Virchows Arch [Pathol Anat] (1983) 400:287–295

Virchows Archiv A

Breast neoplasms containing bone and cartilage

D.V. Spagnolo and K.B. Shilkin
Department of Histopathology, Sir Charles Gairdner Hospital,
The Queen Elizabeth II Medical Centre, Nedlands, Western Australia, 6009

Summary. A total of 307 breast neoplasms and tumour-like conditions were reviewed to assess the frequency with which bone and/or cartilage occurred. Of 90 fibroadenomas, 1 (1.1%) and 2 of 158 breast carcinomas (1.3%) contained bone, one benign mesenchymoma contained cartilage, and one benign "mixed" tumour (pleomorphic adenoma) displayed cartilage and bone. Twenty-two papillomas and 34 cases of gynaecomastia did not contain any cartilage or bone. This study confirms the impression that the occurrence of bone or cartilage in human breast neoplasms is rare. These lesions are briefly discussed with reference to the pertinent literature.

Key words: Breast neoplasms – Cartilage – Bone – Mesenchymoma – Pleomorphic adenoma

Introduction

Breast neoplasms containing cartilage or bone are uncommon and most reported cases have been malignant (Rottino and Willson 1945; Smith and Taylor 1969; Huvos et al. 1973). The recent occurrence of two unusual cases in our department prompted a review of benign and malignant breast neoplasms and some tumourlike conditions to determine the frequency with which cartilage and/or bone occur, and the types of lesions in which they are found.

Materials and methods

The cases for study were retrieved from the Pathology Departments of the Sir Charles Gairdner Hospital at The Queen Elizabeth II Medical Centre, and from the Repatriation General Hospital, Hollywood, Western Australia. The former is a 550-bed adult general hospital, and the latter, of 350 beds, predominantly serves military personnel, veterans and their families.

Offprint requests to: D.V. Spagnolo at the above address

Table 1. Breast neoplasms with cartilage/bone

Diagnosis	Number of cases	Number with cartilage/bone	Incidence cartilage/bone (%)
Fibroadenoma	90	1	1.1
Carcinoma	158	2	1.3
Benign Mesenchymoma	1	1	–
Benign mixed tumour	1	1	–
Papilloma	22	–	–
Gynaecomastia	34	–	–
Phyllodes tumour (malignant)	1	–	–
Sarcoma	0	–	–
Total	307	5	

All cases on file as fibroadenoma, papilloma (including solitary, multiple and florid papillomatosis), gynaecomastia, cystosarcoma phyllodes (phyllodes tumour), sarcoma, and miscellaneous were reviewed. For this study carcinomas diagnosed only in the four year period 1977–1980 were included. Cases of hormonal mastopathy were not considered.

Haematoxylin and eosin-stained (H & E) sections were available in most cases, or were recut and stained when necessary. Step sections of equivocal cases were made. Where necessary, the following special stains were employed: periodic-acid-Schiff with and without diastase digestion (PAS + D), Van Gieson, alcian blue (pH 1.0 and 2.5, with and without hyaluronidase digestion), Masson's trichrome, toluidine blue and Glees and Marsland's reticulin stain.

The average numbers of blocks of lesional breast tissue studied per case were as follows: – fibroadenoma, 2.4; gynaecomastia, 2.5; papilloma, 3.6; carcinoma, 3.7. All lymph nodes from mastectomy specimens were also reviewed but were not included in the above calculation.

Results

A total of 5 cases containing cartilage and/or bone were found. The results are summarized in Table 1. These included one fibroadenoma (incidence 1.1%), two carcinomas (incidence 1.3%), one benign mesenchymoma, and one benign "mixed" tumour similar to the pleomorphic adenoma of salivary glands. One malignant phyllodes tumour did not contain any cartilage or bone and there were no pure breast sarcomas. Clinical details, treatment and follow-up of the 5 cases appear in Table 2.

Pathological findings

Case 1. The specimen was a hard nodule 1.2 cm in diameter with a pale yellow cut surface. Microscopically it was well-circumscribed, surrounded by fibrotic breast tissue, and consisted of extensively hyalinized and calcified hypocellular collagen containing compressed ducts lined by attenuated epithelium. An area of metaplastic lamellar bone, unrelated to any epithelium, was present in the hyaline stroma. The nodule was interpreted as an old hyalinized and calcified fibroadenoma, with focal stromal osseous metaplasia.

