

## Case Report

### **Paget's disease in an Asian woman**

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#### **Abstract**

Extramammary Paget's disease is a rare disease, which mainly occurs in postmenopausal women. The case of Paget's disease of vulva, in a 40 year old Asian woman, who presented with a history of intense itching in vulva for 1 year is being reported. After being medically treated, she was diagnosed on Vulval biopsy. Local excision of the vulval lesion was performed, and histopathology revealed Paget's disease, extending close to the surgical margins. Therefore, a re-excision was performed and patient remained disease free at six months follow up.

**Keywords:** Extramammary Paget's disease, vulval biopsy, local excision.

#### **Introduction**

Paget's disease of the vulva is rare and mainly occurs in the seventh decade of life, primarily among whites,<sup>1</sup> but it

has also been observed increasingly among Asians over the past 4-5 years.<sup>2</sup> Because of its rarity, frequency data are unavailable. Women are more commonly affected than men. The female to male ratio was 4.5 : 1 in one series of 55 patients and 3:1 in another series of 197 patients. It may be a primary lesion or associated with adenocarcinoma originating from local organs such as the Bartholin's gland, the urethra or the rectum, thus deeming it secondary. James Paget had described Paget's disease of the nipple in 1874.<sup>3</sup> Raddiffe Crocker first recognized and reported extramammary Paget's disease as a distinct clinical entity in 1889.<sup>4</sup>

It usually involves the apocrine gland of the anogenital region and is typically confined to the epithelium, but it is associated with invasive disease in 15-25% of cases. The epidermis becomes infiltrated with neoplastic cells showing glandular differentiation. It coexists with other malignancies in 25% of cases, most commonly with carcinoma of the breast. Aggressive

angiomyxoma should be considered in the differential diagnosis of vulvar lesion.<sup>5</sup> Besides Paget's Disease, concurrent disease of the breast and vulva is common, such as in fibromatosis of vulva.<sup>6</sup> Recurrence is common and therefore regular follow up is required to reduce the morbidity associated with this lesion.<sup>7</sup>

### Case Report

The case of a 42 year old Asian woman, para 4+0 (all delivered vaginally) and diagnosed as Paget's disease, and referred to a tertiary care hospital is being presented. She experienced itching in vulva and perineum for 1 year, for which she was prescribed ointments by a general practitioner, yet her condition aggravated. She had also developed heavy menstrual flow. A diagnostic D&C and vulvar biopsy was performed, and the histopathology report revealed secretory endometrium and Paget's disease of vulva. She was then referred to a tertiary care hospital, for further management. A detailed history was taken through which the only local symptom identified was vulval itching. Thorough general physical examination including breast examination was done, which revealed no abnormalities. A preoperative assessment of the lesion showed that cervix was unhealthy (pap smear was negative) and there was no extension of the lesion in the vagina. No abnormal areas were identified on the cervix after the application of 1% acetic acid. Vulvar skin was thick, sharply demarcated, with the typical cake icing effect, involving both sides of vulva, which was also spread across the perineum and involved the superior margin of anal sphincter.

Necessary pre-operative investigations were carried out, including complete blood picture, blood group and Rh factor, random blood sugar and urine analysis.

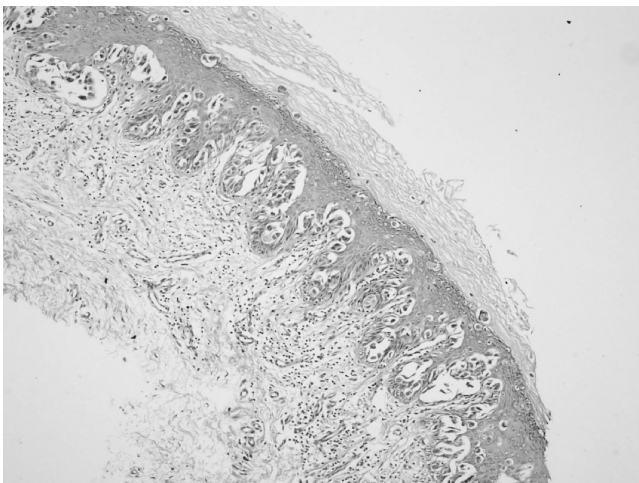


Figure-1: Photomicrograph of Paget's disease of the vulva ,revealing intraepithelial infiltration by sheets and clusters of large neoplastic cells showing clear cytoplasm and hyperchromatic and pleomorphic nuclei with prominent nucleoli. These tumour cells are causing suprabasal clefting with acantholysis. (H&E low power).

