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## Paget's Disease of the Breast : Report of Four Cases

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Paget's disease of the breast is one of the special types of breast cancers of rare incidence; it is characterized by eczematous changes of the nipple and Paget's cell infiltration in the epidermis of the nipple.

We encountered four cases of Paget's disease among the sixty cases of breast cancers we treated in the past five years. The incidence was 6.7 per cent, which is higher than that in other reported series. Two of the four cases had only nipple changes without breast tumors while the other two cases had both nipple changes and breast tumors. The mean age of the patients in the four cases of Paget's disease was 52.3 years while that of the patients with ordinary breast cancers was 53.2 years. The four cases were all treated by radical mastectomy.

It was Velpeau<sup>8)</sup> who first described the lesion of the nipple in 1840, which is known today as Paget's disease. Sir James Paget,<sup>9)</sup> an English surgeon, observed first the association of the erosion with a breast cancer in 1874. But Paget himself thought that the nipple change was a precancerous stage but not the cancer itself.

In 1889, Darier<sup>10)</sup> first described the large cells with pale cytoplasm and prominent irregular nuclei which we now call Paget's cells; but he regarded them merely as degenerated epidermal cells. It was Jacobaeus<sup>11)</sup> who, in 1904, first traced the origin of the Paget's cells from intraductal carcinoma in the nipple ducts. This has been supported by many investigators.

Haagensen<sup>1)</sup> states that... "it can be said that there is today general agreement that in all cases of Paget's carcinoma the disease is found not only in the nipple epidermis but also in the nipple ducts, and that in the great majority of cases there is also intraductal carcinoma of the mammary gland itself."

### Case Reports

#### Case 1

Mrs. N. K., a 42 year old housewife, noticed that her right nipple was crusted and eroded accompanied by an itchy sensation three years before her visit to our hospital. She consulted a dermatologist who treated her with ointment. The erosion of the nipple improved for several weeks but soon it broke out again. As the erosion and itching increased, she consulted the dermatology department of our hospital in July 1977. A nipple biopsy confirmed the diagnosis of Paget's disease of the breast. In 1967, a biopsy of her left breast revealed chronic mastitis.

On her first visit to our clinic, her breasts were symmetric in size. In the right breast, the nipple was flat and erosion involving the surface of the nipple and areola measured  $2.5 \times 3.0$  cm in diameter. There was an orange-peel appearance of the skin in the supra-areola region (Fig. 1). Some induration was felt beneath the areola. There was no palpable axillary lymphnode.

A radical mastectomy including parasternal dissection was carried out on July 22, 1977. There were neither tumors in the breast tissues nor lymphnode metastases. A microscopic examination revealed infiltration of large Paget's cells with pale cytoplasm in the epidermis of the nipple (Fig. 2). Same cells were also found in the nipple ducts but there was no extraductal invasion.

#### Case 2

Mrs. K. S., a housewife aged 47, noted that her right nipple had been crusted and eroded with a few spots of blood on her brassiere for six months. Although she applied a plaster by herself over the eroded nipple, remission and recurrence of the erosion repeated. On examination, an erosion 5 mm in diameter at the tip of the nipple and several bleeding spots were observed in the erosion (Fig. 3). There was no palpable mass in the breast. A few small lymphnodes were felt in the bilateral axillae but they were soft. A biopsy of the nipple, which was done at the dermatology department, revealed that the epidermis was infiltrated by Paget's cells. A radical mastectomy was performed on April 30, 1975. Microscopically we found that Paget's cells had spread not only in the epidermis of the nipple but also into the lactiferous ducts. There were no lymphnode metastases (Fig. 4).

#### Case 3

Mrs. Y. S., 67 year old housewife, who had three children all fed with maternal milk, noticed a mass in the left breast in 1972. It was about 3 cm in diameter underlying the areola. She felt some itchy sensation around the nipple after that. She noted erosion in the areola for these eight months and secretion from the eroded area with occasional bleeding. Her left nipple had always been slightly retracted before she noticed the mass. She said that the mass had gradually enlarged.

On her visit to our clinic, we noticed that left breast was larger than the right and elevated upward. The left nipple was retracted and the skin around the areola showed an orange-peel appearance. In the areola, there was an erosion about 5 mm in width which circumscribed the nipple. A mass was palpable beneath the areola 5 cm in diameter which was adherent to the skin (Fig. 5). Several lymphnodes were palpable in the left axilla.