Table 2. Summary of clinicopathological details

Case	Age/sex	Clinical features	Diagnosis	Treatment	Follow-up (years)
1.	57F	Two weeks left subareolar mass	Old fibroadenoma with focal ossification	Local excision	N.E.D. ($1\ ^1/_2$)
2.	71F	Tender mass deep to left nipple	I.L.C. with stromal osseous metaplasia	Left M.R.M.	N.E.D. (4)
3.	52F	Two weeks tender left sub-areolar mass	I.D.C. with stromal osseous metaplasia	Left M.R.M.	N.E.D. (4)
4.	80F	One month left L.O.Q. mass	I.D.C., one positive node. Incidental benign mesenchymoma in U.I.Q.	Left M.R.M.	Local scar recurrence, bone metastases ($3\ ^1/_2$)
5.	46F	One year firm right subareaolar mass. Nipple discharge	"Mixed" tumour (pleomorphic adenoma)	Local excision	N.E.D. ($2\ ^1/_2$)

Abbreviations: N.E.D. = no evidence of disease; I.L.C. = infiltrating lobular carcinoma; M.R.M. = modified radical mastectoma; I.D.C. = infiltrating duct carcinoma; L.O.Q. = lower outer quadrant; U.I.Q. = upper inner quadrant

Case 2. The tissue removed for frozen section and the subsequent mastectomy specimen showed in-situ and infiltrating lobular carcinoma. There were no lymph node metastases. There was a central collageneous scar containing an area of haemorrhage demonstrating cholesterol clefts, collections of haemosiderophages, and dystrophic calcification. Osseous metaplasia had occurred around the calcific debris (Fig. 1). The bone did not show any relationship to neoplastic epithelium. This was interpreted as osseous metaplasia occurring in an area of calcification within the tumour stroma.

Case 3. The tissue excised for frozen section and the mastectomy specimen revealed an intraduct and infiltrating carcinoma. A microscopic focus of centrally calcified mature bone had arisen in the fibrous stroma of the neoplasm. It was not directly related to any neoplastic epithelium and there was no evidence such as old haemorrhage, to suggest that dystrophic stromal calcification had been the primary event. The bone formation was interpreted as osseous metaplasia within the stroma of a carcinoma.

Case 4. The frozen section tissue and mastectomy specimens showed a lower outer quadrant, poorly differentiated, infiltrating carcinoma with metastases in one axillary node. In the upper inner quadrant there was an incidental 0.5 cm firm white nodule. It was thinly encapsulated, purely mesenchymal,

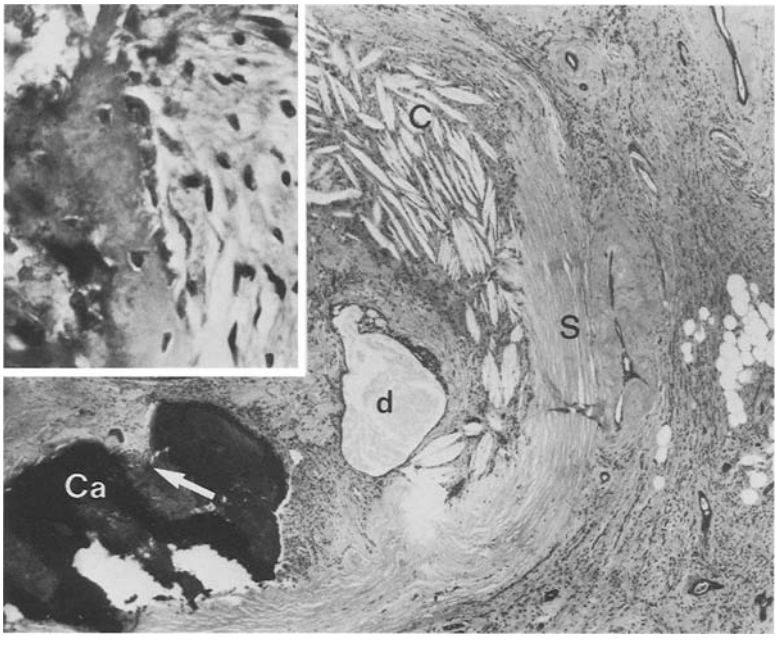

Fig. 1. *Case 2:* Infiltrating small carcinoma cells with residual small ducts (*top*), central hyaline scar (*S*) containing cholesterol clefts (*C*), and bone formation (*white arrow*) in area of dystrophic calcification (*Ca*). *d*= trapped duct showing mild epitheliosis. H & E ×40. *Inset:* Higher power of metaplastic bone formation. H & E ×370

