Virchows Arch. A Path. Anat. and Histol. 385, 117–124 (1979)

Virchows Archiv A

Case Report

Liposarcoma of the Breast

Case Report and Review of the Literature

Jan Rasmussen and Helle Jensen

Department of Pathology, The Finsen Institute, Strandboulevarden 49, DK-2100 Copenhagen, Denmark

Summary. A case of primary liposarcoma of the breast in a 65-years-old woman is described by light- and electron microscopy. The patient had previously had a cystosarcoma phyllodes removed from the same area.

A review of the literature showed 34 previously published cases of liposarcoma of the breast, which regarding age distribution, histological type and pattern of metastasis corresponded to liposarcomas of the lower limbs.

Key words: Liposarcoma – Breast – Histopathology – Electron microscopy.

Introduction

Primary liposarcoma of the mammary gland (l.m.) is rare. In the period 1862 to 1978 only 34 cases were reported. As far as we know, the ultrastructure of the liposarcoma studied by electron microscopy has previously been described a few times (Flenker, 1976; Johannessen, 1977; Kalderon et al., 1973; Kindblom et al., 1979; Qizilbash, 1976; Scarpelli et al., 1962), only one of which involved a mammary gland liposarcoma (Qizilbash, 1976).

Sarcomas represent from 0.5% to 3% of all primary malignant tumours of the mammary gland, while liposarcomas represent from 0.3% to 13% of all sarcomas of the breast (Adair et al., 1946; Fox, 1934; McGregor, 1960).

In 1969 The World Health Organisation classified liposarcomas in the following five types:

a) Predominantly well-differentiated,
b) Predominantly myxoid (embryonal),
c) Predominantly round-cell,
d) Predominantly pleomorphic (poorly differentiated),
e) Mixed type.

Offprint requests to: Jan Rasmussen, Dept. of Pathology, The Finsen Institute, Strandboulevarden 49, DK-2100 Copenhagen, Denmark

0340-1227/79/0385/0117/$01.60

The purpose of this work is to report the 35th case of l.m. and to describe the cellular components studied by light- and electron microscopy. In addition the previously described cases of l.m. are compared with liposarcomas with other localisations.

Case Report

The patient was a woman born in 1913. In 1966 she had a well-circumscribed, soft tumour with a diameter of 3 cm removed from her left breast. Revision of the histological slides indicated a cystosarcoma phyllodes.

The present tumour in the left breast was discovered by the patient herself in July 1978, 12 years after the first tumour, and was preceded by tenderness in the area, but not by trauma. Mammography showed a 4 cm large, round condensation containing small calcifications.

Histological examination of the present tumour showed liposarcoma, and mastectomy was performed with exstirpation of the axillary lymph nodes. After six months no evidence of recurrence had appeared.

Materials and Methods

The tumour tissue removed from the left breast in 1978 was fixed in formalin and examined by light microscopy. Frozen and paraffin sections were treated with the following stains: haematoxylin-eosin, oil-red-O, Alcian-blue and van Kossa.

Formalin-fixed minced tissue was refixed in Karnovsky's fixative (Karnovsky, 1965), rinsed in Cacodylate-buffer and postfixed in s-collidine buffered osmium tetroxide, dehydrated in alcohol and embedded in EPON 812. Ultrathin sections were cut on a Reichert ultramicrotome OM U3, stained with uranyl acetate and Reynold's lead citrate (Reynolds, 1963) and examined by electron microscopy.

Results

Macroscopy

The tumour, measuring 5 cm in diameter, was poorly defined against the surrounding mammary tissue. The consistency was elastic and the cut surface was yellowish, glistening, gelatinous and slightly elevated. There were no skin pathologies in the mastectomy specimen.

Light Microscopy

The tumour tissue was composed of a myxoid, vascular stroma containing two types of cells with mesenchymal characters, partly stellate and partly spindle-shaped cells with sparse mitosis and, in places, cytoplasmatic vacuoles (Figs. 1 and 2). In the frozen sections the vacuoles were positively stained by oil-red-O, indicating lipids. The myxoid intercellular substance was stained slightly positive with Alcian-blue at pH 2.8 for acid mucopolysaccharides. Isolated mammary glands and smaller ducts were scattered throughout the tumour tissue. Staining