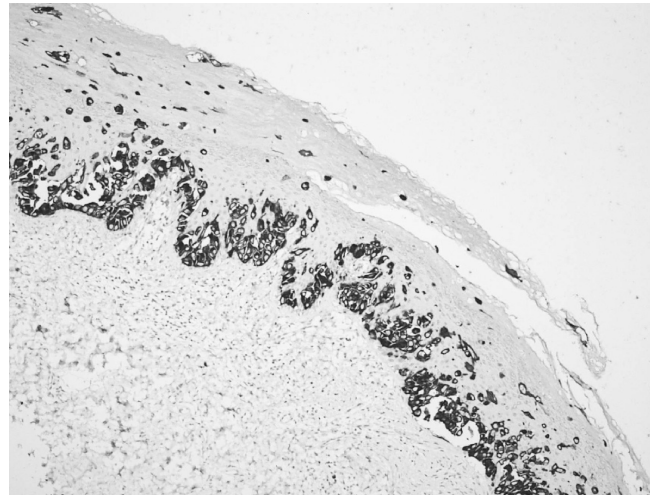


Figure-2: Photomicrograph of the Paget's disease of the vulva showing immunohistochemical positive staining of cytokeritin 7 in clusters of large neoplastic cells. (Immunohistochemical staining. low power).

Mammography and pap smear were also performed, which revealed no abnormalities. After informed consent for surgery, local excision of lesion was performed under general anaesthesia, after marking the lesion with methylene blue. The entire vulval lesion (including skin and subcutaneous tissue) along with the healthy margin of 1.5 cm was excised, along with the cervical punch biopsy and were sent for histopathology.

Primary closure of the wound was performed.

The disease was confirmed by histopathology, as observed in Figure-1 & 2.

Wound toilet was performed daily. Broad spectrum antibiotics were continued for seven days and liquid diet was given for three days, followed by a stool softener. Wound dehiscence (involving skin and subcutaneous tissue) was observed on 4th post operative day. It was managed by daily wound debridement and wet to dry dressings. Histopathology report revealed benign endocervical tissue and Paget's disease, extending up to the closest peripheral surgical margin, while deep margin was tumour free. A reexcision was performed on the 16th postoperative day, in which margins were refreshed and 1 cm of skin and subcutaneous tissue was removed from left side of perineum. A triangular flap of skin (full thickness graft) was removed from medial aspect of thigh and was attached to the wound, anal sphincter and posterior fourchette. Histopathology revealed a foci of Paget's disease, but the margins of the lesion remained free from the lesion.

Patient was followed weekly for 2 weeks, then three monthly and at every visit, a visual examination was performed, in order to determine disease free status. After three months, the entire wound was completely healed, and

she was symptom free.

## Discussion

Most of the benign vulvar tumours arise from the subcutaneous tissue of the vulva.<sup>8</sup>

The vulva is one of the extramammary sites, which has a potential for developing Paget's disease. An underlying sweat gland carcinoma or breast carcinoma is frequently associated with this disease.

It is characterized by the presence of pruritis and tenderness.<sup>9</sup> The lesion may be localized to one labium or involve the entire vulvar epithelium. It may extend to the peri rectal area, buttocks, inguinal area or mons. Vulvar lesions usually are hyperaemic and they may be demarcated sharply and thickened with foci of excoriation and induration. The vulvar skin may be thick, leading to the impression of leukoplakia with the cake icing effect. This classic finding almost is pathognomonic for Paget's disease. Adequate biopsy from the thickened indurated area is required for the diagnosis and to rule out adenocarcinoma. Histologically, large cells of clear cytoplasm in a heavy lymphocytic infiltration in the dermis occurs and can be confused with Melanotic melanoma.

