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A REINVESTIGATION ON MASTOPATHY WITH SPECIAL REFERENCE TO CANCER OF THE BREAST

by

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Numerous studies have been made by various workers based on the view that mastopathy is a precancerous stage of cancer of the breast. However, owing to the basic complexity of the histogical images of mastopathy, it is almost impossible to identify the images under any single category. Thus, it may be said that in order to investigate the true relationship between mastopathy and cancer of the breast it becomes necessary to analyse each and every phase and portion of mastopathy before a conclusion may be reached. Hence, we have conducted a comparative studies on the architectural structure and electronmicroscopic structure of mastopathy with the intent of grasping the significance of mastopathy as a step towards cancerization.

During the past 6 years we have handled 540 cases of mammary tumor (556 mammary glands) on which usual histological studies were made. At the same time, in 30 cases which showed characteristic partial image of mastopathy serial sections were made and electron-microscopic studies were conducted, including normal mammary gland tissue (Table 1).

In the present studies we have only selected true mastopathic mammary glands, in which no cancerous changes or inflammatory changes were seen, as indicated by IMAI, et al. In the histological studies of the above, special care was taken in order to select partial images which more or less came under the 10 types of changes as set forth by STEWART (Table 2).

In the age distribution based on mastopathy, fibroadenoma and the sum total of both, a high degree of incidence was seen between the ages of 30-45 (Fig. 1). In mastopathy alone the same may be said. The main histological feature of mastopathy were cysts (Fig.

Table 1

	Patients	Numbers of mammary glands
Carcinoma mammae	133	133
Mastopathia	294	309
Fibroadenoma	56	65
Gynecomastia	30	31
Mastitis chronica	8	8
Others	19	19
Total	540	556

Table 2

1. Cyst
2. Duct papillomatosis
3. Terminal type of adenosis
4. Sclerosing adenosis
5. Apocrine metaplasia
6. Multiple small cystic changes
7. Duct epithelial hyperplasia and dilatation
8. Tendency to fibroadenoma
9. Fibroadenoma
10. Fibrosis and hyalinization

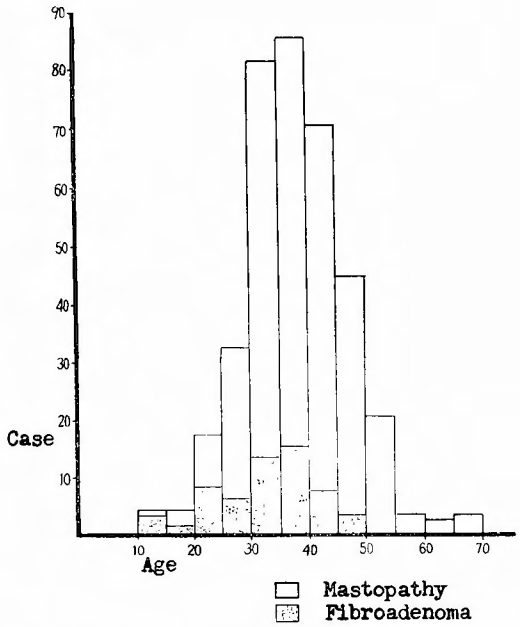

Fig. 1 Age distribution of Mastopathy and Fibroadenoma.

2), duct papillomatosis (Fig. 3), terminal phase of adenosis (Fig. 4), apocrine metaplasia (Fig. 5), dilatation of duct (Fig. 6) and duct epithelial hyperplasia (Fig. 7) etc.. The age distribution of the above showed a shift of peak towards higher ages and in contrast to this in fibroadenoma a shift of peak towards lower age was seen (Fig. 8, 9).

From the above findings, it may be said that fibroadenoma may not come under the same category as mastopathy as pointed out by various workers. When we stop to consider this point, it may become evident that in the histological investigations of mastopathy, since KROMPECHER's report, various workers may have been dazzled and mislead by the spectacular hyperplasia of the epithelium, causing them to overlock or disregard the changes in the interstitium.