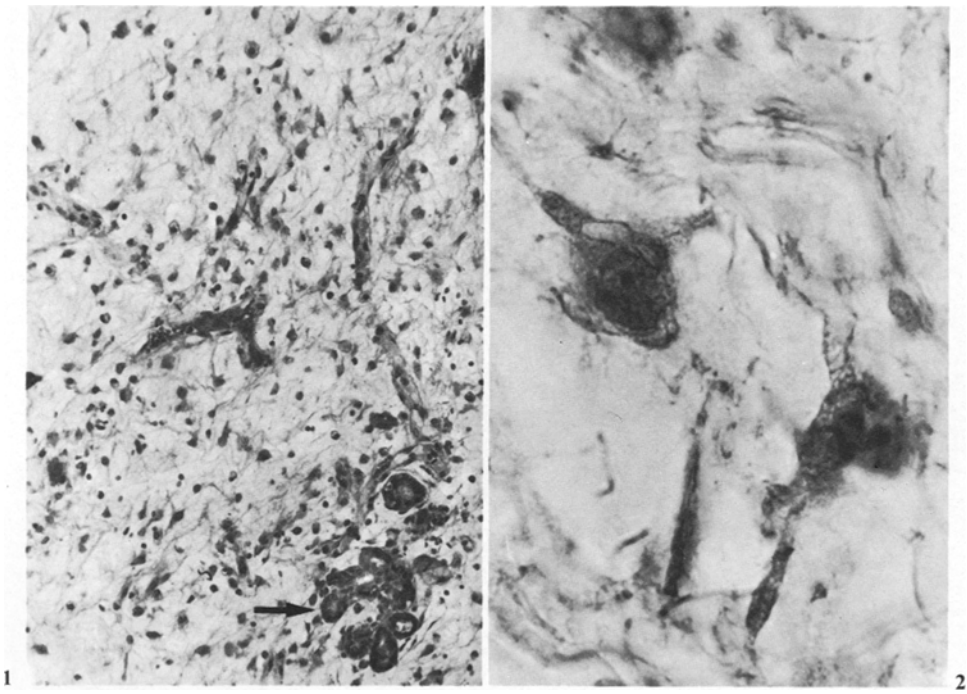

Fig. 1. Liposarcoma with moderate cellularity and a prominently myxoid and vascular stroma. A few breast ducts are visible (*arrow*). Stained by haematoxylin – eosin. Original magnification: ×100

Fig. 2. Lipoblasts of stellate and fibroblast like types. Stained by haematoxylin – eosin. Original magnification: ×1,000

with van Kossa showed solitary small calcifications in the connective tissue.

On the basis of the above findings, the diagnosis of myxoid liposarcoma was made.

Twelve axillary lymph nodes were removed, all without metastasis.

The present tumour tissue was compared with the sections from the cystosarcoma phyllodes which had been removed in 1966. The two tumours were not identical. The cystosarcoma had distinctly long, slightly dilated and, in places, branched epithelial clefts; in some areas the stroma was packed with slightly polymorphical cells and a few mitotic figures were present. In the cystosarcoma there were no liposarcomatous characteristics.

Electron Microscopy

Electron microscopy confirmed the impression given by light microscopy of two types of cells. The first type was fibroblastic (Fig. 3) with smooth to slightly wrinkled nuclear membrane without greater indentations. The chromatin was

