Extramammary Paget's disease of the axilla with adnexal carcinoma in-situ

S Prasad W Kumarasinghe[1], J B C Wijesinghe[2], S Perera[3], M P Kumarasinghe[4]

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Extramammary Paget's disease (EMPD) is an uncommon cutaneous disorder. EMPD is mostly found in areas where there is a high density of apocrine glands; such as the anogenital region and the axilla. In mammary Paget's there is nearly always an associated intraductal carcinoma of the breast. In a large series of in EMPD, only 24% showed evidence of underlying cutaneous adnexal carcinoma, 12% had a concurrent and, another 17% had non concurrent malignancy[1]. EMPD of the axilla is rarer than in the perineum[1-5]. We report a case of EMPD of the axilla of a woman with evidence of associated adnexal carcinoma.

Case report

A 64 year old woman presented with an erythematous pruritic plaque which was slowly increasing in size, in the right axilla of 6 month's duration. She had no past history of malignancies. There were no previous skin diseases. She was on treatment for hypertension for 10 years and has had a cardiovascular accident 3 months before, leading to left hemiparesis. She had used topical antifungals and topical steroids on this lesion without success. On examination she was a thinly built woman on a wheel chair due to the hemiparesis. She had an 8cm × 6cm, moist plaque with well demarcated borders. There were no underlying lumps. There were no other dermatological abnormalities. Examination of breasts was normal, there was no discharge from the nipples. Clinically, EMPD, Bowen's disease and flexural psoriasis were considered in the differential diagnosis. Her basic laboratory tests, ESR, full blood count, blood urea, serum electrolytes and the chest X ray were normal. Skin biopsy was done. The haematoxylin and eosin (H&E) stain revealed epidermal hyperplasia with cells displaying polymorphic nuclei and pale cytoplasm in the epidermis, arranged singly and in collections. A dense inflammatory cell infiltrate composed mostly of lymphocytes and histiocytes was noted in the dermis. There was no exocytosis. Thus a diagnosis of EMPD was made.

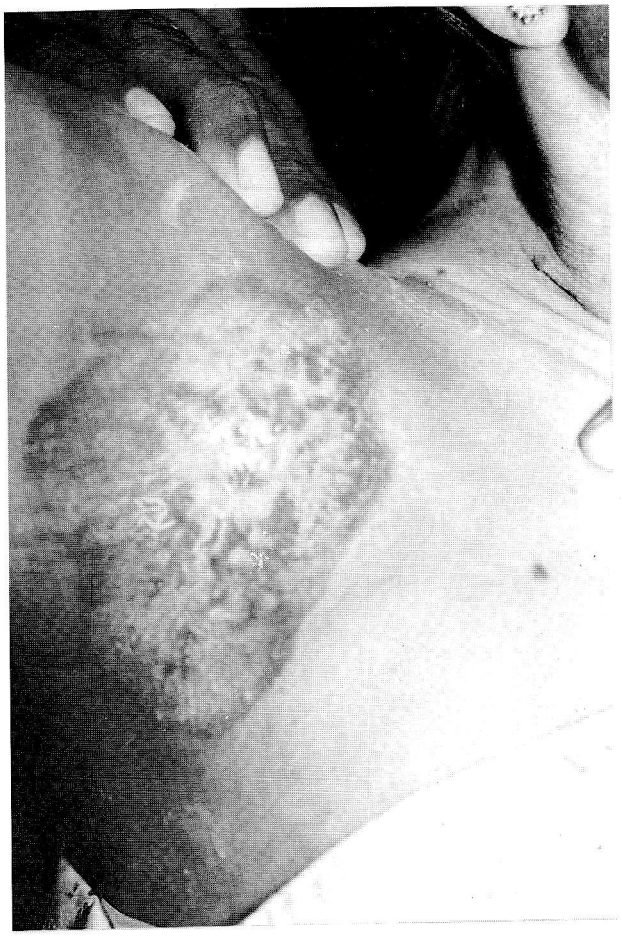

Figure 1. *6 × 8 cm well demarcated, moist, plaque in the right axilla.*

The patient was referred to a surgeon; and complete excision of the lesion was done under local anaesthesia. The surgical specimen was again histopathologically examined. The lesion showed epidermal hyperplasia composed of cells with pleomorphic vesicular nuclei, nucleoli, mitoses and abundant pale cytoplasm. These cells were infiltrating the epidermis in a pagetoid fashion (Figure 2). The infiltration was

