

**CASE REPORT****Metaplastic Breast Carcinomas: A Report of Six Cases**Shahrin NS<sup>1</sup>, Rohaizak M<sup>1</sup>, Naqiyah I<sup>1</sup>, Nurismah MI<sup>2</sup>*Department of <sup>1</sup>Surgery and <sup>2</sup>Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur***ABSTRAK**

'Metaplastic breast carcinoma' (MBC) adalah jenis kanser payu dara yang amat jarang ditemui yang dari segi histologinya, bercirikan karsinoma yang terdiri daripada dua jenis epitelia atau kehadiran karsinoma bersama-sama dengan elemen 'bukan-epitelial'. Ianya adalah agresif dan mempunyai ciri prognosis yang buruk. Ciri-ciri patologi dan klinikal kanser ini dikalangan pesakit kanser payu dara di Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM) telah dikaji dari tahun 2000 sehingga 2007. Daripada 471 pesakit kanser payu dara di PPUKM terdapat enam pesakit wanita dikenal pasti melalui diagnosis histologi mengidap MBC yang mana ianya melibatkan 1.3% dari keseluruhan kes kanser payu dara. Empat daripada mereka adalah dari etnik Melayu manakala dua adalah India dan min umur mereka adalah 51 tahun. Di dalam kesemua kes, kanser ini adalah besar, bersaiz lebih dari 5 sm, gred 3 dan beresepor estrogen negatif. Lima pesakit menjalani mastectomi (empat bersama 'axillary clearance' manakala satu tanpa 'axillary clearance'). Penglibatan kelenjar limfa aksilari didapati pada empat pesakit (tiga pesakit mempunyai tumor jenis epithelia sahaja dan satu tumor dwifasa). Lima pesakit menerima kemoterapi, seorang lagi enggan dirawat secara kemoterapi. Kesemua pesakit mengalami rekuren tumor dengan min masa rekuren selama 9 bulan. Kesimpulannya, MBC jarang berlaku, agresif dan biasanya melibatkan golongan wanita yang sudah menopause. Mereka selalunya bersaiz besar, mempunyai gred histopatologi tinggi dan beresepor estrogen negatif. Saiz tumor yang besar serta penebaran tumor ke kelenjar limfa menjangkakan prognosis buruk. Walaupun dengan rawatan kemoterapi dan radioterapi, pesakit-pesakit ini mempunyai risiko yang tinggi untuk mendapat kanser berulang atau merebak ke organ lain.

*Kata kunci:* kanser metaplastik payu dara, ciri-ciri patologi, kesan klinikal

**ABSTRACT**

Metaplastic breast carcinomas (MBCs) are rare primary breast malignancies characterized histologically by carcinoma of two epithelial types or co-existence of carcinoma with non-epithelial cellular elements. They are aggressive tumours that carry poor prognosis. We reviewed the pathologic features and clinical outcomes of MBCs seen in our institution between the years 2000 to 2007. Out of 471 breast

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cancer patients, six female patients were histologically-proven to have MBCs giving an incidence rate of 1.3%. The patients comprised four Malays and two Indians and their mean age was 51 years old. Five patients underwent mastectomy (four with axillary clearance and one without) and one had wide local excision with axillary clearance. Axillary lymph node involvement was seen in four patients (three with epithelial only type tumour and one with the biphasic tumour). In all the cases, the tumours were bigger than 5 cm in diameter (T3), grade 3 and estrogen receptor negative. Five patients received chemotherapy while one refused. All of the patients had tumour recurrence with a mean time of recurrence of 9 months. In conclusion, metaplastic breast carcinomas are rare and aggressive tumours usually affect the post menopausal age group. They present as aggressive, large sized, high grade tumours that are estrogen receptor negative. Tumour size and axillary lymph node involvement indicate poor prognosis. Despite treatment with chemotherapy and radiotherapy, these patients have high risk of local recurrence and distant metastases which are potentially fatal.