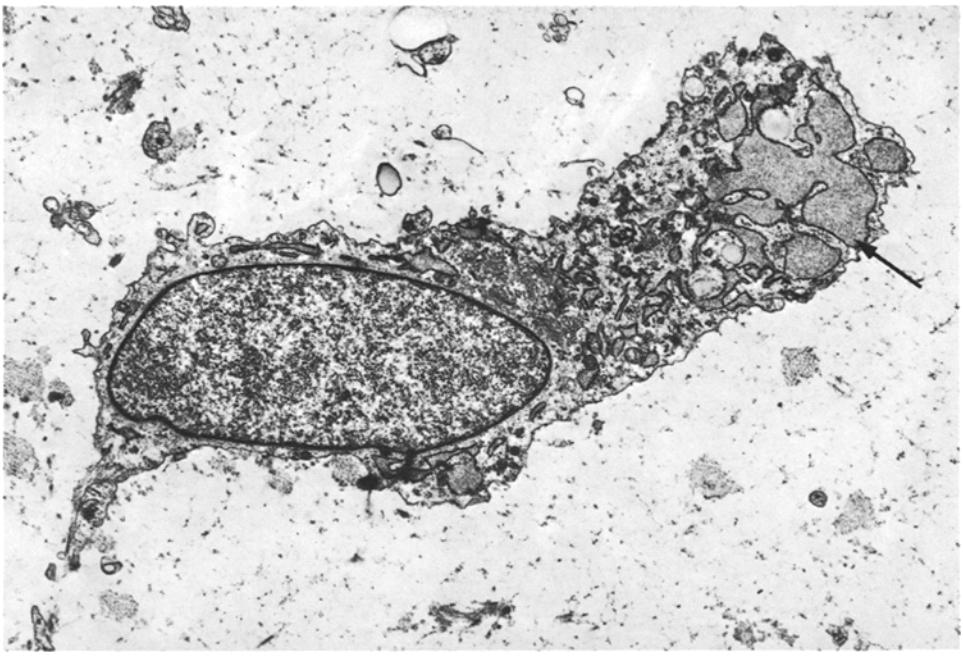

Fig. 3. Fibroblast like cell surrounded by collagen fibers and embedded in fluffy material. The cytoplasm contains a distended rough endoplasmic reticulum (*arrow*). Original magnification: ×5,000

evenly distributed with slightly marginal condensation. There were one or two not prominent nucleoli. The mitochondria in the cytoplasm were poorly preserved because of the primary fixation in formalin. The rough endoplasmatic reticulum (R.E.R.) was prominent and dilated with a matrix of electron-dense material. The Golgi apparatus often appeared prominent. A few small droplets of fat of low electron density and scattered polyribosomes were found. The cells had no lamina basalis or intercellular junctions.

The second type of cell occurred less frequently and was more ovoid or stellate (Fig. 4). Under electron microscopy the nuclei looked like the nuclei of the fibroblastic cell. The cytoplasm contained sparse, poorly preserved mitochondria. Ribosomes and R.E.R. were not prominent, and the Golgi apparatus were visible only in few of the cells. The cytoplasm was dominated by large lipid inclusions with lipid of different saturation. In addition there were small vesicles with a diameter of 700 A.U.

The intercellular substance was electrolucent and contained scattered bundles of collagen fibrils with a periodicity of 600 A.U.

Areas abundant with microcalcification were found, not only intracellular but also, and particularly in the extracellular matrix. The calcifications appeared in electron microscopy as irregular clusters of dark needle-shaped crystals (Fig. 5).