and subdivided by fibrous trabeculae; it consisted mainly of mature adipose tissue and a few islands of mature cartilage. A peripheral cellular and vascular zone was also present composed of bland, ovoid or spindle-shaped cells with vesicular nuclei and scant pale cytoplasm without demonstrable fibrils. In places they were arranged in a perithelial fashion. Numerous mast cells were scattered amongst these cells. This area was rich in reticulin fibres which often separated individual cells, and short, thick collagen bundles were also prominent (Fig. 2). The exact nature of these spindle cells is not certain, but they are possibly related to smooth muscle, pericytic, or glomus cells, This lesion was interpreted as a benign mesenchymoma.

Case 5. The lesion was a well-circumscribed 1.5 cm hard nodule with a glistening, grey cut surface. The tumour was partially enclosed by a collagenous capsule, elsewhere abutting on compressed ductal structures of the surrounding breast parenchyma. The neoplasm was composed of epithelial and mesenchymal elements. There were intimately mixed ductal structures containing PAS-positive secretions, and sheets of epithelium. The ducts were often lined by an inner cuboidal cell layer and an outer layer of larger, pale myoepithelial cells, some of which contained glycogen. Both cell types were intimately admixed in the solid epithelial sheets. Here, the cells gradually spilled over into a prominent basophilic myxochondroid stroma which

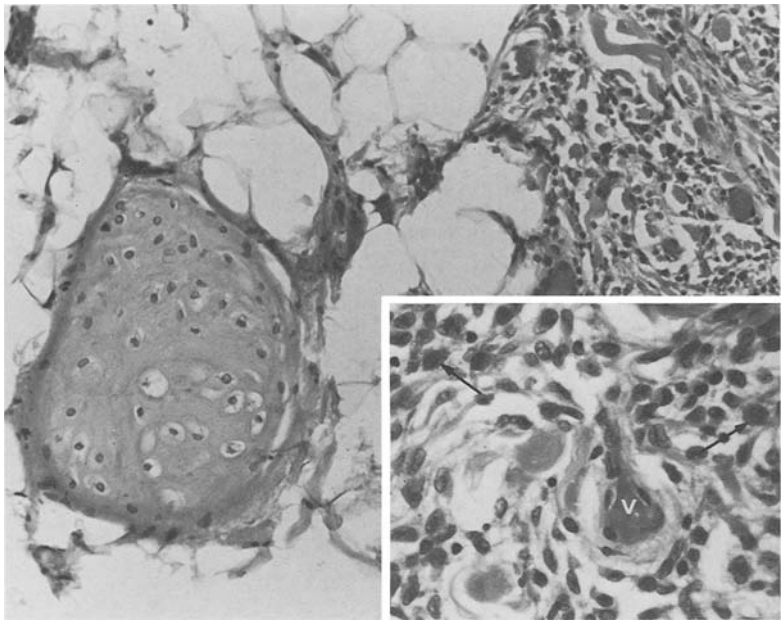

Fig. 2. *Case 4:* Mature cartilage and adipose tissue (*top*) and vascular spindle cell zone (*bottom right*) in benign mesenchymoma. H & E ×150. *Inset:* Bland spindle cells, some concentrically disposed around a central vessel (*v*), and occasional mast cells (*arrows*). H & E ×320

