CASE 7.1
A 60 year-old male from Chanthaburi

Chief complaint:
Chronic rash on genitalia for 1 year

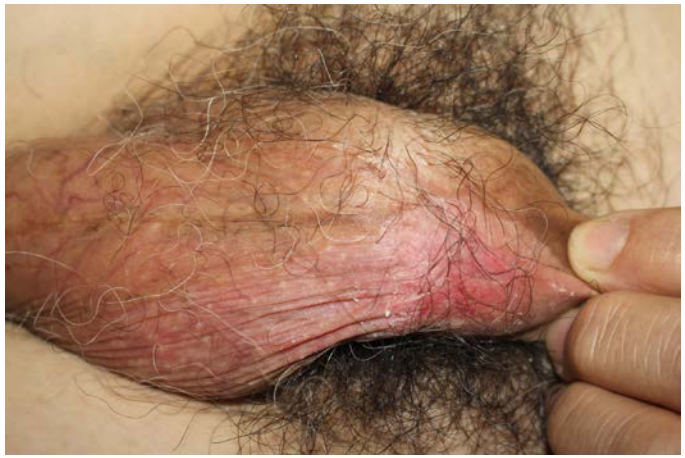

Fig. 7.1.1

Present illness:
The patient complained of longstanding rash on genitalia for 1 year. There has not been significant improvement after the treatment with topical corticosteroid and topical antifungal agent.

Past history:
His underlying disease is bipolar disorder which is currently treated with lithium.

Physical examination:
General appearance: elderly man, not pale, no jaundice
Cardiovascular, respiratory system and abdomen: normal
Lymph node: not palpable

Dermatologic examination: (Fig. 7.1.1)
Large ill-defined scaly erythematous plaques overlying with erosions on the scrotum and shaft of penis

Histopathology: (S17-37896, skin, genitalia) (Fig. 7.1.2)

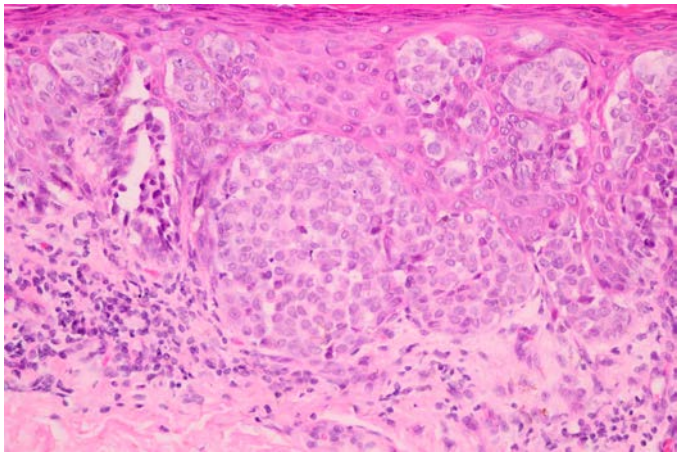

Fig. 7.1.2

- Proliferation of pagetoid cells, both singly and in nest at all layer of the epidermis
- Band like inflammatory cells infiltration in the underlying dermis
- Pagetoid cells shows large pleomorphic nuclei and pale abundant cytoplasm
- Inflammatory cells composed of mainly lymphocytes

Immunohistochemistry: (S17-039252) (Fig. 7.1.3)

