Nigerian Journal of Clincal Practice
December 2006 .Vol 9(2): 179 182

PAGET'S DISEASE OF THE NIPPLE-AREOLA COMPLEX AS SEEN IN BENIN CITY, NIGERIA.

C. E. Ohanaka, A. N. Ollu-Eddo
Department of Surgery and Pathology, College of Medical Sciences, University of Benin,P.M.B. 1154, Benin City, NIGERIA.

ABSTRACT

Out of a total of 240 patients who were managed at the University of Benin Teaching Hospital , Nigeria, for breast cancer over a ten year period (January 1995-December 2004, 8(3.3%)were found to have Paget's disease of the nipple-areolar complex. They were all females aged between 38-60 (mean 47.62 years). Duration of symptoms before presentation was between 5 months and 7 years (mean 20.75 months). The left breast was more affected than the right.

They all presented with itching, excoriation and ulceration of the nipple and diagnosis was by wedge biopsy of the nipple in early cases and by incisional biopsy in late cases. Most presented with advanced disease. Seven patients had mastectomy while one declined surgery. They all had chemotherapy and tamoxifen. Five died within one year of surgery while the remaining three were lost to follow up. Paget's disease, though rare,requires a high index of suspicion for proper diagnosis.

Key words: Paget's disease, nipple, Benin city, Nigeria.

INTRODUCTION

Paget's disease of the nipple has been defined as a lesion in which large pale-staining cells are present within the epidemis of the nipple predominantly in the deep half[1]. It is almost invariably found to be associated with an intraductal carcinoma and less frequently with an invasive carcinoma.

The clinical entity consisting of crusting, bleeding and ulceration of the nipple was first described by Velpeau in 1856[2]. However, it was Sir James Paget who writing in 1874 described "an eruption on the nipple and areolar" with characteristics of "ordinary eczema or psoriasis" and observed that "cancer of the mammary gland has followed at the most two years." He equally noted that the cancer had always taken place in the substance of the mammary gland. Jacobeus in 1904 noted that the carcinoma is derived from the glandular epithelium of the lactiferous ducts[4]. Muir[5] described the phenomenon of "secondary" Paget's disease in which an invasive primary carcinoma of the breast extends directly into the epidermis and accompanied by an intra-epidermal spread of Paget's cell. Paget's disease has assumed a Position of considerable importance because of the presence of an underlying carcinoma.

Correspondences: Dr C. E. Ohanaka

It is rare and has been reported as the presenting sign of breast cancer in 0.5% to 4.3% of all cases[6].

Available literature shows that not much has been written on Pagets disease of the nipple from our environment. This forms the basis for this study. This paper is a ten-year review of Pagets disease of the breast as seen in the University of Benin Teaching Hospital, Nigeria. The peculiarities of presentation in our setting are highlighted coupled with a literature review of the relevant aspects of this clinical entity.

PATIENTS AND METHODS

A review of the Medical Records in the Surgical Wards and Pathology Department was carried out in order to identify the patients who were managed in the University of Benin Teaching Hospital, Nigeria for Paget's disease of the nipple over a ten year period (January 1995-December 2004). The findings from the ward records were cross checked with those of the Pathology Department. Subsequently, the case notes of the patients so identified were pulled out for analysis.

Analysis was in terms of age, sex, duration of symptoms before presentation and relevant clinical features. Others were the investigations carried out, treatment offered, duration of follow up and outcome of treatment.

RESULTS

Within the ten years under review (January 1995-December2004)240 patients were admitted and managed for breast cancer in the University of Benin Teaching Hospital, Nigeria. Of this number, 8(3.3%) were diagnosed as having Paget's disease of the nipple-areolar complex. They were all females aged between 38-60 years (mean 47.62 years). Whereas 6 patients presented within one year of development of symptoms one patient each presented at 2 and 7 years respectively (mean duration of symptoms 20.75 months). The left breast was involved in 6 cases and the right in two . They all presented with breast mass, itching, excoriation and ulceration of the nipple. None presented with nipple discharge.

Diagnosis was by wedge-biopsy of the nipple lesion in two relatively early cases and by incisional biopsy in the other more advanced cases. In one peculiar case, diagnosis could only be made on the post mastectomy breast specimen. Paget's disease of the nipple-areolar complex with an underlying infiltrating duct carcinoma was the histological finding in all the cases.