**Key words:** metaplastic breast carcinomas, pathologic features, outcome

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## INTRODUCTION

Metaplastic breast carcinomas (MBCs) encompass a heterogeneous group of breast cancers characterised histologically by intimate admixture of adenocarcinoma with dominant areas of spindle cell, squamous, and/or mesenchymal differentiation (Devilee & Tavasoli 2003). The tumour may present in pure form of metaplastic spindle cell or squamous cell component without recognizable adenocarcinoma. It can be categorised into purely epithelial (when it is composed of squamous cell carcinoma only or adenocarcinoma and squamous cell) or mixed epithelial and mesenchymal e.g. carcinosarcoma. These tumours are rare, accounting for less than 1% of all breast cancer cases with mean age of presentation at 55 years old (Devilee & Tavasoli 2003). Between 1984 to 2005, there were only 16 published reports of 505 cases discussing the clinical and pathological characteristics of this tumour (Beatty et al. 2006). Due to its rarity, data on the current understanding and management of metaplastic breast carcinomas are

scanty. We report our experience in managing six cases of metaplastic breast carcinomas encountered at our centre over an 8-year study period. The histopathological features and clinical outcomes from these patients are reviewed.

## MATERIALS AND METHODS

Cases were retrieved from the Breast Cancer Database at The Breast and Endocrine Unit, Universiti Kebangsaan Malaysia Medical Center (UKMMC). Information on the demographics, diagnosis, tumour grade, oestrogen (ER) and progesterone (PR) receptors status, HER2 expression, clinical staging, treatment, recurrence status and patient survival was recorded. Information on the patients' survival details were obtained from the medical records and through telephone conversations with their family members. The patients were grouped according to tumour types; epithelial and biphasic histological subtypes. Disease free survival was defined as the time from diagnosis to distant recurrence (or death from cancer in the absence of re-

currence) or last follow-up. Overall survival was defined as the time from diagnosis to the time of death from the cancer or date of last contact for patients who are still alive or who had died from other causes.

## RESULTS

A total of 471 breast cancer patients were operated between 2000 and 2007 at our institution, of which six female patients were histologically confirmed to have MBCs, giving an incidence rate of 1.3%. Ethnically, the patients comprised four Malays and two Indians. The mean age of our patients was 51 years with the epithelial only group being slightly younger age (42 years) than the biphasic group (55 years). The mean tumour size was 9.5cm with the epithelial only group presenting with slightly bigger tumor size (13cm) compared to the biphasic group (8 cm). Histologically, three of the six patients had epithelial only tumours com-

posed of both adenocarcinoma and squamous cell carcinoma while the other three patients were diagnosed with tumours of the biphasic type expressing both carcinoma and sarcomatoid components. All patients had grade 3 tumours and all tumours were ER and PR negative. Only four patients had the HER2 status tested, all of which were negative. Axillary nodal involvement was found in all epithelial only group and one in the biphasic group. Four patients underwent mastectomy with axillary clearance, one patient had mastectomy only and one had wide local excision with axillary clearance. Two patients received neoadjuvant chemotherapy while another three had adjuvant chemotherapy. One patient refused chemotherapy. All of the patients had tumour recurrence with mean time of recurrence of 9 months. Five of them died two to three months after tumour recurrence. Table 1 summarises the relevant clinicopathological findings.

**Table 1** : Summary of metaplastic breast cancer cases

Patient No.	Tumour grade	ER	PR	No of lymph nodes involved	Operation date	Type of operation	Chemotherapy	Recurrence date & site	Death
1	3	negative	negative	12/28	15.01.05	Mastectomy +AC	Yes	12.09.05 local	07.10.05
2	3	negative	negative	1/31	15.10.02	Mastectomy +AC	No	07.05.03 brain	17.06.03
3	3	negative	negative	1/8	28.03.03	Mastectomy +AC	Yes	May - 2004 bone	still alive
4	3	negative	negative	0/7	26.02.05	WLE + AC	Yes	30.09.05 liver	31.10.05
5	3	negative	negative	-	15.06.02	Mastectomy	Yes	Aug – 2002 bone	09.10.02
6	3	negative	negative	0/12	06.08.02	Mastectomy + AC	Yes	July – 2004 lung, liver	05.08.04

**ER**: estrogen receptor; **PR**: progesterone receptor; **AC**: axillary clearance; **WLE** : wide local excision

## DISCUSSION

Metaplastic breast carcinomas (MBCs) are rare types of breast cancer which are difficult to diagnose clinically as they do not have specific imaging patterns. They are also challenging to the pathologists as the tumours have a wide range of histopathological features and the metaplastic area may dominate the whole tumour or occupy a very small area within the lesion. In this report, we identified six metaplastic breast carcinomas and evaluated their clinicopathological parameters. We record an incidence rate of 1.3% which concurs with the reported incidence of 1-2% elsewhere (Roses 2005). Interestingly, the six patients in our series were comprised of four Malay and two Indian ethnicity with no MBC diagnosed among Chinese patients. Similar ethnic differences in risks for MBCs was reported in an earlier study which reported a higher percentage of MBCs among African Americans or Hispanics (Pezzi et al. 2007). The reason for this observation is unclear but probably suggests that racial or genetic factors may underlie the increased risk for MBCs.

