), mucin core protein (MUC) 5-AC, and MUC2. CK20, CK7, and diastase-resistant PAS were stained positively in Pagetoid cells, but CEA was stained with faint. (B) In the left lesion of tumor, MUC 5-AC was clearly observed in Paget cells, but not by MUC-2. Original magnification ×100.

gross cystic disease fluid protein (GCDFP)-15, PAS, and CEA[11,12]. Additionally, it may be appropriate to use a descriptive term, such as pagetoid Bowen's disease or Bowen's disease with pagetoid features. Immunohistochemistry staining, such as CEA, supports the diagnosis of Paget's disease, but histologic features are focally suggestive of Bowen's disease. In this case, the middle area of tumor was typical of Bowen's disease with pagetoid features, which was evidenced by a positive reaction for only in basal pagetoid cells.

There are antigenic differences between primary intraepidermal Paget's disease (CK7 positive, CK20 negative, GCDFP-15 positive) and Paget's disease that has spread from an associated internal carcinoma (CK7 positive, CK20 positive, GCDFP-15 negative)[7,8,11,12]. MUC 5-AC and MUC-2 were positive in primary EMPD, but not in secondary EMPD. In this case, one side of the nodules was occupied by full-thickness atypia and the opposite side was composed of Paget cells. Our case showed the Paget cells stained with PAS, diastase-resistant PAS, CK7, CK20, CEA, and MUC 5-AC, and the underlying tumor was not detected by PET-CT. Therefore, these tumors may be a primary EMPD.

This case interestingly displayed EMPD with Bowen's disease in the same lesion at the same time. In the vulvar area, Bowen's disease with pagetoid features and primary EMPD were present from the right side to left side in order. This is a rare case that has not been reported in Korea.

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