However, when we clinicians are confronted with mastopathy which is one of the mammary gland tumors, actually we become aware of hyperplasis of the interstitium by palpation of the induration. Thus, when mastopathy is reconsidered with the above in mind, we find that in almost all cases of mastopathy, hyperplasia of the interstitium and hyalinization of it within the partial images of mastopathy, namely a formation of fibroadenoma is present (Fig. 10). Thus, we find the above to be one of the main changes of the mastopathy. And in contrast to this, it is not unusual to prove the presence of apocrine metaplasia in the epithelium included in the fibroadenome (Fig. 11). In this sense mastopathy and fibroadenoma would possibly come under the some category, and mastopathy may even be called fibroadenomatosis (cystica), and as Hück reported we agree that in fibroadenoma interstitial hyperplasia is more active and that fibroadenoma should be included in mastopathy. However, it goes without saying that in epithelial tumor, we do not consider that the changes in the epithelium are of a passive nature which is dominated by interstitial hyperplasia but are rather an active hyperplasia.

Since KROMPECHER, apocrine metaplasia has been considered as a characteristic change in mastopathy. In regards to this change, as a result of our observations, the changes were also seen in acinar epithelium and efferent duct epithelium. While in some cases typical apocrine cyst was seen (Fig. 12), in other cases apocrine metaplasia was seen in parts of the duct epithelium which showed an active hyperplasic picture (Fig. 13), a transitional change toward normal epithelium was also shown. When the cells of apocrine metaplasia were observed electron-microscopically, tongue-shaped processes consisting of low density protoplasmic substance were seen in the lumen of the intercellular duct while no microvilli were seen on the surface of the protuberances (Fig. 14). In addition, it was onted that protoplasm other than the protuberances were generally clearer.

Next, when duct epithelium with no apocrine metaplasia was observed in contrast to the simple structure of duct epithelium of usual secreting glands, clear cells resembling the above mentioned cells with numerous vacuoles having limiting membrane in the protoplasm and extremely dark cells were seen mixed together (Fig. 15). This was considered to indicate that in mammary gland the efferent duct epithelium is capable of differentiating into secreting cells, and may possibly be an important key in the elucidation of the complex changes of mastopathic epithelium.

Thut, as reported by HÜCK, it may be considered that in the duct epithelium of the mammary gland it is possible that acinar formation may occur in various sites, and that while maintaining the character of efferent duct it is possible for a multi-branching to occur. And the stimulation which may cause such abnormal hyperplasia, as indicated by various workers, may be of endocrine nature. And, when the influencing factors are considered in regards to whether the differentiation will turn to acinar formation or branching of the efferent duct, it may be said that aside from the nature of the stimulation, the condition of the cell itself on receiving and and the condition of the adjacent connective tissue should be taken into consideration.

As evidence supporting the above, observations on 30 caces of gynecomatia are cited. In all cases, dilatation of the duct, inward hyperplasia of the epithelial cell together with hyperplasis of the interstitium and hyalinization alone were seen with no evidence of acinar formation or duct branching (Fig. 16). As further evidence, no indications of direct acinar formation from large efferent ducts was seen. This was considered to be due to the lack oflatent differentiating ability in the epithelium of large efferent ducts. Even normal mammary glands in adult show to certain extent various regressive and degenerating changes and in some cases even show abnormal pictures. And, if this is considered to be due to different individual reactions of epithelium cells to hormon stimulation, it may be possible to explain the extensive changes in the mastopathic picture neatly to a certain extent.

Of 133 cases of breast cancer examined, 39 cases (29.3%) showed mastopathic changes in the cancerous tissue and adjoining tissue (Fig. 17). Electron-microscopic studies were made on the breast cancer cases which showed a varying tissue picture. As mentioned before, in the present case, we observed both clear and dark cells in all cases, even in gellatinous cancer (Fig. 18~28).

These findings are directly connected with the previously mentioned differentiating

potency or polypotency of the efferent duct epithelium of the mammary gland and at the same time this is considered as subsantiating morphological evidence of a limited varied tissue picture of cancerized cells.