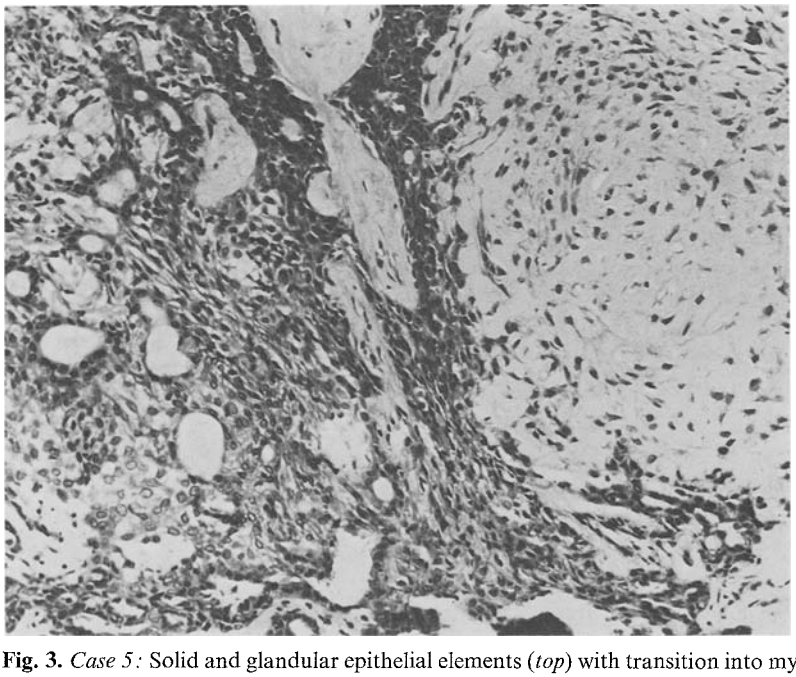

Fig. 3. *Case 5:* Solid and glandular epithelial elements (*top*) with transition into myxochondroid area (*bottom*). Mature cartilage not present in this field. H & E ×150

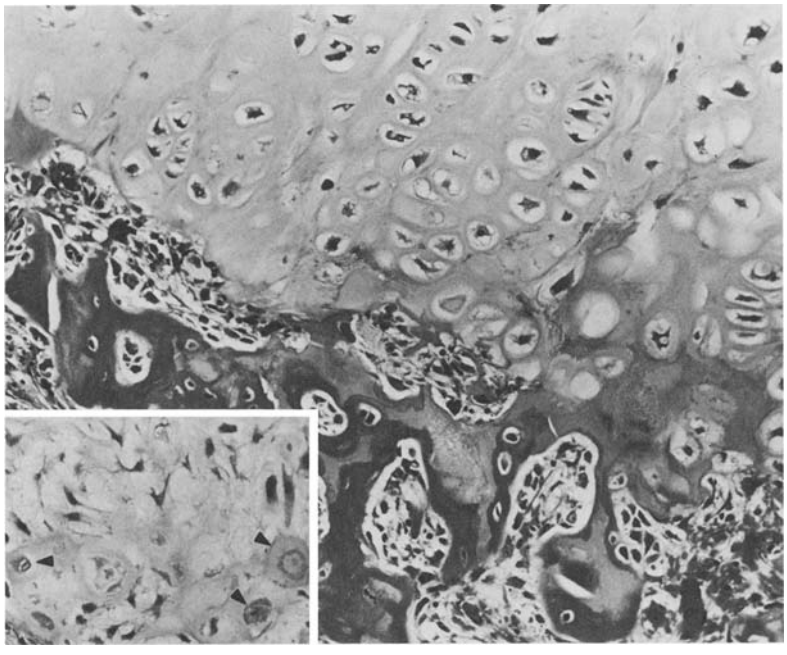

Fig. 4. *Case 5:* Bone arising from mature cartilage by enchondral ossification. H & E ×150. *Inset:* Myxoid spindle cell stroma (*left*) merging with more mature cartilage (*right*) showing cells within lacunae (*arrowheads*) lying in denser chondroid stroma. H & E ×150

was PAS-negative, alcianophilic at pH 1.0 and hyaluronidase resistant (Fig. 3). This stroma gradually merged into large islands of mature hyaline cartilage at the periphery of which there was formation of lamellar bone apparently arising by enchondral ossification (Fig. 4). Remodelling of the bone trabeculae with oseteoblastic and osteoclastic activity was apparent. There was no cellular atypia. The intertrabecular spaces consisted of mature adipose tissue without bone marrow formation.

At the periphery of the nodule, well- defined elastic laminae could be seen in the walls of compressed ducts. In places, this elastic tissue was interrupted by the tumour nodule, and there was evidence that the tumour was growing as a broadbased, polypoid, intraductal lesion which for the most part had obliterated the duct lumen. The nodule was therefore interpreted as a benign "mixed" tumour, possibly arising as an intraductal papilloma, and resembling pleomorphic adenoma of salivary glands.

Discussion

Several neoplasms containing cartilage, bone, or both, have been described in the literature; most have been carcinomas with cartilaginous and/or osseous metaplasia, or sarcomas (Rottino and Willson 1945; Smith and Taylor 1969). The occurrence of cartilage or bone in benign neoplasms is particularly rare (Smith and Taylor 1969; Kaplan and Walts 1977).

