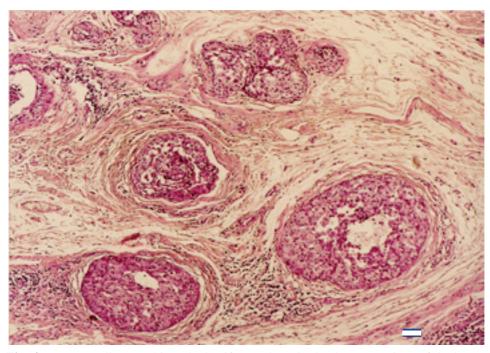
## Paget's disease with intraductal spread



**Fig. 4.** Paget's cells spread into the lactiferous ducts in the deeper portions of the breast (hematoxylin and eosin stain; original magnification  $\times$  40). Bar = 160  $\mu$ m.

fered formalin and embedded in paraffin wax. The histlogical sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS) and elastic van Gieson (EVG) methods to distinguish lactiferous ducts from blood vessels.

Histologically, a large number of Paget's cells with abundant clear cytoplasms and large nucleoli were present in the nipple epidermis (Fig. 2). PAS staining showed granular bodies in the cytoplasms of a few Paget's cells. The cells were distributed in proximal lactiferous ducts underlying the nipple (Fig. 3). Furthermore, extensive intraductal spreads of Paget's cells were found at several branches of the lactiferous ducts in the deeper breast (Fig. 4). There was no invasive carcinoma. All the axillary lymph nodes showed no metastatic tumor.

She remained free from any signs of relapse for 2 years after the operation. The current form implies there was a relapse after 2 years.

## Discussion

Mammary Paget's disease occupies 2% of all breast cancers (Lloyd et al., 2000). The disease does not grow from the nipple epidermis but from the underlying breast carcinoma, which develops secondarily because of spreads due to the extension or migration of malignant cells from underlying breast carcinoma.

Intraductal spread of Paget's cells with the flow, either continuous or discontinuous, has been reported (Rosai, 1996). Mai and coworkers (May, 1999; Mai et al., 1999) reported the discontinuous pattern of intraductal tumor spread identified in the foci of carcinoma in deep breast tissues. They suggested 3 possible mechanisms of this discontinuous pattern of tumor spread: i) tumor cell migration, ii) tumor implantation and iii) multifocal carcinogenesis that most likely affects progenitors of ductal cells in the duct.

In the past, radical or modified mastectomy was the mainstream choice for the surgical treat-

ment of mammary Paget's disease. Recently, breast conservative therapy (excision of the nipple/ areola complex) has been performed for most patients (Pierce et al., 1997). However, there are no randomized trials that provide a specific basis to the selection of an ideal treatment for this condition. Preoperative procedures including ultrasonography, mammography and MRI are uncertain in diagnosing underlying tumors or intraductal spread of Paget's cells which might be overlooked even after careful sectioning of the resected breast (Dixon et al., 1991; Kothari et al., 2002). Kothari et al. (2002) reported that cone excision of the nipple resulted in incomplete excision in approximately 75% of mammary Paget's disease patients. Mammary Paget's disease with extensive intraductal spread seems to be a nonsuitable candidate for breast conservative therapy. Therefore, breast conservative therapy for mammary Paget's disease should be treated as a consideration for possible intraductal spread.

## References

 Dixon AR, Galea MH, Ellis IO, Elston CW, Blaweg RW. Paget disease of the nipple. Br J Surg 1991;78: 722–723.

- 2 Japanese Breast Cancer Society, The. General rules for clinical and pathological recording of breast cancer. 14th ed. Tokyo: 2000. p. 12–14.
- 3 Kothari AS, Beechey-Newman N, Hamed H, Fentiman IS, D'Arrigo Bandy AM, Ryder K. Paget disease of the nipple: a multifocal manifestation of higher-risk disease. Cancer 2002;95:1–7.
- 4 Lloyd J, Flanagan AM. Mammary and extramammary Paget's disease. J Clin Pathol 2000;53:742– 749.
- 5 Mai KT. Morphological evidence for field effect as a mechanism for tumor spread in mammary Paget's disease. Histopathology 1999;35:567–576.
- 6 Mai KT, Yazdi M, Perkins DG. Mammary Paget's disease: evidence of diverse origin of the disease with a subgroup of Paget's disease developing from the superficial portion of lactiferous duct and a discontinuous pattern of tumor spread. Pathol Int 1999; 49:956–961.
- 7 Pierce LJ, Haffty BG, Solin LJ, McCormick B, Vicini FA, Wazer DE, et al. The conservative management of Paget's disease of the breast with radiotherapy. Cancer 1997;80:1065–1072.
- 8 Rosai J. Ackerman's surgical pathology. 8th ed. St. Louis: Mosby; 1996.

Received April 14, 2003; accepted May 26, 2003

Corresponding author: Kunio Araki, MD