和文抄録

乳腺腫瘍とくに乳癌における乳腺症の位置に対する再吟味

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乳腺症の病理発生を追求し，その癌性化への意義を把握せんとして，乳腺症の個々の部分像に関し構築学的検索と，電子顕微鏡的観察をおこない一知見をえた．

乳腺症の部分像としての間質の増生については，乳腺症を Fibro-adenomatosis とみる Hück の説に賛意を表するが，上皮の変化はその増生に支配された受身の病変ではなく，積極的な増殖像とみなすべきであり，また Apocrine 化生を有する腺房ならびに輸出管上皮を電顕的に観察すると，乳腺の輸出管上皮は一般の分泌腺導管と異なつて，分泌細胞への分化能を常在的に有すると考えられる．さらにまた133例の乳癌症例中，その3分の1に癌組織内および周辺部に乳腺症様変化を認め，その電顕所見に乳癌同様 clear cell と dark cell の存在をみたことは，輸出管上皮の Polypotency に直接つながりのある所見と考えられ，一方また成熟期における正常乳腺にも各種の退縮像，寡形成像およびそれらの異常像をふくんでいて，これらの上皮細胞は一定の Hormone 刺戟に対してそれぞれ異なつた反応をなすと考えると，乳腺症および乳癌の組織像の多彩さと，Hormone 依存性をあらわす形態学的根拠となると考えられる．