[1]*Consultant Dermatologist, Teaching Hospital, Colombo North (currently at National Skin Centre, Singapore)* [2]*Senior House Officer in Dermatology, Teaching Hospital, Colombo North,* [3]*Consultant Pathologist, Teaching Hospital, Colombo North,* [4]*Consultant Pathologist, Singapore General Hospital.*

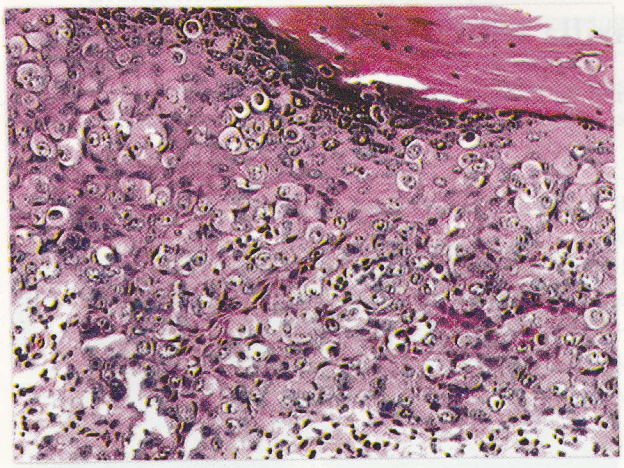

Figure 2. *Characteristic Paget's cells with their abundant pale cytoplasm, large nuclei and nucleoli (H&E × 400).*

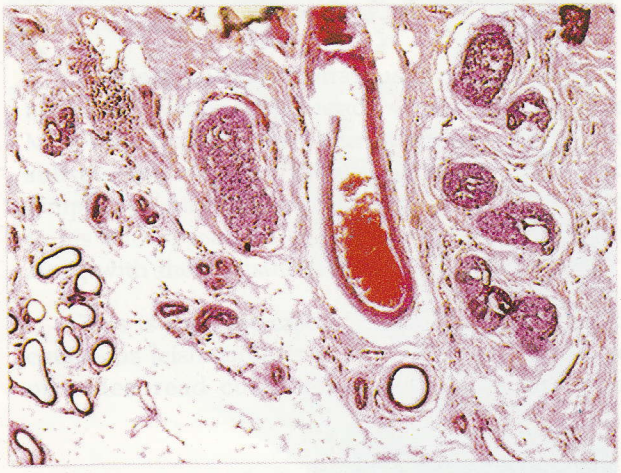

Figure 3. *Ductal structures filled with Paget's cells depicting carcinoma-in-situ with adjacent uninvolved eccrine and apocrine structures. (H&E × 40).*

