## Synchronous Bilateral Breast Carcinoma with Two Different Morphology Subtypes: A Case Report

Božica Vrabec Branica $^1,$  Silvana Smojver Ježek $^{1,4},$  Zrinka Juroš $^1,$  Inja Neralić Meniga $^2$  and Šimun Križanac $^{3,4}$ 

- <sup>1</sup> Department of Cytology, University Hospital for Lung Diseases »Jordanovac«, Zagreb, Croatia
- <sup>2</sup> Department of Radiology, University Hospital for Lung Diseases »Jordanovac«, Zagreb, Croatia
- $^3$  Zagreb University, School of Medicine, Department of Pathology, Zagreb, Croatia  $\,$
- <sup>4</sup> Zagreb University, School of Medicine, Zagreb, Croatia

#### ABSTRACT

We report a case of synchronous bilateral breast cancer with ductal and medullary carcinoma. A 60-year-old woman presented with lesion in both breasts which were mammographicaly found two years ago. Ultrasonography proved two suspected masses in breasts. Fine needle cytology was performed and confirmed bilateral carcinoma but with different cytological findings. The cytological feature of the left breast suggested ductal carcinoma and of the right breast raised possibility of a medullary carcinoma. Patient underwent bilateral quadrectomy with evacuation of axillary lymph nodes. Histological examination showed bilateral carcinoma with two different histological features: ductal in the left and medullary carcinoma in the right breast.

**Key words:** bilateral breast cancer, synchronous, different histological features

#### Introduction

Bilateral synchronous breast cancer is an uncommon event and accounts for 0.3–12% of all breast cancers¹. Bilateral breast cancer was defined as synchronous when contralateral cancer was identified within 6 months² (some physicians consider 3 months and others one year)¹,³ after the first breast cancer. Synchronous bilateral tumours are considered independent when they have characteristics like presence of an intraductal component, different histologies or different degrees of differentiation⁴. Different histological types form 20–30% of bilateral synchronous breast cancer⁵. This is a case with concurrent invasive ductal and medullary carcinoma.

#### **Case Report**

A 60-year-old woman without family history of breast cancer was referred to our hospital for regular breast examination. The patient came with two years old mammographic finding made in another hospital. It showed two masses in breasts: one in the left breast, in the upper outer quadrant and one in the right breast, on the border of outer quadrants. Two years ago it was considered that

neither of these masses required additional diagnostic procedures.

She had a firm mobile palpable lesion about 8 mm in its largest diameter, in the upper outer quadrant of her left breast. Ultrasound examination confirmed there suspected mass, 10 mm in diameter. No masses were palpated in left axilla. In her right breast there was a firm mobile palpable mass, about 20 mm in diameter, on the border of outer quadrants. Ultrasound examination confirmed it as an irregular hipoehogenic mass 10 mm in diameter. She hadn't palpable masses in right axilla.

Fine needle aspiration cytology was performed using 22-gauge needle. Slides were air-dried and stained using the May-Grünwald-Giemsa method. Cytological examination confirmed bilateral cancer. Cytology finding of the lesion in the left breast was ductal carcinoma with epithelial cells round and oval in shape with atypical features, variation in size and nuclear moulding (Figure 1 and 2). Aspirates of fine needle aspiration cytology of right breast, predominantly consisted of structureless sheets of large pleomorphic cells, sometimes with bi-

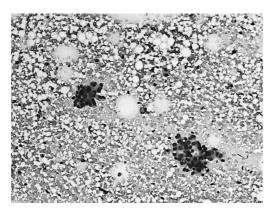


Fig. 1. Ductal carcinoma cells grouped in loose aggregate show atytipical features with nuclear moulding and variation in size (May-Grünwald-Giemsa stain, x200).

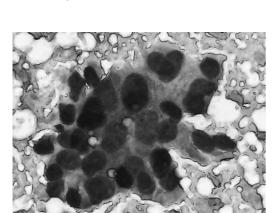
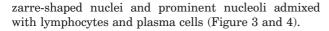


Fig. 2. The nuclei of ductal carcinoma cells vary considerably in size and have round or oval shape with little nuclear border irregularity (May-Grünwald-Giemsa stain, x600)



Medullary carcinoma was suggested but diagnosed only as carcinoma because small areas of lymphoid stroma are quite common in high grade ductal carcinoma, so only histology can confirmed medullary carcinoma using criteria proposed by Ridolfi<sup>6</sup>.

Based on cytology findings, the patient underwent surgical treatment: bilateral quadrectomy with evacuation of axillary lymph nodes. Intraoperative cytology confirmed bilateral carcinoma but of two different types: left as ductal and right suggested possibility of medullary carcinoma. Histopathological examination of the left breast confirmed invasive ductal carcinoma, 5 mm in diameter, with 90% estrogen receptor positive cells and 60% progesteron receptor positive cells by immunohistochemical staining. HER2 was negative. Tumor was composed of atypical epithelial moderately differentiated cells arranged in tubules and sheets in dense collagenous stroma. Seven axillary lymph nodes were free of tumor.