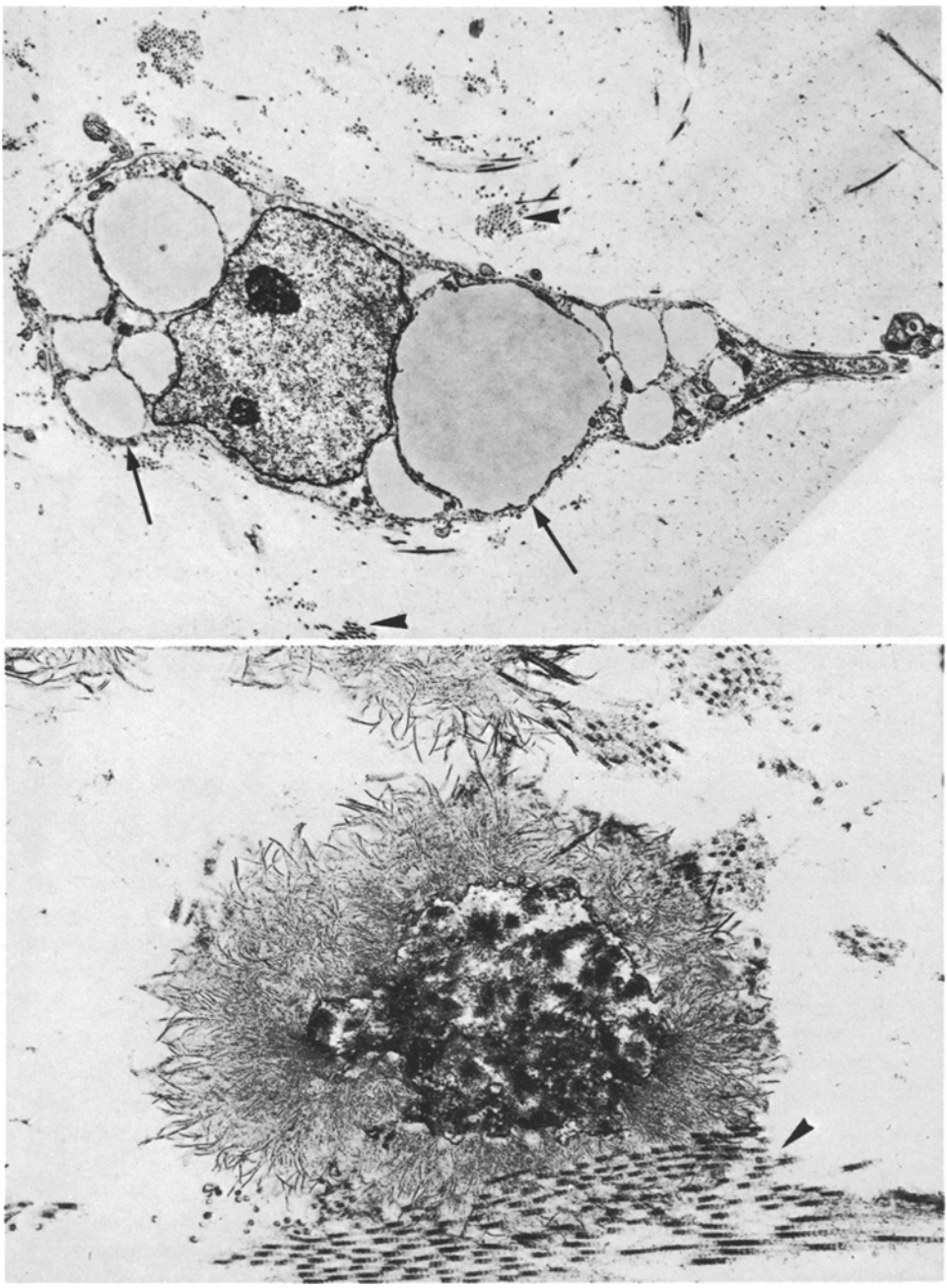

Fig. 4. Multivacuolated tumour cell containing lipid droplets (*arrows*). Collagen fibrils are seen close to the tumour cells (*arrowheads*). Original magnification: ×5,780

Fig. 5. Irregular needle-shaped crystals of calcium surrounding cellular debris. Fibrils of collagen are seen below (*arrowhead*). Original magnification: ×14,200

Discussion and Review of the Literature

A review of the literature revealed 34 previously published cases of l.m. Only one case of liposarcoma was described in a man (Neal, 1933), the remaining 33 having occured in women (Adair et al., 1946; Anderson et al., 1972; Binkert, 1924; Botham et al., 1958; Breckenridge, 1954; Carpanelli et al., 1963; Cuthbertson, 1956; Delage et al., 1904; De Navasquez et al., 1947; Enterline et al., 1960; Fox, 1934; Geschickter, 1943; Hinterberger, 1942; Homes et al., 1962; Hummer et al., 1967; Jackson, 1962; Kristensen et al., 1978; Lifvendahl, 1930; MacFarlane, 1957; McGregor, 1960; Menon et al., 1974; Merkel, 1906; Michalany, 1951; Neumann, 1862; Qizilbash, 1976; Stout et al., 1946; Tedeschi, 1948).

Out of 35 cases the localisation was known in 19; of these, eight were in the right breast, nine in the left, and two cases had bilateral involvement.

The age was mentioned in 26 cases and varied from 16 to 76 years, with an average of 51 years. Kindblom et al. (1975) found the mean age to be 54 years for liposarcomas of the lower extremities and 59 years for the retroperitoneal liposarcomas.

On the basis of text and pictures it was possible in 30 cases to classify the tumours histologically according to WHO (1969). None were well-differentiated, 19 (63%) were myxoid, three (10%) round-cell, five (17%) pleomorphic and three (10%) mixed. The distribution of the major group, the myxoid liposarcomas corresponded to that of the histological types on the lower extremities, while the pleomorphical liposarcoma was the dominant histological type in the retroperitoneal region (Enzinger et al., 1962).

With regard to prognosis, 20 l.m. were followed over a period of three months to 20 years. Six died during this period due to l.m. metastasis. Three had metastasis in the lungs, one had metastasis in the lungs, liver and bones, while one had metastasis only in the bones. In four other cases there was metastasis in the axillary glands. These patients were only followed from less than one month to 11 months, and no deaths occurred during this period. The distribution of metastasis corresponded to the pattern of metastasis for liposarcomas of the lower extremities (Kindblom et al., 1975); however Enzinger et al. (1962) found metastasis in the lymph nodes in only one of 103 patients with liposarcomas.