Fibroadenomas containing bone or cartilage, whilst relatively common in canine tumours, (Cotchin 1958) are uncommon in human examples. Out of ninety fibroadenomas, we found only one which contained bone (but no cartilage), an incidence of 1.1%. In one review of mammary neoplasms containing bone or cartilage (Smith and Taylor 1969) not one fibroadenoma was found. Willis (1967) cites 4 personally observed cases and alludes to 4 other reported cases. The cartilage and bone are presumed to arise by metaplasia from the spindle cell stroma (Willis 1967). A cellular fibroma with cartilaginous metaplasia and totally devoid of any epithelial elements had also been described (Lawler 1969).

Of the 158 carcinomas which we reviewed, two contained foci of histologically benign metaplastic bone, an incidence of 1.3%; there were no cases containing cartilage. The bone had arisen within the tumour stroma and was not directly related to the neoplastic epithelium. Osseous and cartilaginous metaplasia have been reported within the stroma of many neoplasms, and can arise by (i) ossification in relation to calcific debris (ii) metaplasia in areas of tumour-mucin secretion, or (iii) metaplasia without antecedent stromal changes (Willis 1958). In our case 2, the ossification had arisen within an area of dystrophic calcification in the tumour stroma, while in case 3 the bone had arisen directly, presumably by metaplasia, within the tumour stroma which did not show any antecedent abnormalities. This type of bone formation is to be distinguished from that seen in so-called "metaplastic breast carcinomas" where bone and cartilage apparently arise by direct metaplasia from the epithelial elements of the carcinoma (Smith and Taylor 1969; Huvos et al. 1973; Kahn et al. 1978), and not from connective tissue as seen in our two cases.

Another group of neoplasms which may display cartilage or bone formation are true carcinosarcomas, that is, neoplasms whose constituent elements arise from both epithelium and mesenchyme and are often intimately mixed but do not show transitions from one to the other. According to some, these neoplasms are rare and many are in fact metaplastic carcinomas (Azzopardi 1979), but well-documented cases do exist in the literature (Wayte et al. 1970; Harris and Persaud 1974). An even rarer occurrence is the collision between carcinoma and osteogenic sarcoma or chondrosarcoma (Wester and Finlay-Jones 1960). Other malignant neoplasms which may show bone or cartilage formation include the phyllodes tumour (Smith and Taylor 1969; Ludgate et al. 1977; McDivitt et al. 1968; Pietruszka and Barnes 1978) and pure or mixed sarcomas (Smith and Taylor 1969; Ludgate et al. 1977; Norris and Taylor 1968; Barnes and Pietruszka 1977).

One benign mesenchymoma was found in this study (case 4), an incidental finding in a breast removed for carcinoma which was present in another quadrant. The term "mesenchymoma" was coined by Stout (1948) to describe benign or malignant neoplasms composed of a mixture of two or more different mesenchymal elements. Such cartilage-containing benign breast neoplasms are rare. Synonyms include hamartoma, angiomyolipoma, mixed mesenchymal tumour, and benign chondrolipomatous tumour. Haagensen (1971 a), describes 6 patients under the heading of benign mesenchy-

moma, none of which contained cartilage. Kaplan and Walts (1977) reported one case as a benign chondrolipomatous tumor and tabulated 7 other cases in the literature, the last one of which had been reported in 1909. One of these cases probably was a recurrent chondrosarcoma and should be excluded (Cambria 1887, cited by Kaplan and Walts 1977). These neoplasms should be distinguished from fibroadenomas with cartilaginous metaplasia. In the latter, the epithelial and stromal components both proliferate, while in mesenchymomas, although some normal, probably "trapped" breast ducts may be seen (Kaplan and Walts 1977), there should be no proliferation of epithelial elements. These mesenchymomas are also quite distinct from the benign papillomas showing stromal chondroid or osseous metaplasia (Smith and Taylor 1969).

Our case 5 was a benign "mixed" tumour analogous to the "mixed" tumour (pleomorphic adenoma) of salivary glands, a neoplasm that very rarely occurs in the breast. It contained abundant cartilage and bone, the latter arising by enchondral ossification. There was gradual transition from the epithelial elements into the chondroid areas, beginning as a "spilling" of epithelial cells into a prominent myxoid stroma which progressively assumed a more chondroid appearance and eventually formed hyaline cartilage. The epithelial cells could be traced progressively into the cartilage. A very similar example was reported by Sheth et al. (1978) who also reviewed and tabulated other cases reported since 1968. Similar cases developing from sweat glands in the dermis overlying the breast were described by Haagensen (1971 b).

