

Sarcomatoid/metaplastic carcinoma of the breast: a clinicopathological study of 12 cases

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Aims: To analyse the clinical and pathological features with long-term follow-up of a series of 12 cases of sarcomatoid carcinoma of the breast.

Methods and results: The cases were selected from the surgical files of the Department of Pathology, University of Edinburgh, between 1977 and 1988. The following clinical parameters were recorded: the age of the patients, size of tumour, presence or absence of lymph node or distant metastases, and patient survival. Pathological assessment included: the type of epithelial and mesenchymal components, the proportion of monophasic to biphasic tumours and the presence of adjacent in-situ carcinoma/atypical epithelial proliferation. The mean age of the patients was 61 years with a median of 64 and range 46–82 years. The mean size of the tumour was 52 mm (range 22–100 mm). None of the patients had distant metastasis at presentation and only one case had local lymph node metastasis which had a carcinomatous appearance. Five women were still alive after a minimum 12-year follow-up period. Four patients died of their disease (three with lung metastasis only and one with lung and bone metastases), one died of carcinoma of the cervix and two patients were lost to follow-up. Pathologically, four cases (33.3%) had no or almost undetectable epithelial structures by light microscopy, i.e. 'monophasic sarco-

matoid carcinoma'. The remaining cases revealed varying proportions of both epithelial and mesenchymal elements, i.e. 'biphasic sarcomatoid carcinoma'. Of the epithelial component, six (50%) tumours had predominantly carcinoma of no special type, one lobular and one tubular carcinoma. The mesenchymal component was fibromatosis/nodular fasciitis-like, malignant fibrous histiocytoma-like (MFH), osteosarcoma-like and fibrosarcoma-like in five (42%), four (33%), two (17%) and one (8%) tumours, respectively. In 3/4 monophasic tumours, the mesenchymal component was of a low-grade fibromatosis/nodular fasciitis type. In 6/12 (50%) of the cases there was associated in-situ atypical epithelial proliferation (five ductal carcinoma in situ (DCIS) and one atypical ductal hyperplasia).

Conclusions: From this small series it appears that sarcomatoid carcinoma is an uncommon tumour, which is large in size and tends to lack local or distant metastasis at presentation. Pathologists should be alert to the presence of the bland monophasic sarcomatoid carcinoma which has a pure mesenchymal appearance on light microscopy, but epithelial components demonstrated by cytokeratin immunohistochemistry. These showed metastases on long-term follow-up, similar to other histological patterns of sarcomatoid carcinoma.

Keywords: breast, sarcomatoid carcinoma, carcinosarcoma, metaplastic carcinoma

Introduction

Tumours showing both carcinomatous and sarcomatous features are very uncommon and occur in various anatomical sites.^{1–9} Their wide range of microscopic

appearances have resulted in a variety of names such as 'carcinosarcoma',^{8–10} 'carcinoma with pseudo-sarcomatous stroma',^{11,12} 'spindle cell carcinoma',^{13–16} and in the female genital tract 'malignant mixed mullerian tumour'.⁵ In the breast, this tumour is often called 'metaplastic carcinoma'.^{1,17,18} In spite of the differences in terminology in different organ systems, the evidence suggests that these are similar tumours

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developing through a peculiar phenotypic transformation of carcinoma cells into sarcoma.^{16,19–22} This theory is supported by the finding of morphological 'transition' from carcinoma to sarcoma, the detection of epithelial features in sarcomatous cells by electron microscopy or immunohistochemistry, and the predominance of epithelium in the metastases.^{1,16,19,20,22} In the breast, the most popular theory regarding the histogenesis of the sarcomatous component is through transformation of myoepithelial cells.^{1,18,23–25} In support of this is the finding of a cuff-like proliferation of neoplastic myoepithelial cells around residual breast ducts in some tumours.^{1,25} An alternative theory is that malignant epithelial cells undergo myofibroblastic metaplasia.^{26,27} We prefer the term 'sarcomatoid carcinoma' rather than metaplastic carcinoma when referring to these tumours.^{1,19}

