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Metaplastic carcinoma of breast: clinically aggressive tumour case and literature review

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Abstract

A 36 years old Malay woman was presented with 2 months old painless, ulcerating right breast swelling. Multiple right axillary lymph nodes size of about 1cm and palpable was found during examination. Core biopsy of the tumour showed features of phyllodes tumour. Staging CT scan of thorax, abdomen and pelvis reported right breast carcinoma with local invasion to pectoralis major muscle and metastasis to right axillary lymph nodes. Adjuvant

chemotherapy was planned. Patient developed local recurrence at SSG site. During 2nd cycle of chemotherapy, neutropenic sepsis with septic shock developed. Patient passed away 3 months after the initial diagnosis. Patients are treated by using the same principles that govern treatment of IDC. Considering the differences in the clinical and biologic behaviour of these tumours as compared to IDC, multi-institutional clinical trials designed specifically for MBC would be useful to characterize the biology and therapy of this disease.

Keywords: Metaplastic breast carcinoma, tumour, Invasive ductal carcinoma, chemotherapy, neutropenic sepsis.

Introduction

Metaplastic breast carcinoma (MBC) is a very rare tumour and represents a heterogeneous group of lesions. These lesions are divided into purely epithelial (Adenocarcinoma with spindle cell metaplasia; Adenosquamous, Squamous cell and Mucoepidermoid carcinoma) and mixed epithelial-mesenchymal tumours. These lesions are reported with an incidence of less than 1% of all breast tumours. The rarity of MBC does not allow large or randomized studies to define the optimal treatment. Many of the descriptions of MBC are from case reports and small series. Traditionally, all patients with MBC are treated in a similar fashion as typical Invasive Ductal Carcinoma (IDC). However, based on the clinical features, hormonal receptors status and prognosis especially comparing to IDC, MBC have different characteristics and need to be managed differently.

Case report

A 36 years old Malay woman was presented with 2 months history of right breast swelling which was painless, rapidly increasing in size and ulcerating. She was nulliparous, attained menarche at the age of 11, had no family history of cancer and was not taking any hormonal therapy. Clinically, she had locally advanced disease with huge, ulcerated right breast mass size 20x20cm that was hard and fix to underlying chest wall. Multiple right axillary lymph nodes size was about 1cm and was palpable during examination (Figure 1).

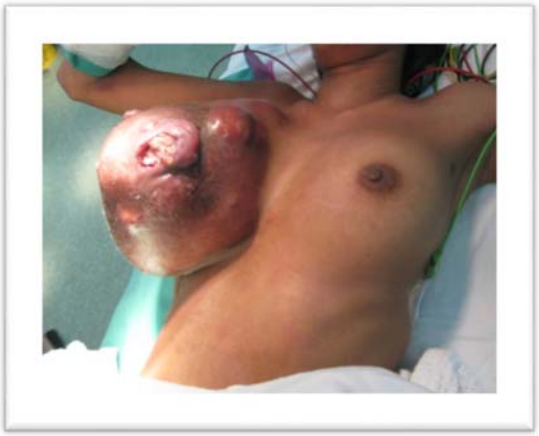

Figure 1: Huge, ulcerating right breast lump

Core biopsy of the tumour showed features of either metaplastic or malignant phyllodes tumour. Staging CT scan of thorax, abdomen and pelvis reported right breast carcinoma with local invasion to pectoralis major muscle and metastasis to right axillary lymph nodes (Figure 2).

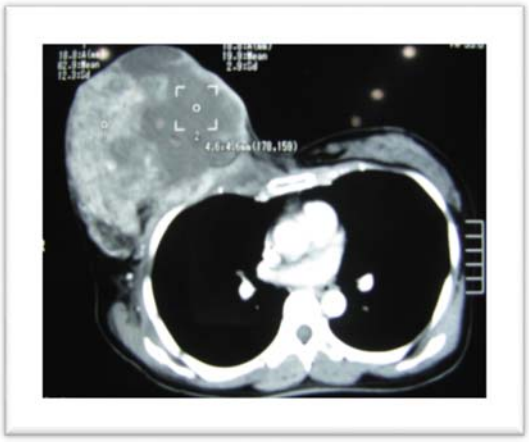

Figure 2: CT scan showed a locally advanced disease with invasion of anterior chest wall.

No distant metastasis was seen. Subsequently she went through right toilet mastectomy with axillary clearance and split skin graft which was successfully performed (Figure 3).

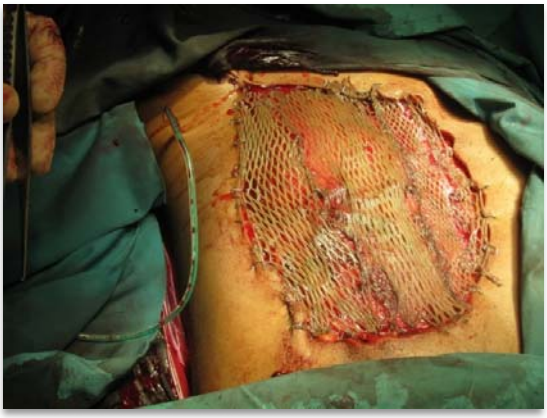

Figure 3: After right toilet mastectomy and split skin graft.