She underwent an extended radical operation including parasternal dissection on July 2, 1976. There was a tumor beneath the areola, measuring  $3 \times 4 \times 5$  cm, and lymphnode involvement in the axilla was obvious. The pathological findings were those of infiltrating duct carcinoma and invasion of the Paget's cells in the nipple epidermis (Fig. 6). There were metastases in four out of nine axillary lymphnodes and there was metastasis in one subclavicular lymphnode. The parasternal lymphnodes were free from metastases. According to the TNM classification, this case belongs to T2N3MO (Stage III).

#### Case 4

A 53 year old married female, gravida 0, noted that the nipple of her left breast was dark-reddened and crusted with an itchy sensation three months before her first visit to our hospital. She consulted a doctor who treated her with ointment. As no noticeable improvement was made,

she was referred to the dermatology department of our hospital, where a biopsy showed Paget's cells.

A radical mastectomy was performed on Nov. 1, 1974. There was a tumor in the breast measuring  $4 \times 4$  cm. A pathological examination revealed infiltrating duct carcinoma without lymph-node metastases. This case was T2NOMO (Stage I). (Fig. 7, 8)

### Discussion

Paget's disease of the breast is known as a special type of breast cancer of rare incidence. Haagensen's Columbia-Presbyterian series<sup>1)</sup> includes 158 women and one man with Paget's disease, which has constituted about 2.5 per cent of all mammary carcinomas. Ashikari<sup>2)</sup> reported 214 cases of Paget's disease which represented 3.2 per cent of all the cases of breast cancer seen at Memorial Hospital, N. Y. during the period 1950 through 1968. In 1972, Senoo<sup>5)</sup> collected 194 cases of Paget's disease in Japan which showed an incidence of 1.2 per cent of all breast cancers (16,342 cases).

During the past five years, we have treated sixty cases of breast cancer, among which four cases were diagnoses as Paget's disease. The incidence is 6.7 per cent, which is higher than other reported series, but the total number of cases of breast cancer in our series is still small.

The mean age in the four cases is 52.3 years while that of the patients with ordinary breast cancer is 53.2 years. But Haagensen<sup>1)</sup> and Sakamoto<sup>4)</sup> pointed out that the average age of patients with Paget's disease is higher than that of patients with common types of breast cancer.

Clinical features of the nipple change are as follows; an itchy or burning sensation in the nipple, redness, roughing and thickening of the epidermis, erosion of the nipple surface. Differentiation of those changes from dermatitis is important but occasionally difficult. Three of our four cases were treated as dermatitis initially. Haagensen<sup>1)</sup> mentioned; "all erosions and dermatitis-like lesions that involve only the nipple epitherium are carcinomatous. Lesions that involve the areola as well as the nipple epitherium and sometimes the skin of the breast are usually carcinomatous, but occasionally they are due to dermatitis. Erosions that involve the areola or the skin of the adjacent breast, leaving the nipple uninvolved are not Paget's carcinoma."

Biopsy of the epithelium of the nipple confirms the diagnosis if there are typical Paget's cells in the epidermis which are large and clear with vacuolated cytoplasm and have hyperchromatic nuclei.

Two of our cases had tumors in the breast while the other two had no tumors. There is clinically an important difference between those patients with tumors in the breast and those patients without tumors. Sakamoto<sup>4)</sup> has classified Paget's disease into two categories; those cases that have only nipple changes without tumors in the breast are named Paget's carcinoma, and those cases that have both nipple changes and tumors in the breast are named Pagetoid carcinoma. The ratio of those cases without to those cases with breast tumors is 40 % to 60 % (Sakamoto) or 42 % to 58 % (Haagensen). In age distribution the two groups are also different. In Haagensen's series, the average age of the patients without breast tumors is 58 years while that of the patients with tumors is 49 years. This tendency is also observed in Sakamoto's series. From this Sakamoto suggests that nipple change does not always precede tumor formation in the breast. Kister & Haagensen<sup>3)</sup> questioned: "does age influence the behavior of the underlying intraductal carcinoma more epidermotrophic in older women?"

Two cases of our Paget's disease without breast tumors showed non-infiltrating duct carcinoma

microscopically and there were no lymphnode metastases, while those two cases with tumors in the breast showed an infiltrating pattern and one of them had axillary and subclavicular lymphnode metastases.

Ashikari<sup>2)</sup> reported that "13 % of 96 patients who did not have a palpable mass preoperatively had axillary lymphnode metastases while 65 % of the 113 patients with palpable masses had axillary lymphnode metastases. In his series, 63 of 96 patients without palpable masses had only intraductal non-infiltrating duct carcinoma. One hundred and six of the 113 patients with palpable masses had infiltrating carcinoma, while 7 showed no evidence of infiltration.