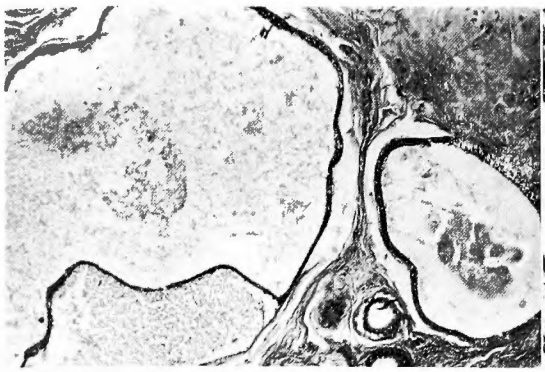

Fig. 2 Cyst

Fig. 3 Duct papillomatosis

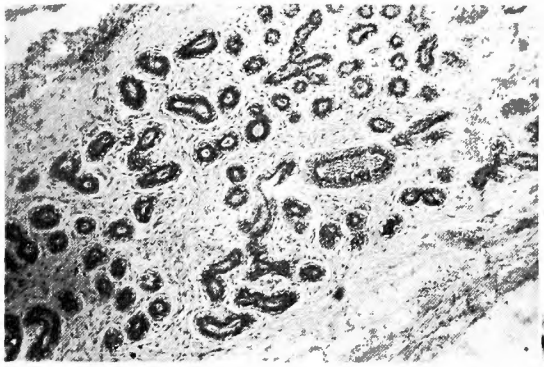

Fig. 4 Terminal Phase of adenosis

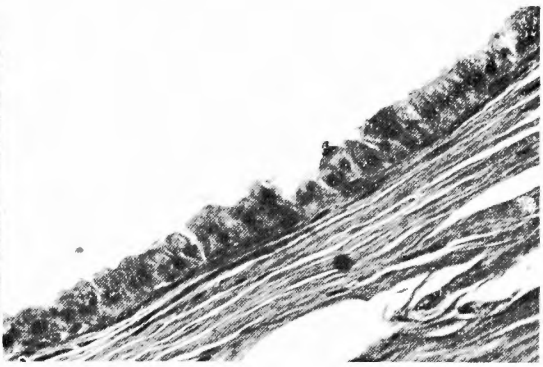

Fig. 5 Apocrine metaplasia

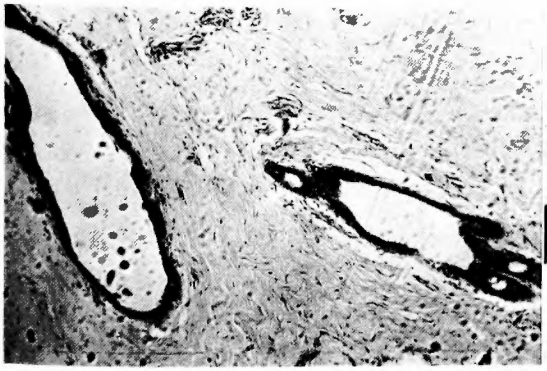

Fig. 6 Dilatation of duct

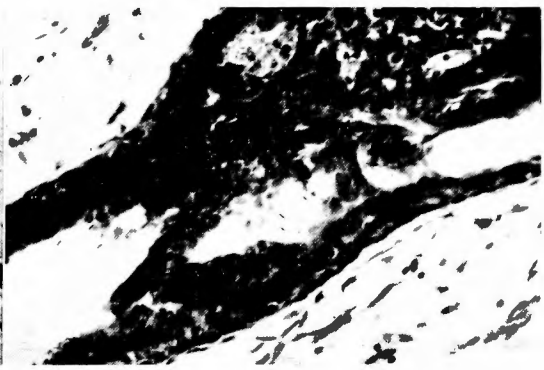

Fig. 7 Duct epithelial hyperplasia

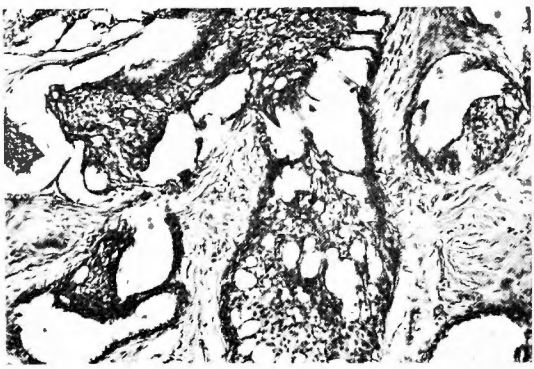

Fig. 8 Duct epithelial hyperplasia

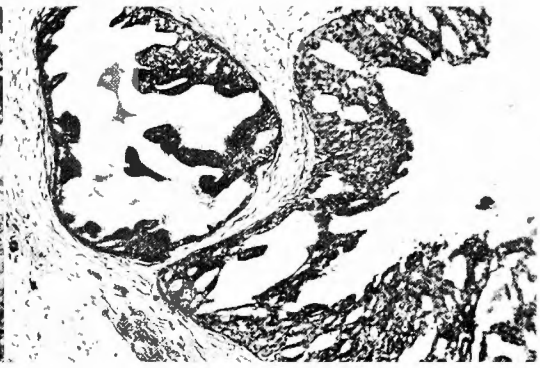

Fig. 9 Duct epithelial hyperplasia

Fig. 10 Fibroadenoma intracanaliculare

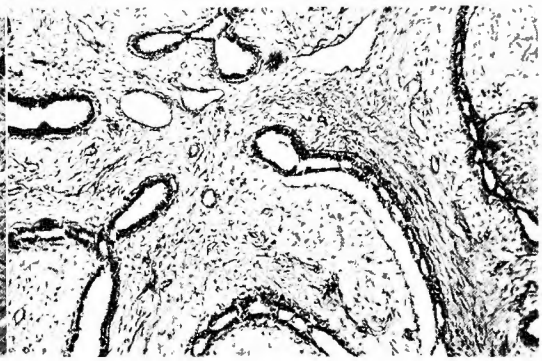

Fig. 11 Fibroadenoma pericanaliculare