MBCs were thought to have either originated as a single entity or clone that originates in the myoepithelial cells or its precursor, or those arising from pre-existing lesions such as papillomas, complex sclerosing lesions and nipple adenoma (Denley et al. 2000; Gobbi et al. 2003; Popnikolov et al. 2003; Reis-Filho et al. 2003). This has been further supported by the fact that these neoplastic cells express vimentin, smooth muscle actin, muscle specific actin and p63 that are commonly associated with myoepithelial cells (Schnitt & Collins 2008). Cytokeratin positivity is seen in the epithelial and mesenchymal component of this tumour and it is thought that it is the metaplasia of the epithelial elements of a carcinoma that could have given rise to

the sarcomatous changes (Saxena et al. 2004).

In most literatures, MBCs are ER and PR negative, as was the case in all patients reported here (Kuo et al. 2000; Khan et al. 2003; Luini et al. 2007; Pezzi et al. 2007). Similarly, most of the MBCs in our series did not express HER2 which is in keeping with a previous study (Barnes et al. 2005). The reported incidences of lymph node involvement in these tumors were between 8%-56% (Kurian & Al-Nafussi 2002; Khan et al. 2003). In this series of cases, axillary nodal involvement was found in the entire epithelial only group and only one of the patients in the biphasic group had nodal metastases. The distinctive lymph node negativity was observed in the presence of spindle cell component which may be due to the nature of sarcoma that tends to metastasize haematogenously rather than through lymphatic channels (Sneige et al. 2001; Gobbi et al. 2003). Despite the lower incidence of axillary lymph node involvement, these tumours had high metastatic potential either locally, to distant organs or both, in more than 50% of cases (Wargotz et al. 1989; Wargotz & Norris 1989a; Rayson et al. 1999). Most distant metastases involve lung or bone (Wargotz et al. 1989; Wargotz & Norris 1989b; Kurian & Al-Nafussi 2002). In our series, we had five patients with distant metastases and one local recurrence (Table 1).

The average size of the tumours in this series was 9.5cm which was bigger than the usual size of infiltrating ductal carcinomas. This is most likely due to the aggressive nature of the tumours with rapid growth rates. Most of these patients had poorly differentiated or undifferentiated tumours (compared to infiltrating ductal carcinoma) which will further lead to rapid growth rates (Pezzi et al. 2007). We were unable to do a statistical analysis on whether the epithelial only group tumours were larger than the biphasic group due

to the limited number of cases. However, in this series the mean tumour size for the epithelial group was greater than the biphasic group. Five of our patients had mastectomy due to the large size of the tumours. Five of the patients had systemic therapy (one refused) and most of them died within a year after surgery. In our series, the mean time of recurrence was 9 months and survival after recurrence was short. This concurs with other studies that showed that MBCs are less responsive to therapy with the conventional regimes that are usually used for infiltrating ductal carcinoma (Wargotz & Norris 1989a; Rayson et al. 1999). There is no survival advantage either with chemotherapy or radiotherapy for distant metastases (Wargotz & Norris 1989a). The median survival after metastases is 8 months after systemic treatment (Rayson et al. 1999). This means that the optimal systemic therapy for metaplastic breast carcinoma still needs further defining.

## CONCLUSION

Metaplastic breast carcinomas are rare types of breast cancers usually affecting the post menopausal age group. These tumours have aggressive clinical behaviour, present with locally advanced disease, are large in size, high grade tumours and triple negative. Despite treatment with chemotherapy and radiotherapy, the patients have a high risk of local recurrence and distant metastases which are potentially fatal.