Paget's disease without breast tumors has a good prognosis, but Paget's disease with breast tumors has a worse prognosis than that of common types of breast cancer. In Sakamoto's series,<sup>4)</sup> for the patients with Paget's carcinoma, the five year survival rate was 90 per cent, and for the patients with Pagetoid carcinoma, it was 60 per cent; this was lower than 70 per cent of the five year survival rate for patients with ordinary breast cancer.

Ashikari<sup>2)</sup> said, "Overall survival of patients without palpable masses was 92 % at 5 years and 87 % at 10 years. Forty-two and a half per cent of patients who had palpable masses survived at 5 years and 37.9 % at 10 years." On the other hand, Kister<sup>3)</sup> & Haagensen reported: "The ten year survival rate is 58 per cent for all patients. For patients without axillary lymphnode metastases the ten year survival rate is 79 per cent and those with axillary lymphnode metastases it is 28 per cent. The same figures for patients with nipple changes only, are 83 per cent and 50 per cent, respectively."

All our four cases of Paget's disease were treated by radical mastectomy. In case 1, there was no tumor in the breast but some induration was felt beneath the areola on palpation, so that parasternal dissection was performed. In case 3, which had a tumor in the breast, there were axillary and subclavicular lymphnode metastases but parasternal lymphnodes were free from metastases, microscopically.

In cases of Paget's disease in which the changes are confined to the nipple only, without a clinically detectable tumor in the breast, some investigators<sup>6) 7)</sup> have suggested simple mastectomy as the treatment of choice. But Haagensen,<sup>1)</sup> Kister,<sup>3)</sup> Sakamoto<sup>4)</sup> and others<sup>12)</sup> maintain redical mastectomy is the treatment of choice for all cases of Paget's disease. Because Paget's disease involving only the nipple ducts can metastasize to the axillary lymphnodes.

Ashikari<sup>2)</sup> of Memorial Hospital, N.Y. recommends; "modified radical mastectomy is the treatment of choice for the patient who does not have a palpable mass. Radical mastectomy should be performed on the patient who has a palpable mass."

### Conclusion

Four cases of Paget's disease of the breast were reported and discussed with reference to studies in the literature. They were all treated by radical mastectomy. Patients with Paget's disease of the breast should be treated in the same way as patients with ordinary breast cancers, whether tumors are present in the breast or not.

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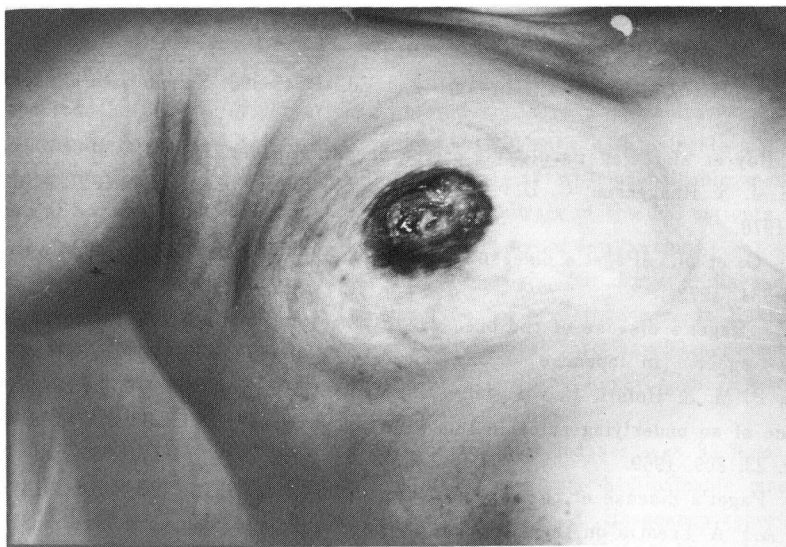


Fig. 1. Erosion involves the surface of the nipple and areola. Orange-peel appearance of the skin.