Classic sarcomatoid carcinoma is a tumour with both epithelial and mesenchymal components, hence the term biphasic sarcomatoid carcinoma.¹ Several reports have described a monophasic variant which appears purely mesenchymal on light microscopy, but which has an epithelial component which can be demonstrated by immunohistochemistry for cytokeratins.^{1,24,28,29} The mesenchymal component can vary between a pleomorphic sarcomatous appearance and a bland appearance which may mimic nodular fasciitis, fibromatosis or a granulation tissue reaction.^{28–30} In a series reported by Gobbi *et al.*, monophasic sarcomatoid carcinoma with a fibromatosis-like appearance has no regional or distant metastasis but a local recurrence rate of 26.7% within a period of 5–72 months follow-up period.²⁹

In the Department of Pathology, Edinburgh University, we obtained 12 cases of sarcomatoid carcinoma of the breast diagnosed between 1978 and 1988. The aim of this study was to analyse the clinical and pathological features of these tumours, determining the epithelial and mesenchymal components, the percentage of monophasic sarcomatoid carcinoma and the status of the adjacent breast tissue. These parameters were examined in the light of a relatively very long (12–22 years) follow-up period.

Materials and methods

CLINICAL DATA

The following parameters were recorded: the age of the patients, size of tumour at presentation, presence or absence of lymph node or distant metastases, treatment modality, and patient survival.

PATHOLOGICAL ASSESSMENT

The files of the Pathology Department, Edinburgh University, were searched from January 1977 to December 1988 for all cases diagnosed as metaplastic carcinoma or carcinosarcoma of the breast (these terms are the most commonly used codes in the department for such tumours). The reviewed material included breast biopsies and mastectomy specimens with axillary node samples or clearances. These were Bouin or formalin fixed and stained with haematoxylin and eosin. Only cases that fulfilled the criteria for sarcomatoid carcinoma were selected. These cases were either biphasic or monophasic. The biphasic tumours had both epithelial and mesenchymal components on light microscopy. The monophasic had a purely spindle mesenchymal appearance on light microscopy but had epithelial components demonstrated by immunohistochemistry for low molecular weight cytokeratins (see Figure 1).

Assessment included the following: the type of the epithelial and stromal components, the proportion of monophasic cases, the presence of adjacent atypical hyperplasia or DCIS, the presence of cystic change, haemorrhage or necrosis.

Results

CLINICAL INFORMATION

The mean age of the patients was 61 years with a median of 64 and range 46–82 years (Table 1). Eight cases were in the left breast and four in the right breast.

The mean size of the tumour was 52 mm (range 22–100 mm) and all were relatively well circumscribed. One woman had a metastatic carcinoma in the axillary lymph node at presentation.

Biphasic:

Classic appearance showing variable combinations of epithelial and mesenchymal tissue

Monophasic:

Bland-looking—mimics fibromatosis or nodular fasciitis. Epithelial foci+/-, mitoses++, Vimentin and CK+

Malignant-looking – mimics fibrosarcoma or malignant fibrous histiocytoma. Epithelial foci+/-, mitoses+++. Vimentin and CK+

Pleomorphic—mimics malignant fibrous histiocytoma, osteo, chondro, rhabdomyosarcoma. Epithelial foci+/-, mitoses++, Vimentin and CK+

Figure 1. Sarcomatoid carcinoma of the breast.

Table 1. The clinicopathological features of 12 cases of sarcomatoid carcinoma of the breast