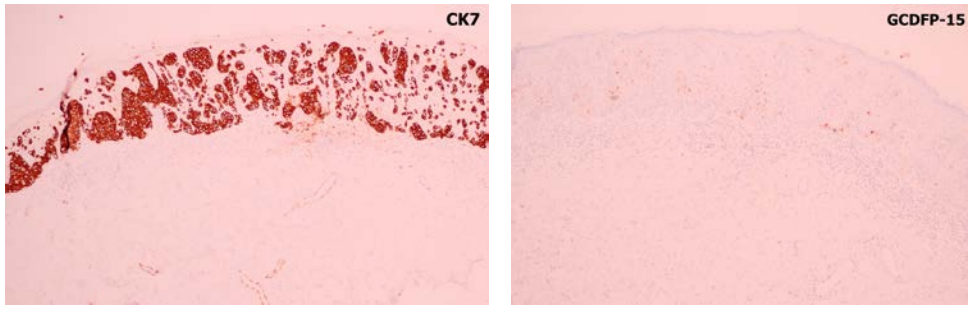

Fig. 7.1.3

Positive: CK7, GCDFP-15
Negative: CK20, S100

Diagnosis: Extramammary Paget's disease

Further investigations:
CBC, urinalysis, Chest X-ray, BUN, Cr, LFT: normal
CEA, PSA: normal
Esophagogastroduodenoscopy: gastritis
Colonoscopy: normal
CT whole abdomen: no liver mass/colonic mass/adrenal gland mass, no significant enlarged node. Few small bilateral renal caliceal stones were seen.
Gastric biopsy: no evidence of malignancy

Treatment: Wide excision with split-thickness skin graft

CASE 7.2
A 53 year-old female from Khonkaen

Chief complaint:
Itchy rash on genitalia for 1 year

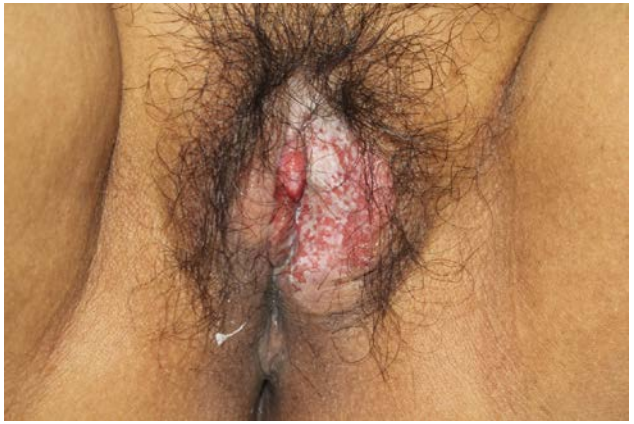

Fig. 7.2.1

Present illness:
The rash developed on her vulvar for approximately 1 year. She had been treated with topical antifungal cream 1 month prior without improvement.

Past history:
She had no underlying disease.

Physical examination:
General appearance: middle-aged woman, not pale, no jaundice
Cardiovascular, respiratory system and abdomen: normal
Breast and nipple: normal
Lymph node: not palpable

Dermatologic examination: (Fig. 7.2.1)
An ill-defined erythematous erosive plaque with overlying whitish patches on labia majora and labia minora

Histopathology: (S18-14887, skin, genitalia) (Fig. 7.2.2)

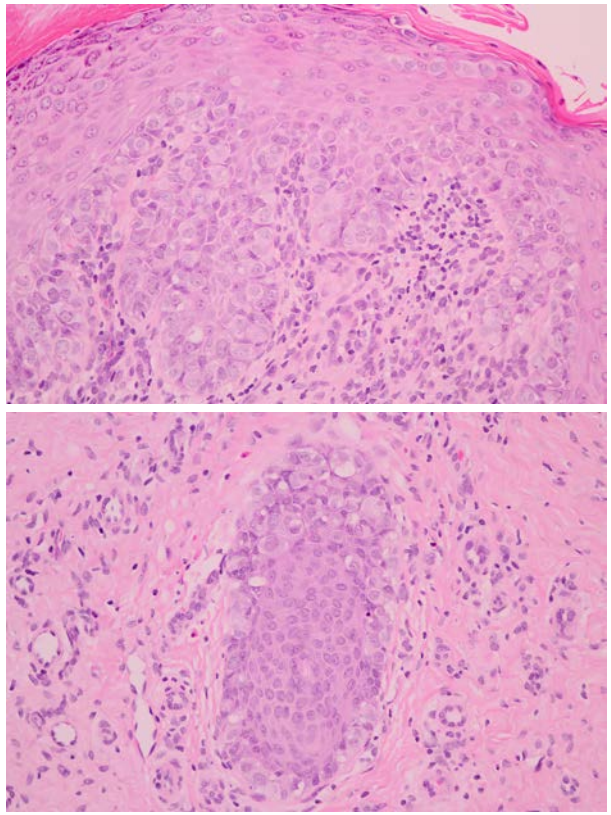

Fig. 7.2.2

- Proliferation of pagetoid cells, both singly and in nest at all layer of the epidermis
- Pagetoid cells also extend deep along dermal eccrine duct

Diagnosis: Extramammary Paget's disease

Further investigations:

- Consultation for gynecologic examination: Pap smear was performed and there was no evidence of malignancy.
- The patient was referred to another hospital due to her health insurance coverage.