Five patients presented with advanced disease. All but one patient had mastectomy (one declined surgery and was lost to follow up). Similarly, five patients died within the first year postmastectomy while the remaining three were lost to follow up. Of the deaths, one died from an unrelated cause (hypertensive crisis).

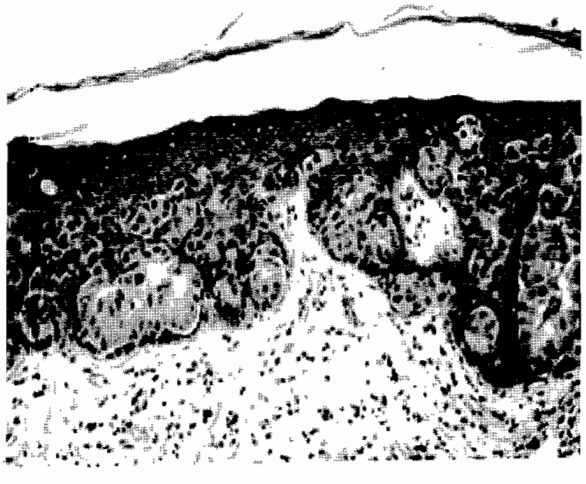

figure 1: Paget's disase of the breast showing clumps and single neoplastic cells infiltrating the epidermis with most of the paget cells are in the lower half of the epidermis x 400

DISCUSSION

Paget's disease of the breast is quite rare. Our incidence rate of 3.3% of all breast carcinomas managed in the hospital is in keeping with figures of 0.5-4.3% generally quoted[6]. Like all breast cancer it is a predominantly female disease. There was no male in this series but about 40 cases of Paget's disease involving the male breast have been reported in the world literature[7,8].

The peak age incidence of Paget's disease of the breast is said to be between 50 and 60 years of age, with a median of 56 years[6]. Our patients were, however, younger (mean age 47.62 years). This is in conformity with the peak incidence of breast cancer being a decade earlier in our environment as compared with the situation in developed countries[9]. Our mean duration of symptoms of 20.75 months is longer than the 6.5 months quoted in developed countries. It is not surprising, therefore, that most of our patients presented with features of late breast disease.

All our cases were unilateral lesions. This is in keeping with other series where bilateral lesions were exceptional[6]. Extramammary Paget's disease occurring in the lateral part of the breast has been reported[10]. Paget's disease of the vulva associated with local adenocarcinoma and previous breast adenocarcinoma has equally been reported[11]. No predilection has been described for any particular breast but in this series the left breast was found to be more affected than the right in the ration 3:1.

The most frequent clinical feature include itching, excoriation, ulceration and crust formation[12]. Nipple discharge is a common symptom but none of our patients had this. About 50% of the patients have a palpable breast mass, positive lymph nodes or both on presentation[8]. Differential diagnosis include eczema, trauma, erosive adenomatosis of the nipple and Bowen's disease (intraepithelial squamous cell carinoma)[13]. Bilateral affectation tends to differentiate the more benign eczema from Paget's disease of the nipple.

Particularly when there is no palpable mass, mammography is useful in the detection and location of sub-clinical underlying tumours, clusters of suspicious micro calcifications or both[6,12]. It also enables an image guided core biopsy of any disease prior to surgery; thus indicating the need for node sampling preoperatively rather than as a delayed

procedure[14] . However, because we are not equipped for these investigations, diagnosis in these cases was based on histology of either the full-thickness wedge biopsy of the nipple in early cases or incisional biopsy in clinically advanced cases. Diagnosis can also be made from a superficial "shave" biopsy of epidermis, or a punch biopsy. These, however, are not as reliable as the wedge biopsy which is able to demonstrate all the structural layers[15]. This is not always easy and straightforward as exemplified by the case mentioned above where a definite diagnosis was made after mastectomy. In this case, inspite of the obvious clinical features, incisional biopsy carried out on two consecutive occasions did not yield any positive result as features were mainly those of fibrosis. The relatives had to prevail on the surgeon and actually signed a consent for a mastectomy to be carried out without a proven histological diagnosis. Section of the excised breast demonstrated Paget's disease. This is also the experience of other authors[15]. Diagnosis is hinged on the presence of large, rounded or ovoid intraepidermal cells with abundant pale cytoplasm. They also have associated large, pleomorphic and hyperchromatic nuclei with large nucleoli. These Paget's cells are the histological landmark of the disease [16] . (Fig 1). The origin of the Paget's cells has been hotly debated. By and large , the epidermotropic theory which postulates that Pagets cells are in essence , ductal carcinoma that have migrated along basement membranes of the underlying duct to the nipple epidermis is widely accepted.