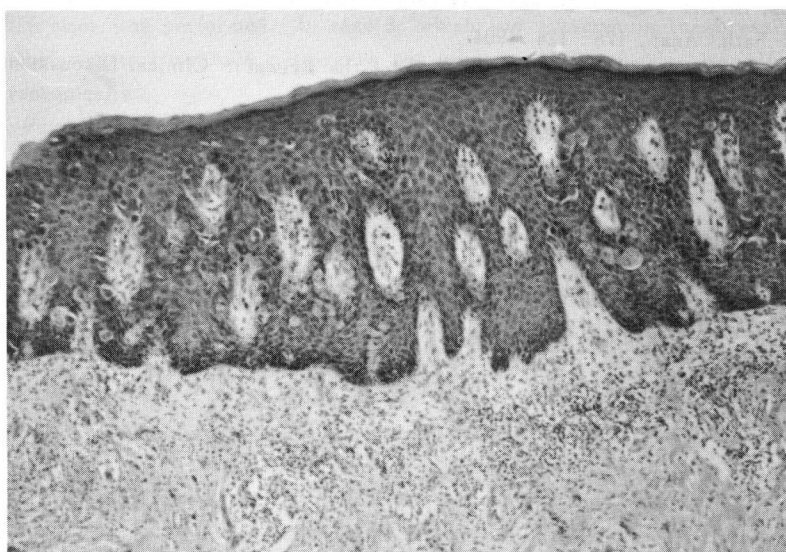


Fig. 2. Infiltration of large Paget's cells with pale cytoplasm in the epidermis of the nipple.



Fig. 3. Erosion of the nipple surface in Paget's carcinoma.

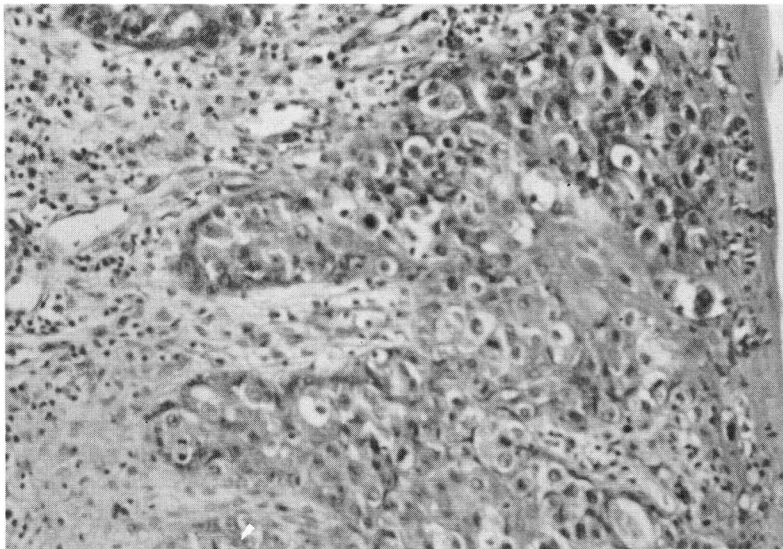


Fig. 4. Infiltration of the epidermis by Paget's cells.



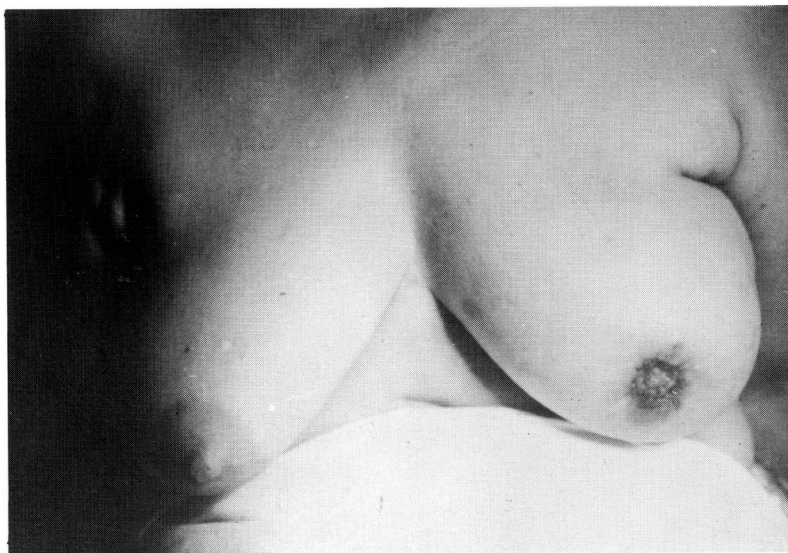


Fig. 5. Elevation of left breast. Retraction of the nipple. Erosion in the areola. Orange-peel appearance of the skin.