Histopathology revealed; metaplastic carcinoma with osteoid, chondroid and rhabdoid differentiation with right axillary lymph nodes involvement (2 positive out of 13 resected lymph nodes). The tumour involved the surgical margin and the immune-histochemical staining was positive for CK and Vimentin. Hormonal receptors (ER, PR) and human epidermal growth factor receptor 2 (HER2) were negative (triple negative).

An oncologist saw the patient and adjuvant chemotherapy was planned. However, she developed local recurrence at SSG site. While receiving 2nd cycle of chemotherapy (Adriamycin and Ifosfamide), she developed neutropenic sepsis with septic shock. She passed away 3 months after the initial diagnosis.

Discussion

Various combinations of adenocarcinoma, mesenchymal, and other epithelial components characterize MBC. It was officially recognized as a distinct pathologic diagnosis in 2000 by WHO [1]. Knowledge about the patient demographics, presentation, tumour behaviour, and response to various treatments is limited. To date, only small series and case reports have attempted to delineate the factors that make MBC different from more common malignant breast histologies [2-6].

MBC is commonly presented as more advanced AJCC stage with larger tumour size

and higher incidence of distant metastasis during diagnosis [5, 6]. A study by M. Pezzi et al on 892 patients with MBC and 255,164 patients with IDC noted that MBC had fewer patients presented as T1 lesions compare to IDC (29.5% vs. 65.2%) [5]. Similar result noted from Jung et al (25.7% vs. 61.2%) and Park et al (13.8% vs. 54.2%) [2, 4]. This difference in size could possibly be explained by the result of a more rapid growth rate in MBC [5]. The incidence of stage IV disease during diagnosis was significantly higher in MBC as reported by Jung et al (8.6% vs. 2.0%, P=0.04) and Park et al (10.3% vs. 0.9%, P=0.002). These indicate that MBC is relatively more aggressive then IDC in terms of tumour growing rate and haematogenous spread. However, most published data on metastases of metaplastic carcinoma have shown haematogenous (lung and bone) metastases rather than lymphatic spread and they are frequently lymph node negative [2, 7]. Where Pezzi and colleagues reported 78.1% (MBC) vs. 65.7% (IDC) patients with no disease ($P < 0.001$), our patient presented with locally advanced disease but her lymph nodes status was positive and without distant metastasis.

Our patient had triple negative disease and this is consistent with the result of all the studies done comparing MBC and IDC [4, 5]. Pezzi et al reported 11.3% of patients with MBC were ER positive compared with 74.1% of patients with IDC ($P< 0.001$). For PR testing, 10.4% of patients with MBC were positive compared with 62.4% of patients with IDC ($P < 0.001$). Jung et al also reported significantly less hormone receptor positivity in the MBC group compared to the IDC group (ER, 5.7% vs. 65.4%, $P<0.001$; PR, 8.6% vs. 55.8%, $P<0.001$), with more triple negative tumour in the MBC group (80.0% vs. 16.7%, $P<0.001$). The very low incidence of hormone receptor positivity in MBC compared with IDC represents another biologic difference in these tumours and this implicates the lack of hormonal therapy as a therapeutic option for adjuvant treatment in MBC.

Within this context, it was suggested that prognosis of metaplastic carcinoma is worse than that of typical breast carcinoma [6, 8] and is supported by recent studies [9, 10]. The prognostic factors that associated with poorer outcome include larger tumour size, lymph node involvement, the presence of distant metastasis at first diagnosis and p53 over-

expression. Another study involving 51 patients reported that the non-triple-negative group had a poor prognosis compared with the triple-negative group in MBC, which is contrary to what has been reported in patients with IDC. Further confirmation fact and future research regarding this is needed [7].

The systemic management of MBC has rarely been reported. The largest series reporting use of either chemotherapy and hormonal by Rayson et al did not find any evidence of benefit for adjuvant chemotherapy, or significant response rates to chemotherapy, or hormonal therapy for those with metastatic disease [8]. A study regarding radiotherapy (RT) that involved 1501 patients reported that in patients receiving RT, overall survival (OS) was 73.2% at 5 years and 60.3% at 10 years versus 56.9% and 48.3% in patients not receiving RT [11]. Disease-specific survival (DSS) for patients receiving RT was 75.9% at 5 years and 71.7% at 10 years compared with 69.0% and 66.1% in patients not receiving RT [11]. These findings supported the use of RT for all patients with MBC following lumpectomy. Post-mastectomy RT is recommended to patients with 4 or more metastatic axillary nodes, gross extra-capsular nodal extension, large (≥ 5 cm) primary tumours, and chest wall invasion.

Conclusion

MBC is a very rare tumour and is different from IDC, with different presenting characteristics, demographics, and tumour biology. Most of the evidence comes from small-scale studies and are insufficient to draw conclusion regarding the best treatment for MBC. Patients are treated by using the same principles that govern treatment of IDC. Considering the differences in the clinical and biologic behaviour of these tumours as compared to IDC, multi-institutional clinical trials designed specifically for MBC would be useful to characterize the biology and therapy of this disease.

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