The lesion from the right breast was histologically diagnosed as a medullary carcinoma, 15 mm in diameter,

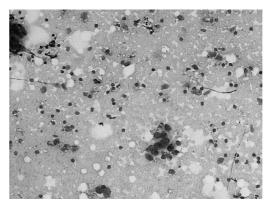


Fig. 3. Structurless sheet of large pleomorphic medullary carcinoma cells with lymphoplasmacytic infiltrate in the background (May-Grünwald-Giemsa stain, x100).

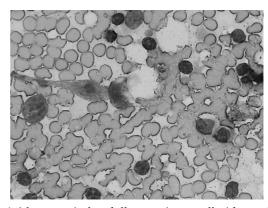


Fig. 4. A large atypical medullary carcinoma cell with prominent nucleoli admixed with lymphocytes and plasma cells (May-Grünwald-Giemsa stain, x400).

with numerous large atypical malignant cells arranged in solid sheets. A dense lymphoplasmacytic infiltrate was observed in the background. There were no estrogen and progesteron receptor positive cells in tumor. HER2 was negative. Thirteen axillary lymph nodes were free of tumor.

According to Elston-Ellis histological grading of breast cancer, ductal carcinoma was evaluated as grade 2 with 6 degree (2 for tubule formation, 2 for nuclear pleomorphism and 2 for mitoses) and medullary carcinoma as grade 3 with 9 degree (3 for tubule formation, 3 for nuclear pleomorphism and 3 for mitoses). The patient received postoperative adjuvant chemotherapy. When seen in follow-up (in November 2008) 41 months postdiagnosis, the physical and mammographical exam findings were negative for metastatic or recurrent disease.

### **Discussion and Conclusion**

Patient with breast cancer have an increased risk of developing either a synchronous or metasynchronous breast cancer which ranges between 0.5% and 0.8% each

year<sup>7</sup>. Several reports showed that the prognosis in bilateral breast carcinoma was worse than that of unilateral breast carcinoma<sup>8–11</sup> and traditional approach to bilateral breast carcinoma is more aggressive than approach to unilateral disease<sup>1</sup>. However, several studies have shown that the prognosis of patients with synchronous bilateral breast carcinoma seems similar to unilateral disease<sup>11–13</sup>. Increase in the incidence of synchronous disease during 1970s coincides with the introduction of routine bilateral mammography in the diagnostic work-up in women with unilateral cancer<sup>14</sup>. This support the role of careful screening of the contralateral breast and follow-up of all patients diagnosed with breast cancer<sup>1</sup>.

The most common breast cancer histologic subtype is infiltrating ductal carcinoma; however, lobular carcinoma is tumour type associated with diffuse or multifocal growth pattern and bilaterality<sup>15</sup>. Medullary carcinoma of the breast is a special type of tumor accounting for 1-6% of all breast carcinomas. It has a better prognosis than the infiltrating ductal carcinoma and than the high degree of epithelial atypia would predict<sup>16</sup> if strict histological criteria proposed by Ridolfi are used. Clinically and mammographically it is a well demarcated lesion and can be mistaken for a fibroadenoma, a colloid or a papillary carcinoma. Cytologists are still facing some difficulties in determining some breast tumour subtypes<sup>17</sup> and medullary carcinoma is one of them. The cytological features of medullary breast carcinoma are rarely detailed in the literature. Based on its cytological features, differential diagnoses are: a poorly-differentiated ductal carcinoma with a lymphocytic infiltrate, metastatic carcinoma in an intramammary lymph node and malignant lymphoma. Nevertheless, it is possible on breast fine needle cytology to suggest that this may be a medullary carcinoma but it must be histologically confirm using the criteria proposed by Ridolfi<sup>6</sup>.

Family history and early age of onset have been reported to increase risk of contralateral breast carcinoma development<sup>18</sup> but other studies have found no such associations<sup>19</sup>. Some reports showed that synchronous cancers are biologically closer to some clonal lesions (metastatic lesions) than metachronous cancers. A biomarker, such as progesteron receptor status, plays a role in addition to the histological parameters, in differentiating metastatic cancers from secondary primary cancers. The rates of the same histopatological type were 93% in synchronous cancers and only 59% in metachronous cancers<sup>2</sup>.

The incidence of synchronous cancer is similar to incidence of unilateral disease but in metachronous cancers is much more common in younger patients from 1980s probably because of the expanding use of adjuvant systematic therapy<sup>3</sup>. Some studies have shown similar prognosis for patients with unilateral and bilateral breast cancer. Gollamudi et al. showed that patients with synchronous bilateral breast cancer don't have a worse prognosis and can be safely treated with bilateral breast conserving surgery<sup>1</sup>.