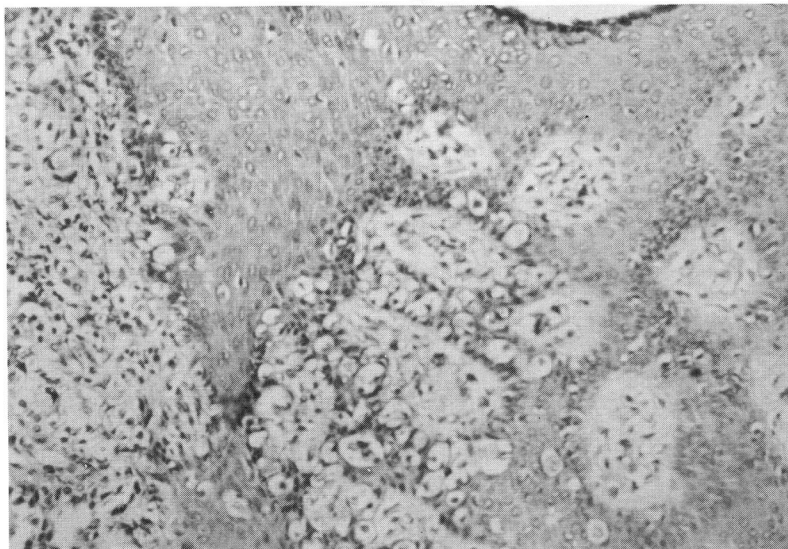


Fig. 6. Infiltrating duct carcinoma with Paget's cells in the epidermis of the nipple.

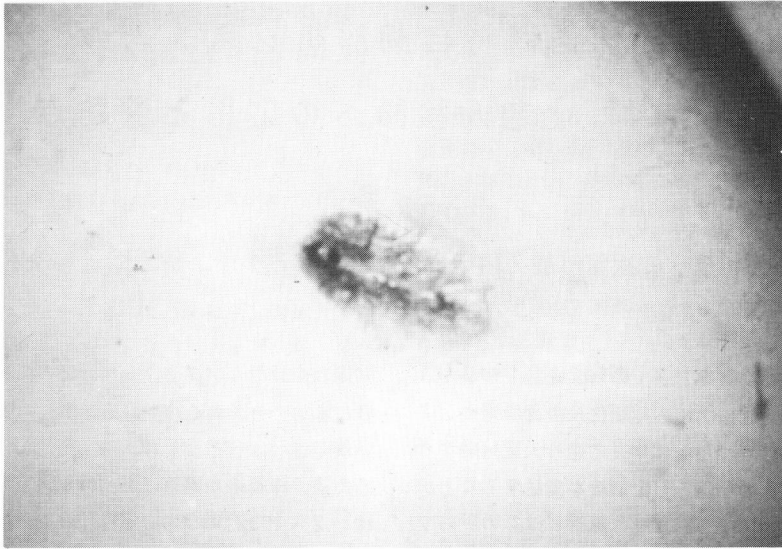


Fig. 7. The nipple is crusted and deformed.

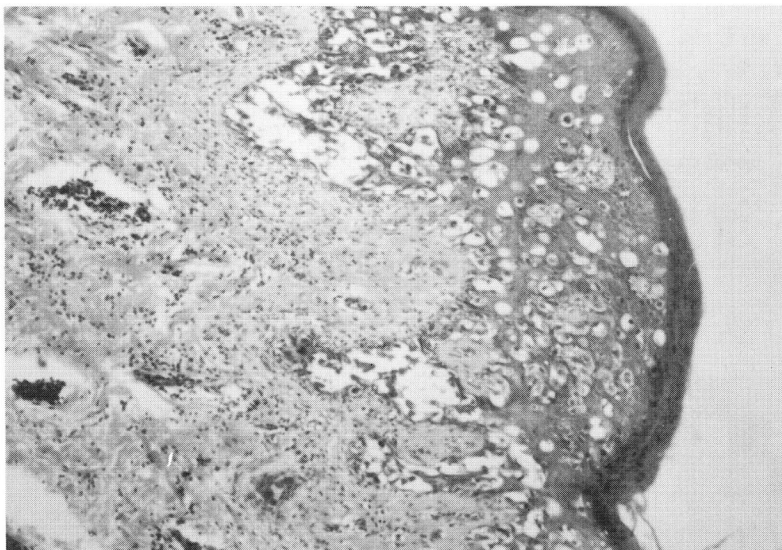


Fig. 8. Erosion of the nipple surface produced by infiltration of the nipple epidermis by Paget's cells.