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Consultant: Ploychompoo Srisuwanwattana, MD

Discussion:
Extramammary Paget's disease (EMPD) is an uncommon intraepithelial neoplasm of apocrine gland-bearing skin. It usually occurs in individuals between the ages of 50 and 80 years and is more common in female and Caucasian. However, in Asain populations, men are more likely to be affected.[1] There are two different forms of EMPD due to distinct mechanisms of pathogenesis.[2] The primary or cutaneous EMPD form seems to originate from the skin. This form is the majority of EMPD cases which is not associated with a distant adenocarcinoma and limited to the epithelium. The precursor cell could correspond to undifferentiated pluripotent cells of the epidermis and/or its adnexa. The secondary form of EMPD is related to an underlying adenocarcinoma or distant tumors. This form would represent an epidermotropic metastasis of the underlying tumor.[3]

For clinical manifestation of EMPD, it commonly presents as a well-demarcated, pruritic eczematous or erythematous plaque. Less commonly, it may present as an annular or hypopigmented plaque associated with scales, excoriations, or erosion. The primary location is the vulva area, followed by the perianal region, scrotum

and penis. Axilla EMPD occasionally presented.[4] Ectopic EMPD arises in non-apocrine-bearing areas has been reported.[5]

Histopathologically, similar to mammary Paget's disease, there are clusters of Paget cells, which are, large cells with faintly basophilic and finely granular cytoplasm with large nuclei, containing prominent nucleolus, in the epidermis and sometimes extend to epithelial of the hair follicle or sweat gland duct. Paget cells (PC) are devoid of intercellular bridges and can be pigmented. They must be differentiated from intraepidermal cell with pagetoid appearance, including melanoma, pagetoid Bowen's disease and mycosis fungoides. PC contain intracellular mucopolysaccharides, therefore, cells frequently show positive staining for diastase-periodic acid-Schiff, mucicarmine, Alcian blue at PH 2.5 and colloidal iron. Immunohistochemistry is beneficial for identification of PC and for differentiation from other pagetoid cells. PC stain positive for carcinoembriogenic antigen (CEA) and mucin core protein 1 (MUC1). CAM5.2 and CK7 are more sensitive markers but CK7 is not specific. Primary EMPD are usually positive for gross cystic disease fluid protein-15 (GCDFP-15) and MUC5AC, whereas secondary EMPD are usually positive for CK20 and MUC2. Melanoma cells, unlike PC, are positive for S100, Melan-A and HMB-45. However, immunohistochemistry can not replace the role of investigation for underlying malignancy in EMPD case.

The association with underlying internal carcinoma is approximately 15 percent. Those are carcinomas of rectum, bladder, urethra, cervix and prostate. Prognosis depends on the presence of an underlying or distant cancer. Primary EMPD has a favorable prognosis that worsens if the lesions become invasive, namely, if the histological depths of invasion exceed 1 mm. The overall mortality is higher in forms associated with an underlying tumor.

The standard treatment of EMPD is wide local excision or Mohs micrographic surgery. The latter provide 16% recurrence rate for primary EMPD and 50% for recurrent EMPD, lower than 33% to 60% recurrence rate from standard surgery.[6] Radiotherapy can be proposed for unresectable lesions or as an adjuvant treatment to surgical excision. The results of treatment are better in primary in situ EMPD. LASER surgery has been reported for treatment, but recurrences occurred.[7-9] Topical 5-fluorouracil may reduce the margins of the lesions or render them better visible, rendering resection more efficacious. Imiquimod has been successfully used in a small number of non-invasive EMPD cases although there is no consensus about the frequency or duration of treatment.[10-12] Studies using photodynamic therapy have been published, however, achieving solely palliative results.

References:

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