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Ectopic extramammary Paget's disease affecting the upper abdomen

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Summary We present 57-year-old man in whom ectopic extramammary Paget's disease (EMPD) affected the upper abdomen. Although the clinical appearance was suggestive of Bowen's disease or superficial basal cell epithelioma (BCE), the biopsy specimen showed EMPD histologically. Only 12 cases of ectopic EMPD have been reported (including this case). In our 20 year experience of 129 EMPD, this is the first ectopic case. Thus, the frequency of ectopic EMPD is 0·78% (one of 129) in our study. The male/female ratio in the reported 12 cases is 2 : 1, nearly the same as EMPD in general (2·1 : 1, in our 129 cases). The mean age of the 12 patients is 65·8 years, which is not significantly different from ordinary EMPD (66·4 years, in our 129 cases). Comparing ectopic EMPD to ordinary EMPD, clinically and histologically, we could find no difference. As they appear to be the same disease, ectopic and ordinary EMPD may share similar origins and mechanisms of occurrence. We support the hypothesis that Paget's cells originate from the remaining pluripotential germinative cells which are able to differentiate into many kinds of secreting glands.

Case report

A 57-year-old man had had an erythematous plaque on the upper abdomen since early infancy. Recently the lesion had increased in size and become desquamative. Several topical treatments had been ineffective. His past history and family history were unremarkable. Examination in December 1991, revealed a polycyclic brown plaque on his left upper abdomen, distinct from the nipple and umbilicus (Fig. 1). The lesion was well demarcated and irregular, measuring 9 × 10 cm in diameter. It was erythematous with pigmentation in the centre. Some dry scaling and a slightly elevated margin, without ulceration or nodules, were present. There were no palpable lymph nodes in the neck, axilla or groin, and the skin elsewhere was normal. Routine blood tests were normal and the serum carcinoembryonic antigen level was also within the normal range. Other investigations, including abdominal echogram, upper gastric investigations, and garium scintigraphy, all showed no significant abnormality.

The clinical findings were suggestive of Bowen's disease or superficial basal cell epithelioma (BCE), and an incisional biopsy was performed. Histology showed many Paget's cells with clear and abundant cytoplasm, proliferating horizontally and forming intraepidermal nests on the basal layer (Fig. 2). The Paget's cells showed nuclear atypia, some with hyperchromatic, large or irregularly shaped nuclei. In the papillary dermis, there was a marked inflammatory cell infiltrate, composed mainly of lymphocytes. Although some hair follicles in the dermis (Fig. 3) were replaced and occupied by tumour cells, there was no dermal invasion. The cytoplasm of the Paget's cells was positive with the periodic acid-Schiff stain, but negative with S-100. Immunohistochemical studies, using the peroxidase–antiperoxidase technique, revealed that all Paget's cells were positive for carcinoembryonic antigen (Fig. 4). The cytoplasm of the Paget's cells was not stained by HMB-45.

Based on these pathological findings, we diagnosed ectopic extramammary Paget's disease (EMPD). We resected the lesion, including 2·5 cm of healthy appearing skin, and closed the defect with a split-thickness skin graft. The excised specimen revealed no dermal invasion at any site and the surgical margin was free of tumour cells. No accessory mammary gland could be found. The patient is free of the disease, 36 months after surgery.

Discussion

EMPD usually occurs in the genital, axillary or perianal regions, where the apocrine glands predominate. Occurrence in other sites is very rare. In 1934, Kojima[1] first reported a case of ectopic EMPD affecting the

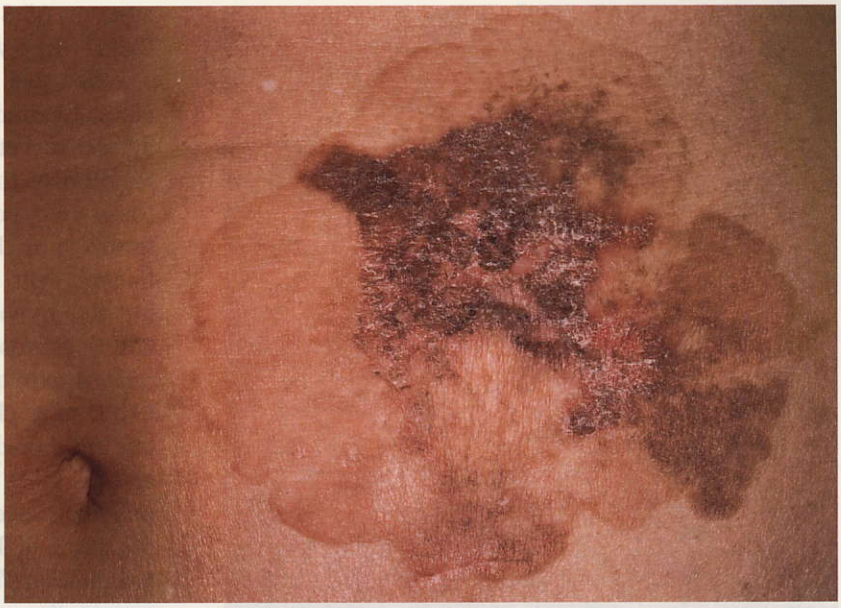

Figure 1. Irregular, erythematous, pigmented lesion, showing dry scaling.