Case	Age (years)	Site/size (mm)	In situ	Epithelial pattern	Mesenchymal pattern	Lymph node metastases	Distant metastases	Secondary features	Treatment	Follow-up
1 (b)	48	L 45	DCIS	NST (foci of squamous & clear cell)	MIFH	No	No	Necrosis	Mastectomy	Alive
2 (b)	66	R 50	DCIS	Tubular	MIFH	No	No	Haemorrhage	Mastectomy, axillary clearance	Alive
3 (b)	54	L 30	DCIS	NST	Fibrosarcoma	No	No	Necrosis	Mastectomy	Died/lung metastasis 1 year
4 (b)	49	R 58	-	NST (foci of squamous)	Fibromatosis/nodular fasciitis	No	No	-	Mastectomy, axillary clearance	Alive
5 (b)	54	L 50	DCIS	NST	MIFH	No	No	-	Mastectomy	Died (ca. cervix) 3 years
6 (b)	82	R 60	-	NST (foci of apocrine)	Osteosarcoma	No	No	Haemorrhage Necrosis	Mastectomy, axillary clearance	Alive
7 (b)	68	L 100	-	NST	MIFH	No	No	Necrosis	Mastectomy, axillary clearance	Lost to follow-up
8 (b)	61	L 50	-	Lobular	Fibromatosis/nodular fasciitis	No	No	-	Mastectomy	Lost to follow-up
9 (m)	46	L 58	-	-	Fibromatosis/nodular fasciitis	No	No	Cystic change	Mastectomy	Alive/R. papillary DCIS
10 (m)	63	R 65	-	-	Osteosarcoma	No	No	Haemorrhage Necrosis	Mastectomy	Died/Lung/Bone metastasis 2 years
11 (m)	69	L 40	-	-	Fibromatosis/nodular fasciitis	Yes	No	Haemorrhage	Mastectomy	Died/Lung/Bone metastasis 5 years
12 (m)	56	L 22	ADH	-	Fibromatosis/nodular fasciitis	No	No	-	Wide local node sample	Died/Lung metastasis 7 years

b, Biphasic; m, monophasic.

Eleven patients were treated by mastectomy, five of these were combined with axillary node clearance and one patient had wide local excision with axillary node sample.

Five women were still alive 12–22 years after presentation, four died of their disease (three with lung metastases only and one with lung and bone metastases), and one died of carcinoma of the cervix. Two patients were lost to follow-up.

PATHOLOGICAL FEATURES

Eight women (66.6%) had biphasic tumours and four (33.3%) had monophasic tumours.

The mesenchymal component in these 12 cases was as follows: fibromatosis/nodular fasciitis-like ($n = 5$) (Figure 2), malignant fibrous histiocytoma-like ($n = 4$) (Figure 3), osteo/chondrosarcoma ($n = 2$) (Figure 4), and fibrosarcoma ($n = 1$). Coexisting DCIS was found in five cases (41%) and atypical ductal hyperplasia in one case (8%). Of the secondary features identified, five cases showed areas of haemorrhage, three focal necrosis and two cystic changes.

In the biphasic group, the epithelial component was as follows: carcinoma of no special type (NST) ($n = 6$), lobular carcinoma ($n = 1$) (Figure 5a,b) and tubular carcinoma ($n = 1$). Three out of the six cases with carcinoma of NST showed small foci of specialized differentiation: one had squamous, one had both squamous and clear cell and one had apocrine change.

In the monophasic group, 3/4 tumours were of the fibromatosis/nodular fasciitis pattern and one was osteo/chondrosarcoma-like.

CLINICOPATHOLOGICAL CORRELATION

Eleven women had mastectomies (five with axillary lymph node clearances) and one had a wide local excision with axillary node sample.

Four patients died from their disease 1 year, 2 years, 3 years and 7 years following diagnosis (average survival of 3 years and 7 months). The tumour sizes of these four patients averaged 39 mm. Three out of these four women had monophasic tumour (two bland fibromatosis-like appearance and one osteo/chondrosarcoma-like) and the fourth woman had a biphasic tumour (an NST epithelial component with a fibrosarcoma-like mesenchymal element).

Discussion

In this study we have found that the clinical presentation and survival of women with sarcomatoid

carcinoma is comparable to previously reported series.^{1,17,18,24,26,31} The mean age of women in our series was 61 years (range 46–82 years) and their tumours were relatively large and well circumscribed. It has been previously suggested that the size at initial excision is one of the best predictors of survival.¹⁷ However, in this study the mean tumour size of those who died of their disease was smaller (39 mm) compared with the overall average size (52 mm).

Only one woman had a local lymph node involvement by carcinoma at presentation, while the rest lacked local or distant metastasis. This confirms previous evidence that suggests that the majority of sarcomatoid carcinomas have not metastasized at presentation despite their large size.¹⁷

Our series includes significantly longer term follow-up than previous reports, with patients monitored between 12 and 22 years after diagnosis. However, the overall survival in our series is consistent with previous reports, with 4/12 (33.3%) dying of their disease. Most published data on metastases of sarcomatoid carcinoma have shown haematogenous rather than lymphatic spread, in keeping with the sarcomatous phenotype.^{1,11,17,18,24,25,32,33} In this series, four patients developed haematogenous metastases (lung and bone) resulting in their death. One of these patients had carcinoma in a lymph node at presentation.

