

Quadruple Extra-mammary Paget's disease

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Sir,

Extra-mammary Paget's disease may occur simultaneously in the genital area and, unilaterally or bilaterally, in the axillary region (1). Such cases have been reported as double or triple extra-mammary Paget's disease. We describe here a patient with quadruple extra-mammary Paget's disease, who developed the erythematous eruption in the genital, bilateral axillary and umbilical regions.

CASE REPORT

A 73-year-old Japanese man presented with a 20-year history of an erythematous eruption in the genital area. His medical history and family histories were unremarkable. On physical examination, there was a centrally eroded, scaly erythematous lesion, 5 cm in diameter, on his left groin, spreading to the scrotum (Fig. 1 a). In addition, ill-defined, irregularly shaped, erythematous lesions were present on both axillae (Fig. 1 b, c) and umbilicus (Fig. 1 d). No lesions were seen in the other apocrine-bearing regions, including breasts, perianal area, or external auditory canals. Superficial lymph nodes were not palpable in the axillary regions. Results of complete blood counts and blood chemistry examinations, including carcinoembryonic antigen (CEA), were normal. There was no evidence of internal malignancy on clinical and X-ray examinations.

Biopsy specimens taken from the 4 lesions showed the presence of large pale cells with prominent nuclei infiltrating diffusely or focally in the epidermis. A diagnosis of multiple extra-mammary Paget's disease was made, and all of the lesions were surgically removed, with a 2-cm free margin from the lesional border. The excisional specimens were investigated histologically and immunohistochemically with anti-CEA, anti-epithelial membrane antigen (EMA) and anti-cytokeratin (CK) antibodies. The genital lesion exhibited a moderate acanthosis of the epidermis filled with Paget's cell nests (Fig. 2 a). In both the axillary lesions and the umbilical one, Paget's cells were

located in the thin epidermis (Figs 2 b–d). The tumour cells in all the lesions were positive histochemically for periodic acid-Schiff stain and immunohistochemically for CEA and EMA. In CK stainings, there was no immunoreactivity with 34 β B4(CK1), DE-K10(CK10) or Ks13.1(CK13) antibodies in any of the lesions. Epithelial CKs recognized by 35 β H11(CK8), RCK102(CK5,8) and RCK108(CK19) were expressed by the tumour cells of all 4 lesions, suggesting the same origin or differentiation of the neoplastic cells. In addition, since this CK staining pattern was the same as found in 5 patients with genital Paget's disease, the tumour cells in this case had no peculiar phenotypic feature.

DISCUSSION

Extra-mammary Paget's disease develops in apocrine-bearing areas other than the breasts, i.e. genital, perianal and axillary lesions (1). Therefore, it seems to be derived from apocrine glands, although other origins might exist. Since the first report by Kawatsu & Miki (1) in 1971, approximately 60 Japanese cases of triple extra-mammary Paget's disease have been reported, mostly in the Japanese literature, and only 4 cases in the English literature (2–4). However, there has been only one case report of triple extra-mammary Paget's disease from outside Japan (6). The patient described here is the second case of quadruple extra-mammary Paget's disease (5), indicating its extreme rarity. In Japan, men are affected with extra-mammary Paget's disease twice as often as women (7), whereas women are predominantly affected in western countries (8). All Japanese patients reported with triple or quadruple Paget's disease are men, and one patient from Europe is female (6). Thus, the incidence of extra-mammary

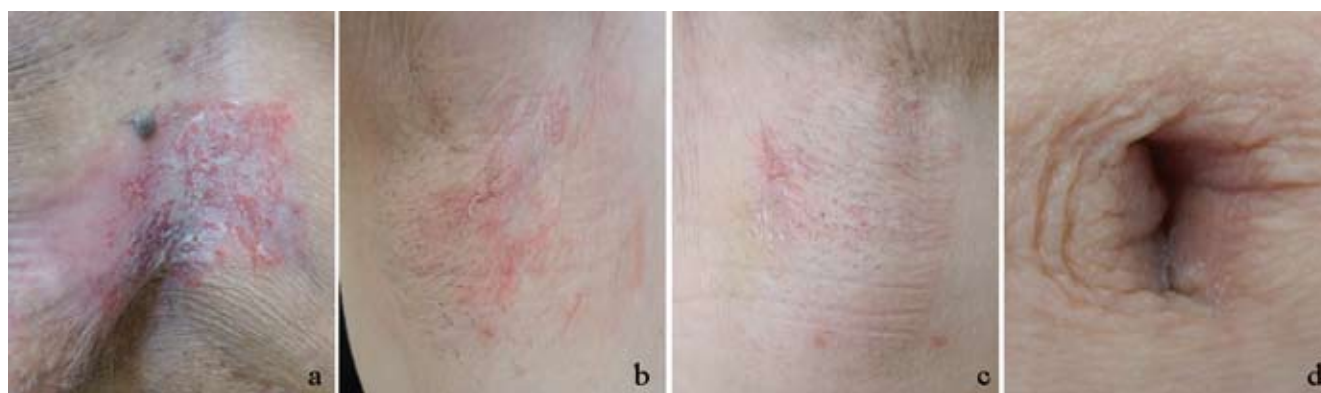


Fig. 1. Skin lesions in: (a) left inguinal area, (b) right axilla, (c) left axilla, and (d) umbilicus.

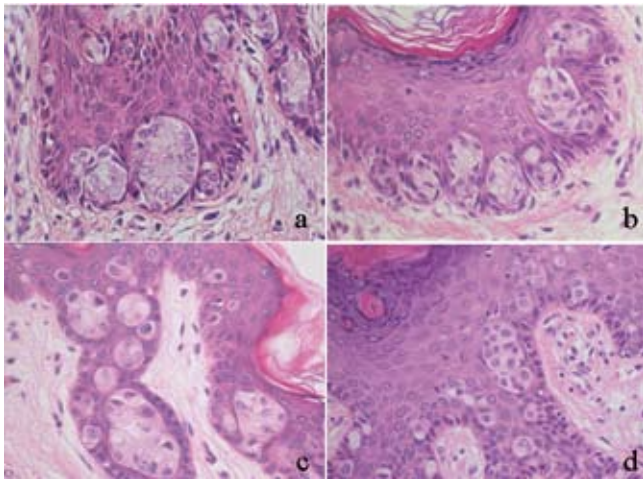


Fig. 2. Histology of excised specimens from: (a) inguinal area, (b) right axilla, (c) left axilla, and (d) umbilicus.

Paget's disease seems to depend on the ethnic origin of the patient.

Ordinary genital Paget's disease has a high potential for local growth and metastasis, but if there is no underlying malignant tumour the prognosis may be excellent. On the other hand, there have been no reports of patients exhibiting highly invasive or metastatic axillary tumours. Prior to our immunohistochemical study, therefore, we had expected that there might be some differences in the profile of CK expression among the different sites of quadruple extra-mammary Paget's disease. The lack of difference in this study is

consistent with the previous observation by Ohnishi et al. (4), and supports the homogeneity of the tumour cell nature irrespective of the site. In triple or quadruple extra-mammary Paget's disease, the racial and gender differences in incidence, the pathophysiology underlying simultaneous distant occurrence of three or four lesions, and their malignant potentials are the matters to be elucidated.

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