

## Case 3 : Extramammary Paget's Disease

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### CASE SUMMARY

#### History

An eighty-five year old man presented with an insidious onset of progressive itchy perianal skin rash for several years. It was found incidentally when he was admitted to hospital for increasing low back pain due to vertebral collapse. He also had prostatism as well as gastrointestinal symptoms including rectal bleeding, constipation and weight loss. His past health was otherwise good.

#### Physical examination

Physical examination revealed well demarcated bilateral erythematous scaly plaque at the perianal area with maceration (Figure 1). There was no pallor or lymphadenopathy. The abdomen was soft with no palpable mass. Rectal examination showed an enlarged prostate only.

#### Investigations

Skin biopsy showed clusters of mucinous cells with eccentric nucleus in the epidermis. The basal layer of melanocyte was unremarkable. Dense inflammatory cells were present in the superficial dermis. No underlying tumour or invasion was found. The diagnosis was **extramammary Paget's disease**.



**Figure 1: Bilateral well demarcated erythematous scaly plaque at perianal region**

Complete blood picture, renal function test and alpha-feto protein level were all normal. Alkaline phosphatase level was 179mmol/L, whereas the prostatic specific antigen was 67.8ug/L. X ray of the lumbosacral spine revealed T12 and L2 vertebral collapse. Ultrasonography of the prostate showed bilateral small hypoechoic and cystic lesions with biopsy showing changes of benign prostatic hyperplasia only. A two cm sessile polyp was found in the descending colon but biopsy showed only tubulovillous adenoma and moderate dysplasia. The bone scan was also normal.

### Management

Local radiotherapy was given to his cutaneous lesion and the patient had defaulted follow up since then.

### Discussion

Dermatopathologist emphasized that immunohistochemical staining with gross cystic disease fluid protein 15 was important in distinguishing primary from secondary disease. Dermatologist also commented that photodynamic therapy could be one of the future therapy.

## REVIEW ON EXTRAMAMMARY PAGET'S DISEASE

Extramammary Paget's disease is defined as a neoplasm of anogenital and axillary skin which resembles Paget's disease of the nipple histologically and clinically. It was first described by Crocker in 1888, involving the scrotum.<sup>1</sup>

It occurs more often in women than men, usually after the fifth decade. It may be associated with underlying adnexal adenocarcinoma. Around 20-40% of patients also have primary carcinoma of other organ such as rectum, cervix, breast, prostate and bladder.<sup>2</sup>

### Clinical features

It consists of insidious onset of well defined erythematous plaques, with a velvety surface with

scaling, crusting, exudation or lichenification. Lymphadenopathy and distant metastasis can occur. It commonly involves the vulva, perianal region, scrotum and axilla. Occurrence at other sites such as umbilicus or presternal area have also been reported. Very often, it is misdiagnosed as eczema or fungal infection. Typically, the disease progresses despite application of topical steroid or antifungal agent.

Differential diagnoses include eczema, intertriginous candida infection, tinea corporis, erythrasma, Bowen's disease, superficial spreading melanoma and human papilloma virus induced intraepithelial neoplasia. The diagnosis is confirmed by biopsy.

### Pathogenesis

The pathogenesis is unclear. The fact that Paget cells is PAS positive and diastase resistant and the disease occurs at sites where apocrine glands predominate, supports its glandular origin. It can be an in-situ extension from appendageal glandular tissue or occur de novo within the epidermis.<sup>1</sup> It is also believed to be a retrograde extension from an underlying adenocarcinoma.<sup>2</sup> The presence of the disease at ectopic sites may also raise the possibility of the presence of pluripotential germinative cells as origin<sup>3</sup>.

### Histology

The Paget cells, which are large cells with abundant pale cytoplasm and prominent nucleolus, are scattered in the basal layer. They may extend into the adnexal structures which should not be regarded as invasion. Adnexal adenocarcinoma may be present. The dermis usually shows chronic inflammatory reaction. Those with associated malignant disease have indistinguishable histological pattern.<sup>4</sup>

Histochemical staining shows that the Paget cells are 93%CEA, 71%Cam 5.2 (a monoclonal antibody that stains low molecular weight keratin) and 96% mucin positive respectively.<sup>5</sup> Those primary extramammary Paget's disease is positive for gross cystic disease fluid protein 15, as opposed to those secondary one.

## Therapy

Local excision with wide margin (>1cm microscopic clearance of surgical margin) is the standard therapy. Recurrence rate is between 31% to 61%.<sup>6</sup> Radiotherapy can be adopted as single therapy in those patients who are unfit for surgery, whose tumor recurs after surgery or those unwilling to undergo mutilating surgery.<sup>1</sup> It can be used as an adjunctive therapy in those patients without associated adenocarcinoma. Topical 5-fluorouracil may be applied preoperatively to delineate the surgical margin more clearly.<sup>7</sup> Paget cells which have high metabolic rate, are very sensitive to 5-fluorouracil. The subsequent necrosis of Paget cells will reflect as inflammatory cutaneous response. Prolonged application for several months may show clinical regression.<sup>6</sup>

## Prognosis

This is related to the existence of an underlying malignancy. Observations suggest that those with associated malignancy have early metastasis and early death whereas those with extramammary Paget's disease alone run a benign course.

### **Learning points:**

***Extramammary Paget's disease should be suspected in long standing progressive eczematous lesions of the genitalia, perineal and perianal areas.***

## References

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