In view of the various names given to this tumour, the literature regarding the epithelial component differs according to the term used. Those reports describing metaplastic carcinoma have identified a significant squamous component.^{1,17,18} However, those referring to carcinosarcoma have shown a predominant carcinomatous component of NST.^{1,17,18,24,26} In this study the commonest epithelial element was carcinoma of NST. This occurred in six cases (50%) and was associated with smaller foci of squamous, clear cell or apocrine metaplasia. In addition, we identified one case with lobular carcinoma (Figure 5a,b,c), which to our knowledge has not been described previously. This is important for pathologists, as lobular carcinoma cells are usually uniform and small in size and therefore could easily be obscured by the mesenchymal component.

In-situ ductal carcinoma has been reported in up to 25% of mammary sarcomatoid carcinoma²³ and up to 66% of cases of ordinary invasive breast carcinoma of no special type.³⁴ In this study 50% of our cases showed DCIS or atypical epithelial proliferation. This further supports the epithelial origin of these tumours.

A recent report has identified a relationship between metaplastic carcinoma of the breast and complex

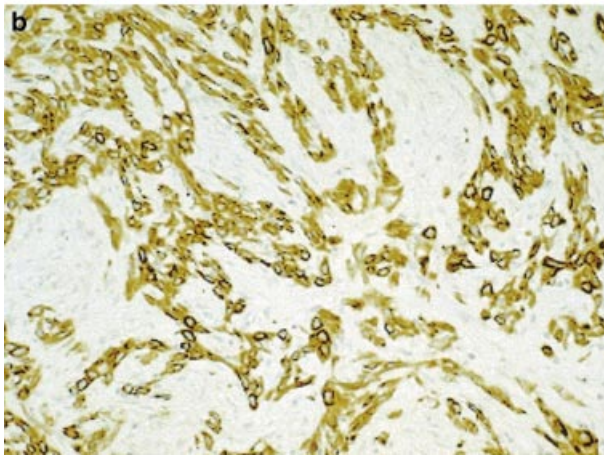
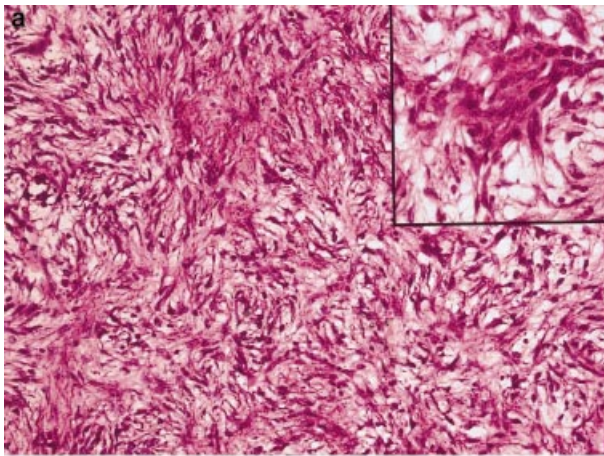


Figure 2. Monophasic sarcomatoid carcinoma. **a**, Nodular fasciitis-like appearance. **b**, Cytokeratin staining highlights the extensive epithelial component.

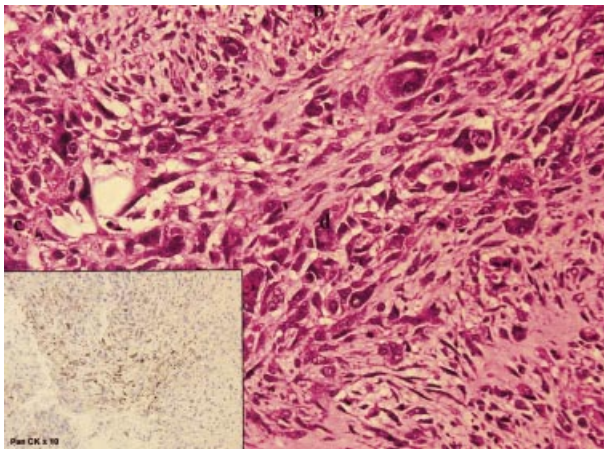


Figure 3. Monophasic sarcomatoid carcinoma: Malignant fibrous histiocytoma-like appearance. Inset: cyokeratin staining highlights the epithelial component.