Review of literature shows delay of average 3.4 years in the diagnosis of Paget's disease of vulva in 7 patients, who were treated at the Cancer Hospital Chinese Academy of Medical Sciences (for the period from 1960 to 2002).<sup>9</sup> The mean age of their patients was 67.3 years (range 54-81 years).<sup>9</sup> However, in the reported case, the patient was 40 years old and the condition was diagnosed earlier.

Margin controlled surgical excision of the affected area to an adequate depth is the standard treatment for extramammary Paget's disease. Treatment of Paget's disease is complicated by the extension of microscopic disease beyond the visible margins of the lesion, as was observed in our case.

Microscopically positive margins following surgical excision of vulvar intraepithelial Paget's disease is a frequent finding and disease recurrence is common, regardless of surgical margin status. Black D had reviewed the medical record of 28 women with intraepithelial Paget's Disease and out of which 20 had microscopically positive margins and 14 (70%) had developed recurrence of disease.<sup>10</sup> Most women with Paget's disease of the vulva have a good prognosis. Review of 100 women with this cancer found that only 4% had an additional cancer called adenocarcinoma.

Recurrences are more likely to occur, if tumour cells

are present at the margin of the excision. Unfortunately, even with negative margins, recurrences are possible, and new lesions can be treated in the same manner as the primary disease. These may occur years after diagnosis of the primary lesion. Al Saad et al. have previously reported a patient, who was initially diagnosed as Paget' disease of the vulva, but later on presented with primary vulvar apocrine adenocarcinoma.<sup>11</sup> Therefore, a strict follow up is mandatory to reduce the morbidity associated with the lesion.

Recurrence is common, so patients should be re-examined every 3 months after surgery for the next 2 years, after which annual follow ups are recommended. At every visit a visual examination is necessary in order to determine disease free status.

## Conclusion

Persistence of vulval itching needs early vulval biopsy. Once the disease has spread, a wide local excision is required. This needs grafting and may have delayed wound healing and breakdown of wound.

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## References

1. Creasman WT, Malignant Vulvar Lesions, e medicine specialties, Gynecologic Oncology 2007. (Online) Available from URL: <http://emedicine.medscape.com/article/264898-overview>.
2. Elizabeth M. Prognosis for Vulvar Paget's disease called excellent (extramammary Paget's disease). Ob Gyn News article, 2005. (Online) Available from URL: <http://www.highbeam.com/doc/1g1-147876464.htm>.
3. Extramammary Paget's disease- Wikipedia, the free encyclopedia. (Online) 2011 (Cited 2009 Jan). Available from URL: Available from URL: <http://www.wikipedia.org/wiki/extramaammry-paget-s-disease>.
4. Wilde JL, Paget's Disease, Extramammary emedicine, 2007. (Online) Available from URL: <http://www.emedicine.com>.
5. Shazia NI, Rauf A, Naqi AH. Aggressive Angiomyxoma of the Vulva Biomedica 2004; 20: 67-8.
6. Sachdev PS. Concurrent Fibroadenoma of breast and Fibromatosis of vulva and thigh. J Coll Physicians Surg Pak 2005; 15: 661-2.
7. Petkovic S, Jeremic K, Vida Kovic S, Jeremic J, Lazovic G. Paget's disease of the vulva- a review of our experience. Eur J Gynaecol Oncol 2006; 27: 611-2.
8. Perveen S. Benign Tumours of the Vulva. J Coll Physicians Surg Pak 2004; 14: 537-9.
9. Hua L, Zhang WH, Zhan R, Bai P, Li HJ. Clinical analysis of extra mammary Paget's disease of vulva. Chinese J Cancer Resear 2004; 16: 212-6.
10. Black D, Tornos C, Soslow RA, Auitrey CS, Barakat RR, Chi DS. The Outcome of patients with positive margins after excision for intraepithelial Paget's disease of the Vulva. Gynecol Oncol 2007; 104: 547-50.
11. Al Saad KO, Obaidat N, Dube V, Chapman W, Ghazarian D, Vulvar apocrine adenocarcinoma: a case with nodal metastasis and intermodal mucinous differentiation. Pathol Res Pract 2009; 205: 131-5.