The therapeutic implication of the epidermotropic theory is that treatment must take cognizance of the underlying carcinoma. Mastectomy with or without axillary dissection therefore remains the standard treatment of Paget's disease of the breast[8]. Five of our patients had toilet mastectomy due to advanced disease, two had modified radical mastectomy while one rejected surgery. It has , however , been found that there is a place for more conservative surgery and irradiation in patients who present without clinically and mammographically detected mass[6]. None of our patients qualified for this owing to late presentation.

Adjuvant chemotherapy, radiation and tamoxifen are also employed depending on the nodal and receptor status of the tumour[8]. All our patients had chemotherapy and tamoxifen.

The prognosis of Paget's disease of the nipple is more a reflection of the underlying carcinoma; be it intraductal or infiltrating. Most of our cases presented late as evidenced by five of them confirmed to have died in hospital within one year of surgery. A similar fate could have befallen those who were lost to follow up.

CONCLUSION:

Paget's disease of the breast is rare. Diagnosis is hinged on a high index of suspicion. Any dermatological involvement of the nipple-areolar complex should be taken seriously. There should be no hesitation in resorting to biopsy and histological confirmation when in doubt. The treatment modality and prognosis are based on the underlying carcinoma.

REFERENCES

1. **World Health Organisation.** Histological typing of breast tumours. 2nd ed. International classification of tumours No.2. Geneva; World Health Organisation, 1981: 19

2. **Velpeau S.** A treatise on disease of the breast and mammary region, 1856, London Syndenham Society.

3. **Paget J.** On disease of the mammary areolar preceding cancer of the mammary gland. St Barthiolomew's Hosp. Rep. 1874; 10: 87-89.

4. **Jacobeus H C.** Paget's disease und sein Verhaitnis zum Milchdrusen carzinom. Virchow Arch 1904: 178: 124-142.

5. **Mui R.** Paget's disease of the nipple and its relationships. J. Pathol Bactriol 1927: 30: 451-471.

6. **Jamali F R., Ticci A I, Deckers P.I.** Paget's disease of the nipple-areolar complex. Surg. Clin N Amer. 1996; 76(2): 365-381.

7. **Semur F, Birkefield S.** Amsterdam. Paget's disease of the male breast cancer 1988; 62: 601.

8. **Desal D.C Brennan E J Jr, Carp NZ.** Pagets disease of the male breast AM Surg 1996; 62(12) 1068-1072.

9. **Edino S T, Oicha O, Alhassan S, Mohammed A.Z, Ajayi O.O.A** Histopathological review of breast cancer in Kano. Nigeria Journal of Surgery, 2000;7(2):70-75.

10. **Friss M.L, Johansen T, Daliland E, Ejstrud P.**Extramammary Paget's disease interpreted as psoriasis. Ugestr-laeger, 1999; 161(9) 1276-1277.

11. **Farrell A.M., Charnock F.M., Millard P.R, Wojua-rowska F.** Paget's disease of the vulva associated with local adenocarcinoma; report of two cases. Br J Dermatol 1999; 141(1): 9 146-149.

12. **Badoe E.A., Baako BN.** The breast . In Principles and Practice of Surgery ,3rd edition, Ghana Publishing Corporation;200:461.

13. **Adant J.P, Paguet P,Bluth F,Nelssen X, Pierard G.** Erosive adenomatosis of the nipple. Report of 2 cases. Ann Chir Plast Esthet 1997; 42(6): 638-641.

14. **Ceccherim A F, Evans A J, Pinder S E, Wilson A R, Ellis I O, Yeoman L J.** Is ipsilateral mammography worthwhile in Paget's disease of the breast. Clin Radiol 1996;51 (1): 35-38.

15. **Rosen P P.** Pagets of the Nipple; In Rosen's Breast Pathology by PP, Lippinsott Raven, Philaldelphia: 493-506.

16. **Cheatle G L, Cutter M.** Paget's disease of the nipple. Arch Pathol 1931; 12: 435.