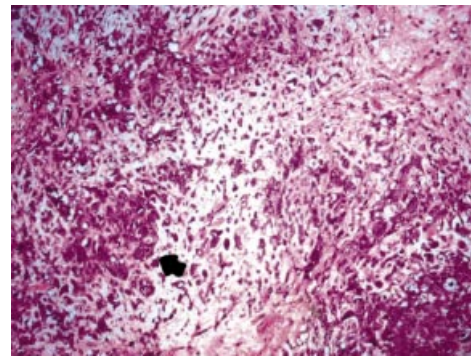


Figure 4. Biphasic sarcomatoid carcinoma: a mixture of undifferentiated carcinoma (arrow) with an osteo/chondrosarcomatous component.

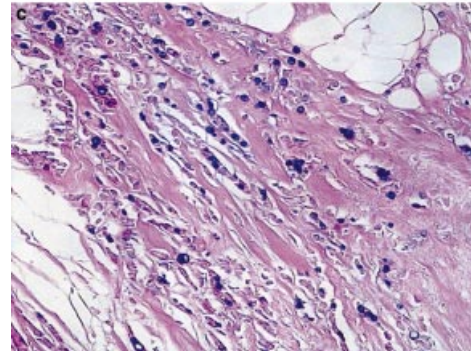
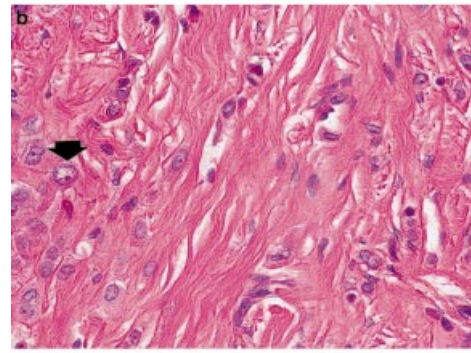
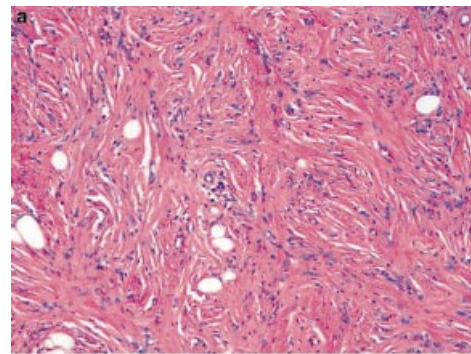


Figure 5. Biphasic sarcomatoid carcinoma. **a**, Storiform pattern of the mesenchymal component. **b**, Lobular carcinomatous epithelial element (see arrow). **c**, Mucin stain (AB/PAS) highlights the intracytoplasmic mucin within lobular carcinoma.

sclerosing lesions/radial scars.³⁵ However, in the latter study four out of five cases were low-grade adeno-squamous carcinomas. In our series none of the cases of sarcomatoid carcinoma was associated with radial scars.

In this report we have identified eight cases (66.6%) of biphasic sarcomatoid carcinoma compared with four cases (33.3%) of monophasic sarcomatoid carcinoma. The percentage of monophasic sarcomatoid carcinoma in this series is comparable to those previously reported.^{1,23,24,28,32} In the largest series of 100 cases of sarcomatoid carcinoma, described by Wargotz *et al.* only 17 cases were of monophasic sarcomatoid carcinoma.²⁴ However, in the series reported by Gobbi *et al.*²⁹ 10 out of 30 cases (33%) of metaplastic breast carcinoma were monophasic.