Five women had previously had benign breast tumours. Of these one had a lipoma, two had adenofibromata, and two had cystosarcoma phyllodes. Recent Danish investigations of cystosarcoma phyllodes have found areas with liposarcomatous characteristics but no development of liposarcomas (Blichert-Toft et al., 1977).

Our patient had 12 years earlier had a cystosarcoma phyllodes removed from the same area in the breast and a development of liposarcoma from remnants of liposarcomatous parts of cystosarcoma phyllodes can not totally be excluded.

The treatment was stated for 32 of the patients. In eight cases only the tumour was excised, in 18 mastectomy were combined with X-rays, and in three cases the sole treatment was actinic. The six patients who died of l.m. had all had a primary mastectomy and one of these had also X-ray treatment.

In previous electron microscopical investigations of liposarcoma (Flenker, 1976; Johannessen, 1977; Kalderon et al., 1973; Kindblom et al., 1979; Qizilbash, 1976; Scarpelli et al., 1962) two types of cells were frequently described: the fibroblastic and the ovoid or stellate. The former was spindle-shaped with large, often folded nuclei, abundant R.E.R., well-developed Golgi apparatus, and a varied number of mitochondria, fine fibrils and free ribosomes were found in the cytoplasm. The cells were found in close association with collagen fibrils. The second cell type was irregular with many cytoplasmatic pseudopodias. R.E.R. was dilated, and there was a varied quantity of small and large droplets of fat in the cytoplasm. The nuclei was large with a folded membrane and even distribution of the chromatin.

The l.m. described in this paper also contained two types of cells, demonstrated by light as well as by electron microscopy. Under light microscopy single calcifications were found, while the electron microscopy revealed areas with many microcalcifications. This could possibly have diagnostic value.

On reviewing the literature we found that in a few cases l.m. had developed in histologically benign tumours of breast such as lipoma, adenofibroma and cystosarcoma phyllodes.

The l.m. and liposarcomas of the lower limbs corresponded with regard to age distribution, prognosis, distribution of histological types and pattern of metastasis, while lower limb liposarcomas differ from the liposarcomas of the retroperitoneal space in the abovementioned respects. The prognosis was found to be most favourable for liposarcomas of the breast and the lower limbs, which might be due to anatomical conditions resulting in a quicker and easier diagnosis in the more superficial localised tumours than in the retroperitoneally localised tumours, which are less accessible and more difficult to remove radically.

Acknowledgements. We are grateful to Mr. Allan Henchel for technical assistance and to Miss Lis Jensen for typing the manuscript.

References

Adair, F.E., Herrmann, J.B.: Sarcoma of the breast. Surgery **19**, 55–73 (1946)

Anderson, D.K., Kafrouni, G.I.: Mammary liposarcoma. Int. Surg. **57**, 67–69 (1972)

Binkert, M.: Fibrolipoadenoma intracanaliculare sarcomatodes xanthomatodes mammae. Frankf. Z. Pathol. **30**, 498–511 (1924)

Blichert-Toft, M., Hansen, J.P.H., Hansen, O.H., Schiødt, T.: Cystosarcoma phyllodes of the breast. Ugeskr. Læg. **139**, 2501–2504 (1977)

Botham, R.J., McDonald, J.R., Clagett, O.T.: Sarcoma of the mammary gland. Surg. Gynec. Obstet. **107**, 55–61 (1958)

Breckenridge, R.L.: Liposarcoma of the breast. Report of a case. Am. J. Clin. Pathol. **24**, 954–956 (1954)

Carpanelli, J.B., Lempel, G., Gatta, C.: Sobre un caso de liposarcoma de glandula mamaria. La Semana méd. **123**, 321–322 (1963)

Cuthbertson, A.N.: Liposarcoma of breast. Postgrad. Med. **20**, 160 (1956)

Delage, J., Massabiau: Les lipomes du sein et de la région mammaire. Rev. Chir. (Paris) **30**, 484–506 (1904)

De Navasquez, S., Horton, R.E.: Liposarcoma of the breast. Guy's Hosp. Rep. **96**, 57–59 (1947)