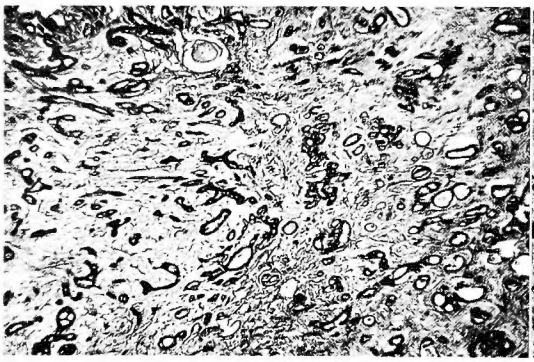

Fig. 12 Formation ef fibroadenoma in mastopathy

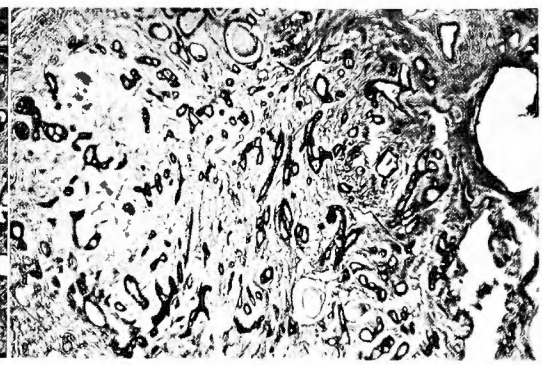

Fig. 13 Formation of fibroadenoma in mastopathy

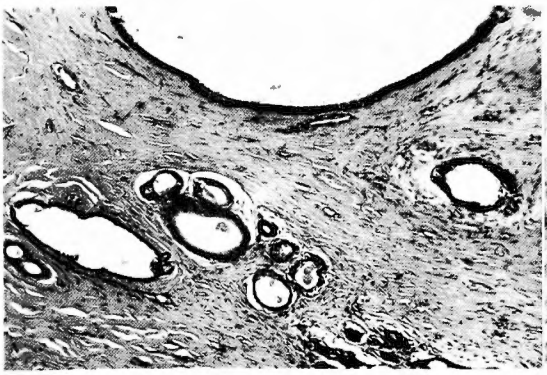

Fig. 14 Apocrine metaplasia in the epithelium included in fibroadenoma

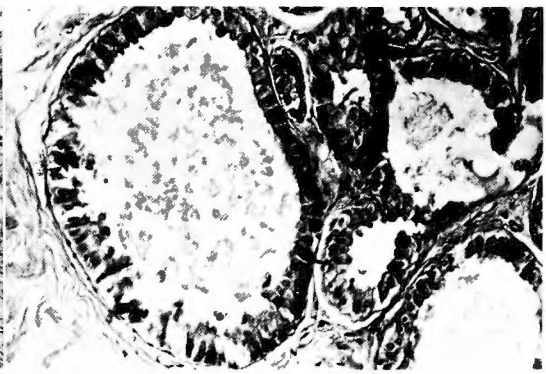

Fig. 15 Apocrine metaplasia in acinar epithelium

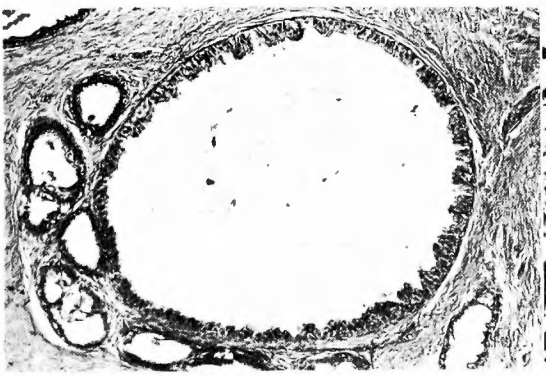

Fig. 16 Apocrine cyst

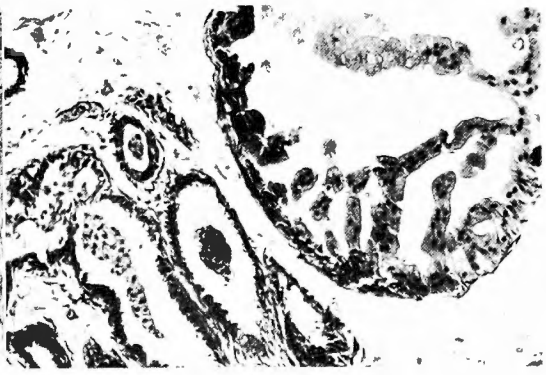

Fig. 17 Apocrine metaplasia of duct epithelium

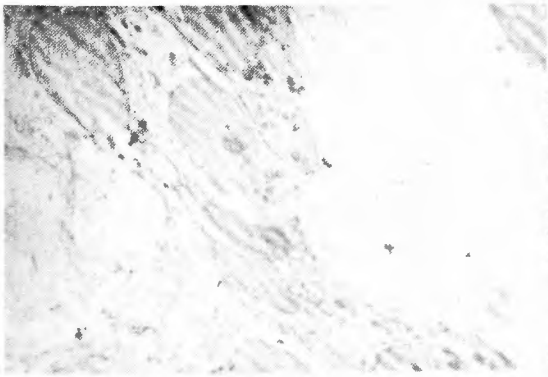

Fig. 18 Electron-microscopic feature of mastopathy, apocrine cells.