The diagnosis of sarcomatoid carcinoma should be considered in the differential diagnosis of any biphasic or monophasic sarcomatoid tumour of the breast.³⁶ The main differential diagnosis of these tumours includes phyllodes tumours and primary breast sarcomas.³⁶ The problem in the pathological diagnosis of sarcomatoid carcinomas lies with the monophasic variant. Diagnosis can be established with the use immunohistochemistry for low molecular weight keratins, which can identify epithelial islands with a deceptive spindle morphology. Epithelial membrane antigen is usually confined to clearly recognizable epithelial structures. Vimentin is expressed in both the epithelial and sarcoma-like components.^{19,29}

The question remains whether the histological patterns of sarcomatoid carcinoma have an influence on patients' survival. The differences in survival among the various subgroups of sarcomatoid carcinoma are said to be minor.^{11,17,24} From our small series, patient survival appeared to be independent of pattern. However, it should be noted that our two cases of monophasic sarcomatoid carcinoma with a bland fibromatosis-like appearance behaved aggressively, resulting in the patients' death 5 and 7 years after diagnosis. This is unlike those that have been reported by Gobbi *et al.*,²⁹ where metaplastic carcinoma of the breast with a fibromatosis-like picture has demonstrated no regional or distant metastasis 5–88 months following diagnosis. It may well be that tumour metastasis occurs later in the natural history of these particular tumours.

In summary, from this small series it appears that sarcomatoid carcinoma is a rare pattern of breast cancer (12 cases in a 10-year period). Although the lesion is relatively large in size, it tends to lack local or distant metastasis at presentation. The epithelial

component of sarcomatoid carcinoma can include lobular carcinoma. Lastly, the bland monophasic sarcomatoid carcinoma with the fibromatosis/nodular fasciitis-like appearance metastasizes similar to other sarcomatoid carcinomas.

References

1. Foschini MP, Dina RE, Eusebi V. Sarcomatoid neoplasms of the breast: proposed definitions for biphasic and monophasic sarcomatoid mammary carcinomas. *Sem. Diagn. Pathol.* 1993; **10**: 128–136.
2. Nappi O, Wick MR. Sarcomatoid neoplasms of the respiratory tract. *Sem. Diagn. Pathol.* 1993; **10**: 137–147.
3. Mark RW, Fitzgibbon J, Swanson PE. Cutaneous sarcomas and sarcomatoid neoplasms of the skin. *Sem. Diagn. Pathol.* 1993; **10**: 148–158.
4. Lampertico P. Anaplastic (sarcomatoid) carcinoma of the thyroid gland. *Sem. Diagn. Pathol.* 1993; **10**: 159–168.
5. Robetto P, Colombi. Sarcomatoid carcinomas of the female genital tract (malignant mixed mullerian tumors). *Sem. Diagn. Pathol.* 1993; **10**: 169–175.
6. Iezzoni JC, Mills SE. Sarcomatoid carcinomas (carcinosarcomas) of the gastrointestinal tract: a review. *Sem. Diagn. Pathol.* 1993; **10**: 176–187.
7. Reuter VE. Sarcomatoid lesions of the urogenital tract. *Sem. Diagn. Pathol.* 1993; **10**: 188–201.
8. Bleiweiss IJ, Huvos AG, Lara J, Strong EW. Carcinosarcoma of the submandibular salivary gland: Immunohistochemical findings. *Cancer* 1992; **69**: 2031–2035.
9. Siegal A, Freund U, Gal R. Carcinosarcoma of the stomach. *Histopathology* 1988; **13**: 350–353.
10. Weidner NZ. Carcinosarcoma of the colon: Report of a unique case with light and immunohistochemical studies. *Cancer* 1986; **58**: 1126–1130.
11. Kaufman MW, Marti JR, Gallager HS, Hoehn JL. Carcinoma of the breast with pseudosarcomatous metaplasia. *Cancer* 1984; **53**: 1908–1917.
12. Steeper TA, Pisciole F, Rosai J. Squamous cell carcinoma with sarcoma-like stroma of the female genital tract: clinicopathological study of four cases. *Cancer* 1983; **52**: 890–898.
13. Evans HL, Smith JL. Spindle cell squamous carcinoma and sarcoma-like tumor of the skin: A comparative study of 38 cases. *Cancer* 1980; **45**: 2687–2697.
14. Ellis GL, Langloss JM, Heffner DK, Hyams VJ. Spindle-cell carcinoma of the aerodigestive tract: An immunohistochemical analysis of 21 cases. *Am. J. Surg. Pathol.* 1987; **11**: 335–342.
15. Matsui K, Kitagawa M. Spindle cell carcinoma of the lung. A clinicopathologic study of three cases. *Cancer* 1991; **67**: 2361–2367.
16. Battifora H. Spindle cell carcinoma: Ultrastructural evidence of squamous origin and collagen production by the tumor cells. *Cancer* 1976; **37**: 2275–2282.
17. Oberman HA. Metaplastic carcinoma of the breast: A clinicopathologic study of 29 patients. *Am. J. Surg. Pathol.* 1987; **11**: 918–929.
18. Wargotz ES, Norris HJ. Metaplastic carcinomas of the breast. III. Carcinosarcomas. *Cancer* 1989; **64**: 1490–1499.
19. Guarino M, Tricomi P, Giordano F, Cristofori E. Sarcomatoid carcinomas: pathological and histogenetic considerations. *Pathology* 1996; **28**: 298–300.