#### REFERENCES

1. TOUSIMIS E, Breast Cancer Online, accessed 29.04.2005. Avaliable from: URL: www.bco.org 8 (4) (2005). — 2. GONG SJ, RHA SY, JE-UNG HC, ROH JK, YANG WI, CHUNG HC, Jpn J Clin Oncol, 37 (2007) 487. — 3. HARTMAN M, CZENE K, REILLY M, ADOLFSSON J, BER-GH J, ADAMI HO, DICKMAN PW, HALL P, J Clin Oncol, 25 (2007) 4210. - 4. GOLLAMUDI S, GELMAN R, PEIRO G, SCHNEIDER L, SCHNI-TT S, RECHT A, SILVER B, HARRIS J, CONNOLLY J, Cancer, 79 (1997) 250.-5. HUSSAIN ST, ALLUM WH, J R Soc Med, 86 (1992) 550.-6.AOUNI NL, ATHANASIOU A, MANSOURI D, MARSIGLIA H, MATH-IEU MC, SUCIU V, VIELH P, Diagn Cytopath, 34 (2006) 701. — 7. INTRA M, ROTMENSZ N, VIALE G, MARIANI L, BONANNI B, MASTROPAS-QUA M, GALIMBERTI V, GENNARI R, VERONESI P, COLLEONI M, TOUSIMISE E, GALLI A, GOLDHIRSCH A, VERONES U, Cancer, 101 (2004) 905. — 8. TAKAHASHI H, WATANABE K, TAKAHASHI M, TA-GUCHI K, SASAKI F, TODO S, Breast Cancer, 12 (2005) 196. — 9. LEVI F, RANDIMBISON L, TE VC, LA VECCHIA C, Breast, 12 (2003) 89. -

10. CARMICHAEL AR, BENDALL S, LOCKERBIE L, PRESCOTT R, BATES T, Eur J Surg Oncol, 28 (2002) 388. — 11. KOLLIAS J, ELLIS IO, ELSTON CW, BLAMEY RW, World J Surg, 25 (2001) 1117. -MA Y, OWAKI T, YOSHINAKA H, AIKOU T, Surg Today, 33 (2003) 606. 13. HUNGNESS ES, SAFA M, SHAUGHNESSY EA, ARON BS, GAZ-DER PA, HAWKINS HH, LOWER EE, SEESKIN C, YASSIN RS, HAS-SELGREN PO, Surgery, 128 (2000) 702. — 14. HUNGNESS ES, SAFA M, SHAUGHNESSY EA, ARON BS, GAZDER PA, HAWKINS HH, LOWER EE, SEESKIN C, YASSIN RS, HASSELGREN PO, Surgery, 128 (2000) 702. — 15. KOLLIAS J, ELLIS IO, ELSTON CW, BLAMEY RW, Eur J Surg Oncol, 25 (1999) 584. — 16. TROTT PA, Breast Cytopathology (Chapman & Hall, London, 1996). — 17. RAMLJAK V, ŠARČEVIĆ B, VRDO-LJAK DV, BOBUŠ KELČEC I, AGAI M, TRUTIN OSTOVIĆ K, Coll Antropol, 34 (2010) 201. — 18. FISHER ER, FISHER B, SASS R, WICKER-HAM L, Cancer, 54 (1984) 3002. — 19. EARLY BREAST CANCER TRIALISTS'GROUP, Lancet, 365 (2005) 1687.

#### B. Vrabec Branica

 $Department\ of\ Cytology,\ University\ Hospital\ for\ Lung\ Diseases\ "Jordanovac",\ Jordanovac\ 104,\ 10000\ Zagreb,\ Croatia\ e-mail:\ bozica.vrabec.branica@zg.t-com.hr$ 

# ISTOVREMENI OBOSTRANI KARCINOM DOJKE RAZLIČITOG MORFOLOŠKOG SUBTIPA: PRIKAZ SLUČAJA

#### SAŽETAK

Prikazujemo slučaj istovremenog obostranog karcinoma dojke: duktalnog i medularnog. Radi se o 60-ogodišnjoj ženi s obostranim promjenama u dojkama koje su mamografski utvrđene dvije godine ranije. Ultrazvučni pregled potvrđuje nalaz dviju suspektnih promjena u dojkama. Citološkom punkcijom dijagnosticira se obostrano karcinom ali s različitom citološkom slikom. Citološki nalaz lijeve dojke upućivao je na duktalni karcinom, a desne dojke postavio sumnju na medularni karcinom. Pacijentici se učini obostrana kvadrektomija sa evakuacijom aksila. Histološki pregled potvrđuje karcinom dojke obostrano i to različitog histološkog subtipa: duktalni karcinom u lijevoj, a međularni u desnoj dojci.