## REFERENCES

- Barnes, P.J. Boutilier, R., Chiasson, D. 2005. Metaplastic breast carcinoma: clinical-pathologic characteristics and HER2/neu expression. *Breast Cancer Research and Treatment* **91**:173-178.
- Beatty, J. D., Atwood, M., Tickman, R. & Reiner, M. 2006. Metaplastic breast cancer: clinical significance. *Am J Surg* **191**:657-664.
- Denley, H., Pinder, S.E., Tan, P.H., Sim, C.S., Brown, R., Barker, T., Gearty, J., Elston C.W. & Ellis, I.O. 2000. Metaplastic carcinoma of the breast arising within complex sclerosing lesions: a report of five cases. *Histopathology* **36**: 203-209.
- Devilee, P. & Tavassoli, F.A. 2003. World Health Organisation Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. Lyon, IARC Press.
- Gobbi, H., Simpson, J.F., Jensen, R.A., Olson S.J. and Page, D.L. 2003. Metaplastic breast tumours arising within papillomas, complex sclerosing lesions and nipple adenomas. *Mod Pathol* **16**: 893-901.
- Luini, A., Aguilar, M. & Gatti, G. 2007. Metaplastic carcinoma of the breast, an unusual disease with worse prognosis: the experience of the European Institute of Oncology and review of the literature. *Breast Cancer Res Treat.* **101**:349-353.
- Khan, H. N., Wyld, L., Dunne, B., Lee, A. H. S., Pinder, S. E., Evans, A. J. & Robertson, J. F. R.. 2003. Spindle cell carcinoma of the breast: a case series of a rare histological subtypes. *Eur J Surg Oncol* **29**: 600-603.
- Kuo, S. H. Chen, C. L. Huang C. S. & Cheng, A. L. 2000. Metaplastic carcinoma of the breast: analysis of eight Asian patients with special emphasis on two unusual cases presenting with inflammatory-type breast cancer. *Anticancer Res* **20**: 2219-2222.
- Kurian, K.M. & Al-Nafussi, A. 2002. Sarcomatoid/metaplastic carcinoma of the breast: a clinicopathological study of 12 cases. *Histopathology* **40**:58-64.
- Pezzi, C.M., Patel-Parekh, L., Cole, K., Franko, J., Klimberg, V.S. & Bland, K. 2006. Characteristics and treatment of metaplastic breast cancer: Analysis of 892 cases from National Cancer Data Base. *Annals of Surgical Oncology.* **14**(1):166-173.
- Popnikolov, N.K., Ayala, A.G., Graves, K. & Gatalica, Z. 2003. Benign myoepithelial tumours of the breast have immunophenotypic characteristics similar to metaplastic matrix-producing and spindle cell carcinomas. *Am J Clin Pathol* **120**(2):161-167.
- Rayson, D., Adjei, A.A., Suman, V.J., Wold, L.E. & Ingle, J.N. 1999. Metaplastic breast carcinoma cancer: prognosis and response to systemic therapy. *Ann Oncol* **10**: 413-419.
- Reis-Filho, J.S., Milanezi, F., Paredes, J., Silva, P., Pereira, E.M., Maeda, S.A., de Carvalho, L.V., Schmitt, F.C. 2003. Novel and classic myoepithelial/ stem cell markers in metaplastic

- carcinomas of the breast. *Appl Immunohistochem Mol Morphol* **11**:1-8.
- Roses, D.F. 2005. Breast Cancer: 2nd Edition. Churchill Livingstone; 117-119.
- Saxena, S., Bansal, A., Mohil, R.S. & Bhatnagar, D. 2004. Metaplastic carcinoma of the breast – a rare breast tumour. *Indian J Pathol Microbiol* **47**: 217-220.
- Schnitt, S.J. & Collins, L. 2008. Biopsy Interpretation of the Breast: 1st Edition. Lippincott Williams and Wilkins; 327.
- Sneige, N., Yaziji, H., Mandavilli, S.R., Perez, E.R., Ordonez, N.G., Gown, A.M., Ayala, A. 2001. Low grade (fibromatous-like) spindle cell carcinoma of the breast. *Am J Surg Pathol* **25**:1009-16.
- Wargotz, E.S., Deos, P.H. & Norris, H.J. 1989. Metaplastic carcinoma of the breast: II. Spindle cell carcinoma. *Human Pathol* **20**(8): 732-740
- Wargotz, E.S. & Norris, H.J. 1989a. Metaplastic carcinoma of the breast: I. Matrix producing carcinoma. *Human Pathol* **20**(7): 628-635.
- Wargotz, E.S. & Norris, H.J. 1989b. Metaplastic carcinomas of the breast: III. Carcinosarcoma. *Cancer* **64**(7):1490-1499.