sternal region and, since then, there have been 11 reports, including our own. These 12 cases have been located on the buttock, back, hypochondrium, medial side of nipple, and on other sites (Table 1).[2–11] We excluded cases which had an associated underlying carcinoma adjacent to the EMPD. These included EMPD of the eyelid with Moll's gland carcinoma,[12,13] EMPD of the external ear canal with ceruminous gland carcinoma,[14] and EMPD of the oesophageal epithelium with invasive epidermoid carcinoma.[15] Such cases might constitute secondary EMPD,[16] as a result of direct cutaneous invasion from an adjacent carcinoma. Similarly, reports on apocrine-dominant regions, like the umbilicus,[17] have also been excluded. In our 20 year experience of 129 EMPD cases (Table 2),[18] this was our first ectopic case. Thus, the frequency of ectopic EMPD is 0·78% (one of 129) in our study. In the reported 12 cases of ectopic EMPD, the male/female ratio is 2·0 : 1, nearly the same as EMPD in general (2·1 : 1, in our 129 cases). The mean age of these 12

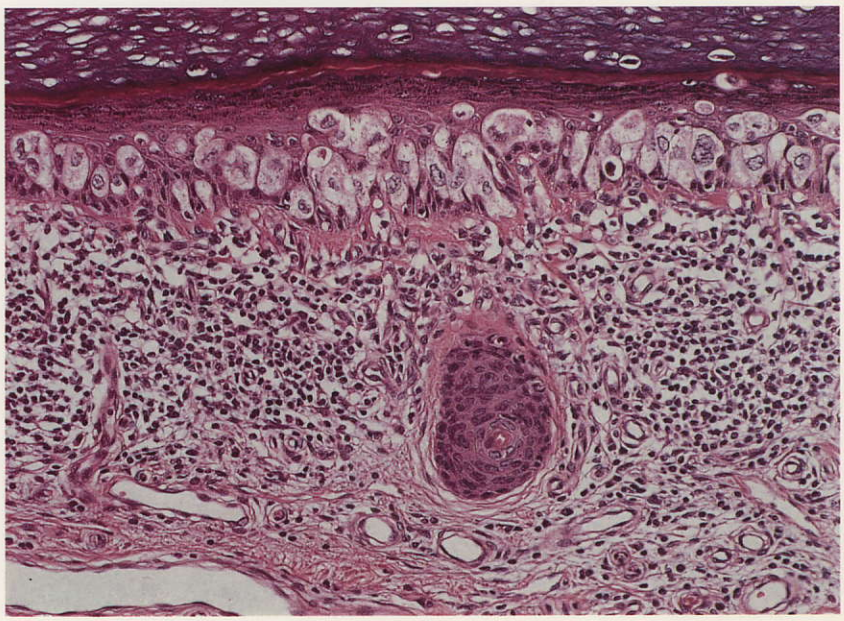

Figure 2. Histological features of the biopsy specimen. Paget's cells are seen proliferating horizontally and forming intraepidermal nests (haematoxylin–eosin ×200).

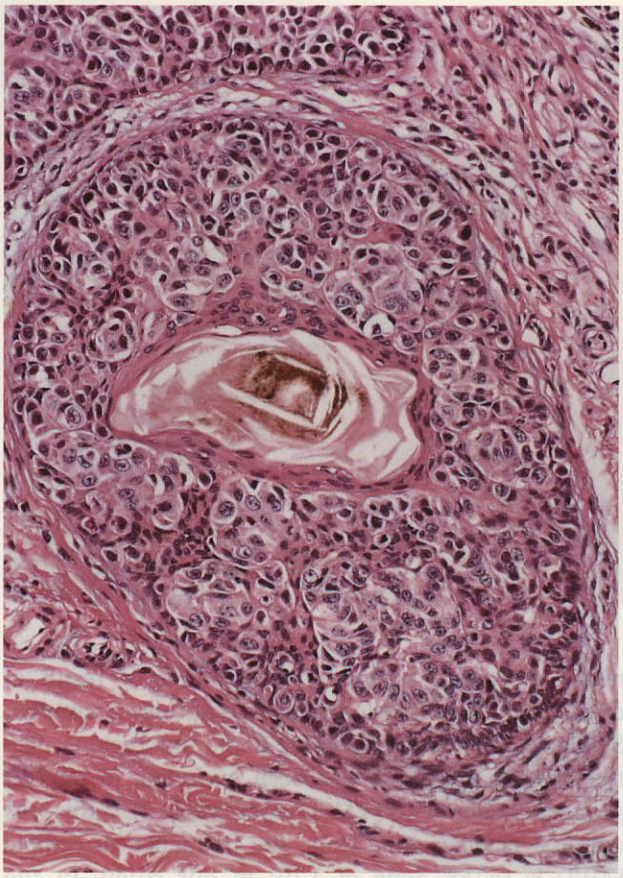

Figure 3. Hair follicle replaced and occupied by tumour cells (haematoxylin–eosin ×200).

cases is 65·8 years, also no different from ordinary EMPD (66·4 years, in our 129 cases).