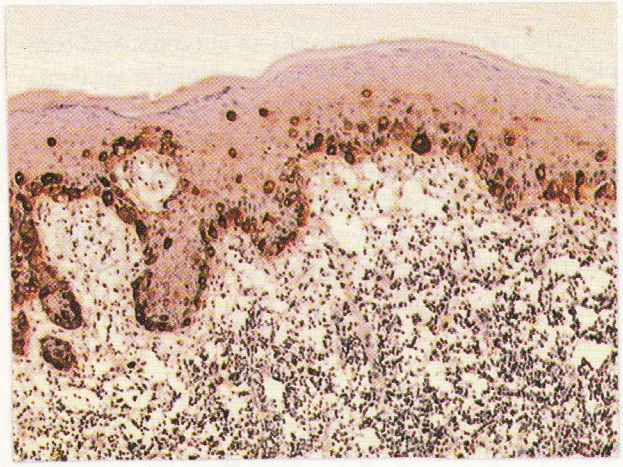

Figure 4. *Paget's cells stained by CEA × 100.*

seen within the epithelium of skin appendages and deep seated ducts (Figure 3). Deep seated foci were not in direct continuity within the epithelium and appeared to represent carcinoma in situ rather than direct sprend into the adnexal epithelium. Some uninvolved ducts showed apocrine differentiation. There was no stromal infiltration to suggest invasive carcinoma. Therefore a diagnosis of EMPD with adnexal carcinoma-in-situ was made. Excision margins were clear of the lesion. Immunohistochemical stains were performed at the Department of Pathology, Singapore General Hospital. As expected, Paget's cells were positive for carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA) and Gross Cystic Disease Fluid Protein (GCDFP); a marker for apocrine cells (Figure 4). The latter stain suggested the morphological impression of apocrine carcinoma-in-situ. These cells also showed mucin secretion as confirmed by mucicarmine stain.

The patient was screened in a limited way for any other associated malignancy, and there was none found.

Discussion

Morphologically, lesions of EMPD are similar to those of areolar lesions, but may go undiagnosed and become more extensive. EMPD usually presents as an erythematous, eczematoid, pruritic, slow growing plaque. Pruritus may be severe in some cases. The size of the lesion usually correlates with the duration of the condition. Older persons are more prone to EMPD. Usually it is a single lesion, but rarely multiple lesions have been reported in different regions of the body. Clinically EMPD may mimic lichen simplex chronicus, Bowen's disease, flexural psoriasis or an inflamed fungal infection.

There may be underlying malignancy associated with EMPD. In one study 50% patients with EMPD had elevated levels of carcinoembryonic antigen levels[6]. Whenever there is a case of EMPD an attempt should be made to detect any underlying malignancy. About 25% have an underlying cutaneous adnexal carcinoma, mostly of the apocrine type[5]. Rarely, eccrine carcinoma has been associated with EMPD. Sometimes the differentiation whether the glandular structures associated with EMPD are of apocrine or eccrine origin can be difficult, as in this case[5]. EMPD has been reported to be associated with carcinoma of the rectum, prostate, cervix uteri, bladder, urethra etc.[5].

Histologically EMPD has to be differentiated from Bowen's disease and superficial spreading or Pagetoid malignant melanoma[5]. The histopathological

and immunohistochemical features were diagnostic of EMPD in the case discussed here. In Bowen's disease malignant cells are of squamous origin and will not show positive staining for CEA, EMA or Gross cystic disease fluid protein (GCDFP). Melanoma cells also will be negative for above stains and will be positive for melanoma markers. A simple mucin stain will also make the differentiation as Paget's cells will contain abundant mucin. Small skipped areas devoid of mucin have been reported[5]. Histochemical and immuno-histochemical stains are specially useful in making the diagnosis in small punch biopsies. GCDFP and apocrine epithelial antigen are thought to be specific markers of apocrine cells[5]. In the biopsy of this patient, malignant Pagetoid cells showed apocrine differentiation as confirmed by GCDFP stain.

Surgical removal of the lesion is the treatment of choice in EMPD. There is poor correlation with clinically apparent margins and histological margins and thus local recurrence of EMPD is common. Generally the prognosis of EMPD is good except in cases where there is an underlying carcinoma. Our patient did not wish to undergo mammography or investigation for carcinoembryonic antigens. According to the excision biopsy histopathology, the excision margins were clear of the tumour. She is currently on follow-up.

To our knowledge, this is the first reported case of EMPD of the axilla associated with adenexal carcinoma in situ with apocrine differentiation, in Sri Lanka.

Acknowledgements

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