Enterline, H.T., Culberson, J.D., Rochlin, D.B., Brady, L.W.: Liposarcoma. A clinical and pathological study of 53 cases. Cancer **13**, 932–950 (1960)
Enzinger, F.M., Winslow, D.J.: Liposarcoma. A study of 103 cases. Virchows Arch. Path. Anat. **335**, 367–388 (1962)
Enzinger, F.M., Lattes, R., Torlino, H.: Histological typing of soft tissue tumours, p. 20. Geneva: WHO 1969
Flenker, H.: Myxoid liposarcoma. Light and electron microscopic investigation. Virchows Arch. A Path. Anat. and Histol. **371**, 171–176 (1976)
Fox, S.L.: Sarcoma of the breast. With a report of sixty cases. Ann. Surg. **100**, 401–421 (1934)
Geschickter, C.F.: Diseases of the breast. 2nd ed., p. 386. Philadelphia: J.B. Lippincott Co. 1943
Hinterberger, H.: Zur Kenntnis des Sarkoma phyllodes lipomatodes mammae. Wien. Klin. Wochenschr. **55**, 28–32 (1942)
Homes, R.S., Leis, H.P.: Liposarcoma of the female breast. Review of the literature and report of a case. J. Am. Geriatrics Soc. **10**, 455–459 (1962)
Hummer, C.D., Burkart, T.J.: Liposarcoma of the breast. A case of bilateral involvement. Am. J. Surg. **113**, 558–561 (1967)
Jackson, A.V.: Metastasising liposarcoma of the breast, arising in a fibro-adenoma. J. Pathol. Bacteriol. **83**, 582–584 (1962)
Johannessen, J.V.: Diagnostic electron microscopy. Part 2, pp. 38–39 and pp. 70–71. London: Philips and LKB 1977
Kalderon, A.E., Fethiere, W.: Fine structure of two liposarcomas. Lab. Invest. **28**, 60–69 (1973)
Karnovsky, M.J.: A formaldehyde-glutaraldehyde fixative of high osmolarity for use in electron microscopy. J. Cell Biol. **27**, 137a–138a (1965)
Kindblom, L.G., Angervall, L., Svendsen, P.: Liposarcoma. A clinicopathologic, radiographic and prognostic study. Acta Pathol. Microbiol. Scand. Sect. A Suppl. **253**, 1–71 (1975)
Kindblom, L.G., Säve-Söderbergh, J.: The ultrastructure of liposarcoma. A study of 10 cases. Acta Pathol. Microbiol. Scand. Sect. A **87**, 109–121 (1979)
Kristensen, P.B., Kryger, H.: Liposarcoma of the breast. A case report. Acta Chir. Scand. **144**, 193–196 (1978)
Lifvendahl, R.A.: Liposarcoma of the mammary gland. Surg. Gynecol. Obstet. **50**, 81–84 (1930)
MacFarlane, A.: Liposarcoma of the breast. Br. J. Surg. **45**, 106–107 (1957)
McGregor, J.K.: Liposarcoma of the breast. Case report and review of the literature. Canad. Med. Ass. J. **82**, 781–783 (1960)
Menon, M., van Velthoven, P.C.M.: Liposarcoma of the breast. A case report. Arch. Pathol. **98**, 370–372 (1974)
Merkel, H.: Über ein Pseudolipom der Mamma. Beitr. Path. Anat. **39**, 152–157 (1906)
Michalany, J.: Liposarcoma da glandula mamaria. Hospital (Rio de Janeiro) **39**, 655–661 (1951)
Neal, M.P.: Malignant tumors of the male breast. Arch. Surg. **27**, 451–465 (1933)
Neumann, E.: Beiträge zur Casuistik der Brustdrüsengeschwülste. Virchows Arch. Path. Anat. **24**, 316–328 (1862)
Qizilbash, A.H.: Cystosarcoma phyllodes with liposarcomatous stroma. Am. J. Clin. Pathol. **65**, 321–327 (1976)
Reynolds, E.S.: The use of lead citrate at high pH as an electron-opaque stain in electron microscopy. J. Cell Biol. **17**, 208–212 (1963)
Scarpelli, D.G., Greider, M.H.: A correlative cytochemical and electron microscopic study of a liposarcoma. Cancer **15**, 776–789 (1962)
Stout, A.P., Benanke, M.: Liposarcoma of the female mammary gland. Surg. Gynecol. Obstet. **83**, 216–218 (1946)
Tedeschi, C.G.: Mammary lipoma. Arch. Pathol. **46**, 386–397 (1948)

Received July 26, 1979