These neoplasms need to be distinguished from the "mixed tumours" described by Smith and Taylor (1968). Their 9 cases did not show any transition between the epithelial and mesenchymal components, and were regarded as intraductal papillomas with stromal chondroid and osseous metaplasia. Our case 5 did show one point of similarity to these cases. The presence of interrupted ductal structures with elastic laminae at the tumour's periphery suggested that it may have arisen as an intraductal growth; however, the pathogenesis of the mesenchymal elements in our case was not by stromal metaplasia, but as for the "mixed" tumours of salivary glands (Azzopardi and Smith 1959).

This study provides an indication of the frequency of bone and cartilage in benign and malignant neoplasms of the human breast and confirms that this is indeed an uncommon occurrence.

Acknowledgements. The authors thank Miss L. Gardiner and Miss L. Duvnjak for secretarial assistance, and Professor M.N.-I. Walters for reviewing the manuscript.

References

Azzopardi JG,, Smith OD (1959) Salivary tumours and their mucins. J Pathol Bacteriol 77:131–140

Azzopardi JG (1979) Problems in breast pathology. In: Bennington JL (ed) Major problems in pathology, vol 11. WB Saunders, London, Philadelphia, Toronto, pp 373–376

Barnes L, Pietruszka M (1977) Sarcomas of the breast. A clinicopathologic analysis of ten cases. Cancer 40:1577–1585

Cotchin E (1958) Mammary neoplasms of the bitch. J Comp Pathol 68:1–22
Haagensen CD (1971) Diseases of the breast. WB Saunders, Philadelphia, (a) pp 313–315 (b) pp 328–330
Harris M, Persaud V (1974) Carcinosarcoma of the breast. J Pathol 112:99–105
Huvos AG, Lucas JC, Foote FW (1973) Metaplastic breast carcinoma. Rare form of mammary cancer. NY State J Med 73:1078–1082
Kahn LB, Uys CJ, Dale J, Rutherfoord S (1978) Carcinoma of the breast with metaplasia to chondrosarcoma: a light and electron microscopic study. Histopathology 2:93–106
Kaplan L, Walts AE (1977) Benign chondrolipomatous tumour of the human female breast. Arch Pathol Lab Med 101:149–151
Lawler RG (1969) Cartilaginous metaplasia in a breast tumour. J Pathol 97:385–387
Ludgate CM, Anderson TJ, Langlands AO (1977) Sarcoma of the female breast – report of a series of 30 cases. Clin Oncol 3:97–105
McDivitt RW, Stewart FW, Berg JW (1968) Tumors of the Breast. In: Atlas of Tumour Pathology, Second series, Fascicle 2, Armed Forces Institute of Pathology, Washington DC, pp 117–132
Norris HJ, Taylor HB (1968) Sarcoma and related mesenchymal tumours of the breast. Cancer 22:22–28
Pietruszka M, Barnes L (1978) Cystosarcoma phyllodes. A clinicopathologic analysis of 42 cases. Cancer 41:1974–1983
Rottino A, Willson K (1945) Osseous, cartilaginous and mixed tumours of the human breast. Arch Surg 50:184–193
Sheth MT, Hathway D, Petrelli M (1978) Pleomorphic adenoma ("mixed" tumour) of human female breast mimicking carcinoma clinico-radiologically. Cancer 41:659–665
Smith BH, Taylor HB (1969) The occurrence of bone and cartilage in mammary tumours. Am J Clin Pathol 51:610–618
Stout AP (1948) Mesenchymoma, the mixed tumour of mesenchymal derivatives. Ann Surg 127:278–290
Wayte DM, Stewart JB, McKenzie CG (1970) A composite malignant tumour of the elderly female breast. J Clin Pathol 23:414–422
Wester JG, Finlay-Jones LR (1960) Osteogenic sarcoma of the breast. Trop Geographic Med 12:222–228
Willis RA (1958) The borderland of embryology and pathology. Butterworths and Co, London, pp 543–547
Willis RA (1967) Pathology of tumours. 4th edn. Butterworths, London, pp 215

Accepted April 14, 1983