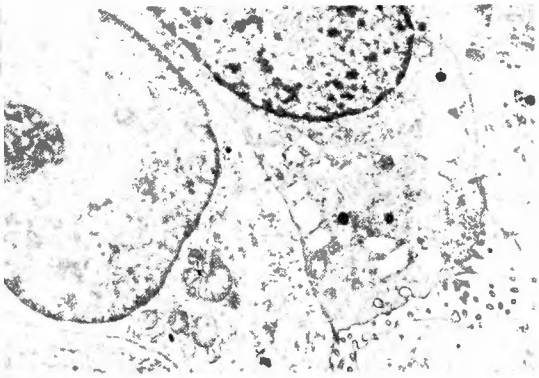

Fig. 19 Electron-microscopic feature of mastopathy, clear cells and dark cells.

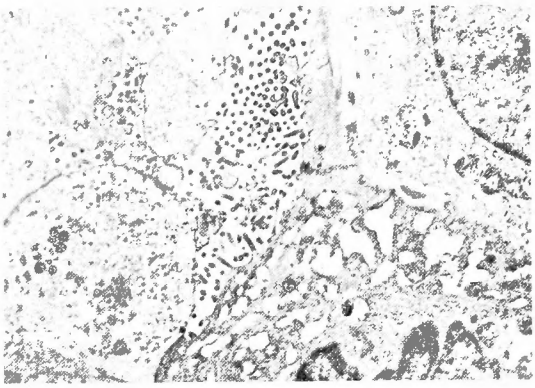

Fig. 20 Electron-microscopic feature of mastopathy, clear cells and dark cell.

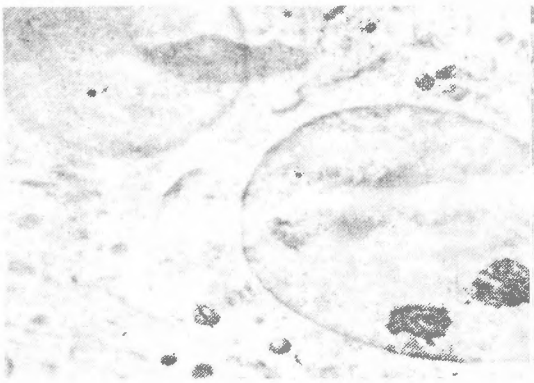

Fig. 21 Electron-microscopic feature of cancer of fhe breast, adenocarcinoma-1. Clear cells.

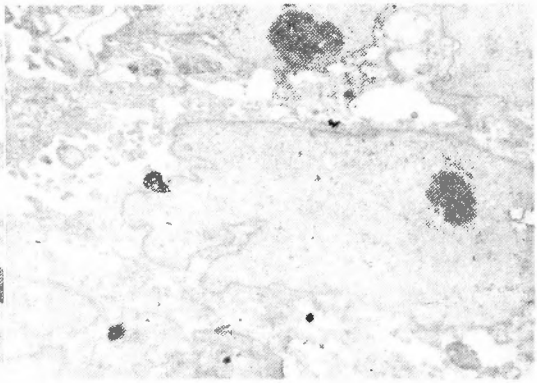

Fig. 22 Electron-microscopic feature of cancer of the breast, adenocarcinoma-2. Dark cells.

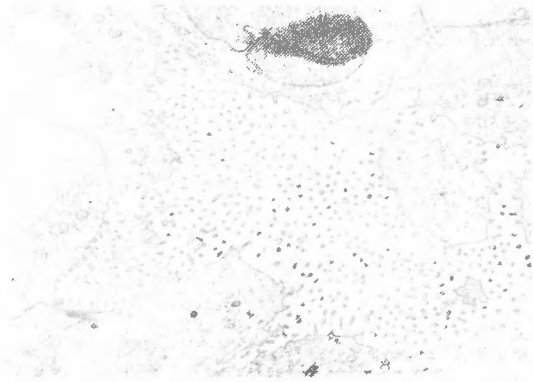

Fig. 23 Electron-microscopic feature of cancer of the dreast, carcinoma simplex-1. Clear cells.