When we compare ectopic and ordinary EMPD clinically and histologically, we find no significant difference between these two groups except for the location of the disease. Therefore, we conclude that these two conditions have an identical biological nature and behaviour. It is generally agreed that Paget's cells originate in the apocrine sweat gland, but this hypothesis does not apply to cases of ectopic EMPD, because they occur in non-apocrine predominant regions, as in our patient. Some authors[5,7] suspect ectopic EMPD to be closely related to the germinative milk line, but this would not explain the occurrence on the back[3] and the scalp.[10] In order to explain these ectopic sites, a unifying concept is needed. In 1979, Jones *et al.*[2] studied 55 cases of EMPD histopathologically, including one ectopic case. They proposed the existence of pluripotential germinative cells as the origin of Paget's cells. These cells are thought to be able to differentiate not only into apocrine glands but also into eccrine glands. For two reasons, we believe this hypothesis is useful in the understanding of the characteristics of both ordinary and ectopic EMPD. First, in the opinion of Jones *et al.*, EMPD can occur on any site of the body when some presumptive carcinogenic factors stimulate the remaining pluripotential germinative cells. Secondly, this hypothesis gives a more rational explanation of the characteristics

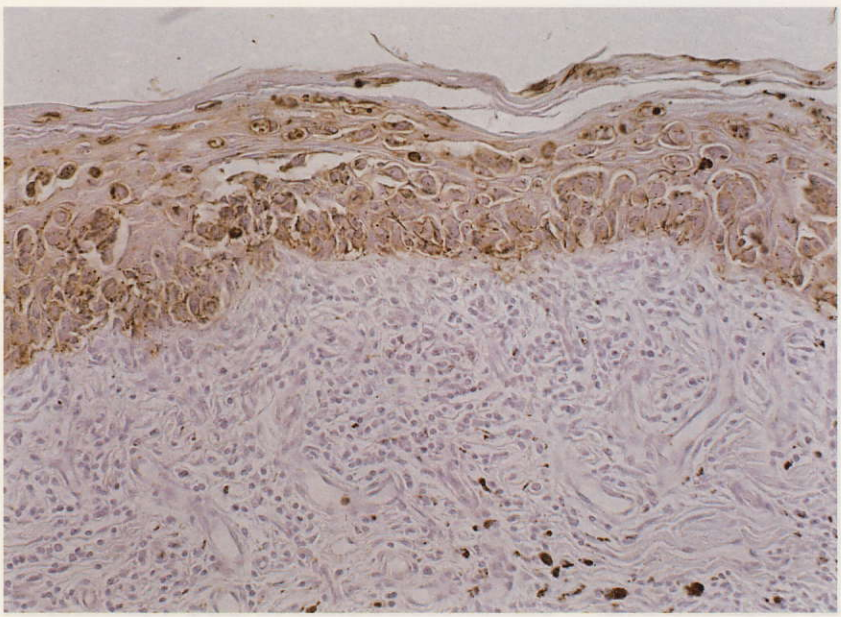

Figure 4. Tumour cells positively stained by carcinoembryonic antigen (peroxidase–antiperoxidase ×200).

Table 1. Reported cases of ectopic extramammary Paget's disease

No.	Age	Sex	Site	Source
1	68	M	Sternal region	Kojima (1934)[1]
2	78	F	Buttock	Jones *et al.* (1979)[2]
3	69	F	Back	Inada *et al.* (1985)[3]
4	54	M	Lower anterior chest	Saida and Iwata (1987)[4]
5	44	F	Lateral chest	Takatsuka *et al.* (1987)[5]
6	44	F	Chest	Ishi *et al.* (1988)[6]
7	54	M	Lateral chest, medial side of nipple (multiple)	Kitahara *et al.* (1990)[7]
8	79	M	Lateral chest	Urabe *et al.* (1990)[8]
9	82	M	Lateral chest	Honda *et al.* (1991)[9]
10	81	M	Scalp	Sai *et al.* (1994)[10]
11	79	M	Hypochondrium	Susaki *et al.* (1995)[11]
12	57	M	Upper abdomen	Our patient

Table 2. Our experience of EMPD (1973–94) (Modified from Ohara *et al.*[18])

Site	No. of lesions	No. of patients (%)
Genital	122*	117 (90·7)
Axillary	6	6 (4·7)
Unilateral axilla	1	1 (0·8)
Unilateral axilla and genital	3	3 (2·3)
Bilateral axilla and genital	2	2 (1·6)
Perianal	5	5 (3·9)
Ectopic	1	1 (0·8)
Total	134	129 (100)

*Including five cases of double and triple EMPD.

of Paget's cells with regard to apocrine and eccrine differentiation. It seems attractive to consider the possibility that pluripotential germinative cells are the origin of EMPD.

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