20. George E, Manivel JC, Dehner LP *et al*. Malignant mixed mullerian tumours: an immunohistochemical study of 47 cases with histogenetic considerations and clinical correlation. *Hum. Pathol.* 1991; **22**: 215–223.
21. Fromowitz FB, Bard RH, Koss L. The epithelial origin of a malignant mesodermal mixed tumor of the bladder: report of a case with long-term survival. *J. Urol.* 1984; **132**: 978–981.
22. Guarino. Epithelial-to-mesenchymal change of differentiation. From embryogenetic mechanism to pathological patterns. *Histopathology* 1995; **10**: 171–184.
23. Wargotz ES, Norris HJ. Metaplastic carcinomas of the breast. I. Matrix-producing carcinoma. *Hum. Pathol.* 1989; **20**: 628–635.
24. Wargotz ES, Deos PH, Norris HJ. Metaplastic carcinomas of the breast. II. Spindle cell carcinoma. *Hum. Pathol.* 1989; **20**: 732–740.
25. Sapino A, Papotti M, SanFilippo B, Gugliotti P, Bussolati G. Tumour types derived from epithelial and myoepithelial cell lines of R3230AC rat mammary carcinoma. *Cancer Res.* 1992; **52**: 1553–1560.
26. Ferrara G. Sarcomatoid carcinoma of the breast: pathology of four cases. *Breast Dis.* 1995; **8**: 283–294.
27. Balercia G, Bhan AK, Dickersin GR. Sarcomatoid carcinoma: an ultrastructural study with light microscopic and immunohistochemical correlation of 10 cases from various anatomic sites. *Ultrastructural Pathol.* 1995; **19**: 249–263.
28. Ostrowski JL, Horgan K, Krausz T, Quinn CM. Monophasic sarcomatoid carcinoma of the breast. *Histopathology* 1998; **32**: 184–186.
29. Gobbi H, Simpson JF, Borowsky A, Jensen R, Page DL. Metaplastic breast tumours with a dominant fibromatosis-like phenotype have a high risk of local recurrence. *Cancer* 1999; **85**: 2170–2182.
30. Weidner N. Malignant breast lesions that may mimic benign tumours. *Sem. Diagn. Pathol.* 1995; **12**: 2–13.
31. Rayson D, Adjei AA, Suman VJ, Wold LE, Ingle JN. Metaplastic breast cancer: prognosis and response to systemic therapy. *Annal. Oncol.* 1999; **10**: 413–419.
32. Eusebi V, Cattani MG, Ceccarelli C *et al*. Sarcomatoid carcinomas of the breast: an immunocytochemical study of 14 cases. *Prog. Surg. Pathol.* 1989; **10**: 83–89.
33. Gersell DJ, Katzenstein AA. Spindle cell carcinoma of the breast. *Hum. Pathol.* 1981; **12**: 550–561.
34. Matsukuma A, Enjoji M, Toyoshima S. Ductal carcinoma of the breast: An analysis of proportions of intraductal and invasive component. *Pathol. Res. Pract.* 1991; **187**: 62–67.
35. Denley H, Pinder SE, Tan PH *et al*. Metaplastic carcinoma of the breast arising within complex sclerosing lesion: a report of five cases. *Histopathology* 2000; **36**: 203–209.
36. Al-Nafussi AN. Spindle cell tumours of the breast: practical approach to diagnosis. *Histopathology* 1999; **35**: 1–13.