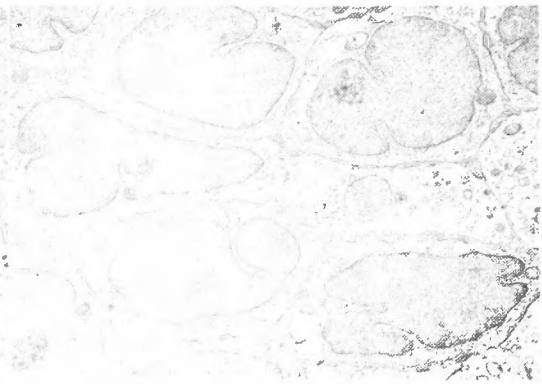

Fig. 24 Electron-microscopic feature of cancer of the breast, carcinoma simplex-2. Dark cells.

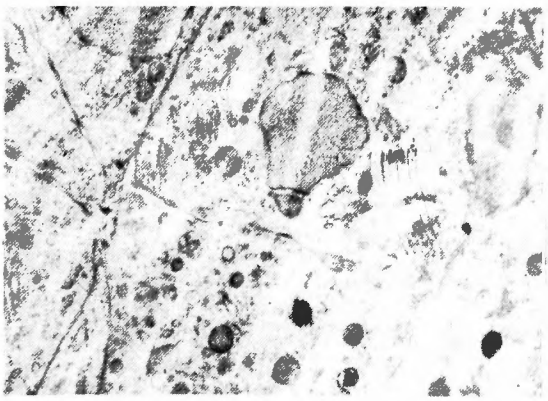

Fig. 25 Electron-microscopic feature of cancer ef the breast, medullary cancer-1. Clear cells.

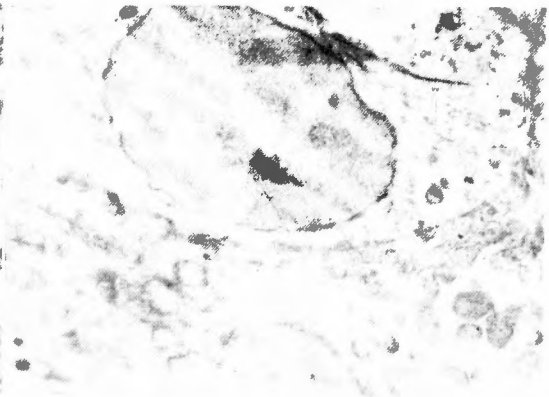

Fig. 26 Electron-microscopic feature of cancer of the breast, medullary cancer-2. Dark cells.

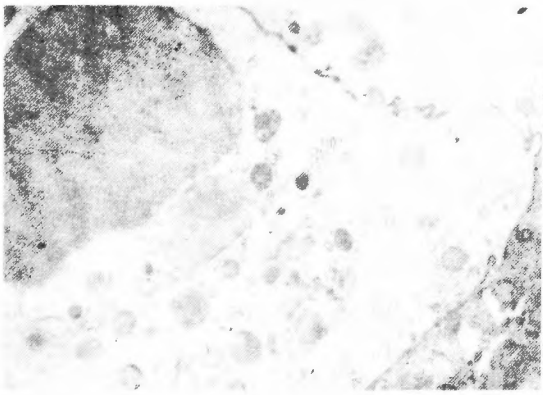

Fig. 27 Electron-microscopic feature of cancer of the breast, gellatinous cancer-1. Clear cell.

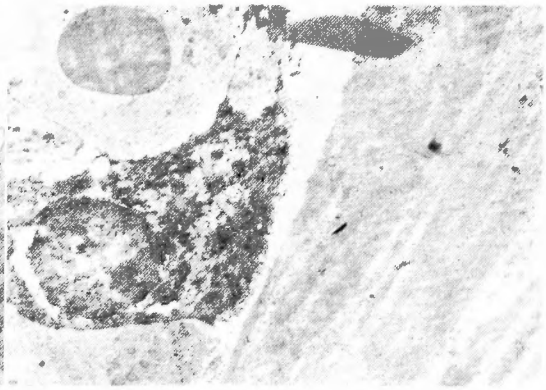

Fig. 28 Electron-microscopic feature of cancer of the breast, gellatinous cancer-1. Dark cell.