

Case Report**Choriocarcinoma of the breast; a case report and review of literatures\****Simin Hemati<sup>1</sup>, Omid Esnaashari<sup>2</sup>, Mohamadreza Mohajeri<sup>3</sup>, Mostafa sarvizadeh<sup>4</sup>***Abstract**

Choriocarcinoma is an extremely rare pathology among breast malignancies. It is introduced by two distinct terms in the literatures: breast cancer with choriocarcinomatous features and metastatic choriocarcinoma to the breast. In this case report, the history, physical examination, laboratory findings, imaging studies, and pathological findings of breast choriocarcinoma in a 41-year-old woman are described and previous literatures about choriocarcinoma in the breast are reviewed.

**KEYWORDS:** Choriocarcinoma, Breast, Carcinoma, Choriocarcinomatous, Metastatic.

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**H**istology of choriocarcinoma in the breast is distinctly unusual.<sup>1, 2</sup> There are two distinct terms for choriocarcinoma in the breast: metastatic choriocarcinoma to the breast and breast cancer with choriocarcinomatous features.<sup>3</sup> The breast is an uncommon site for metastasis from extra-mammary neoplasms. It is not common for metastasis to be formed in the breast from extra-mammary neoplasms. The rate of happening in different series, ranged from 0.5 to 6.6 of all breast malignancies. In order of frequency, the most usual primary tumor sources for breast metastases are lymphomas, melanomas, rhabdomyosarcomas, lung tumors, and ovarian tumors.<sup>4</sup>

Choriocarcinoma represents fewer than 10% of all gynecological malignancies. Metastatic disease occurs in about 4% of patients after local management of hydatiform moles and very rarely after term pregnancies or abortions (1 in 40000). Metastases are found in lung (80%), vagina (30%), pelvis (20%), brain (10%), and liver (10%). Other rare sites are spleen, kidneys, and gastrointestinal tract. Indeed, breast is very rare site for metastasis of choriocarcinoma.<sup>3,4</sup>

Few case reports of metastatic choriocarcinoma to the breast are reported till now.<sup>1-11</sup> The most common appearances of breast metastasis are of one or more well-circumscribed masses that are fixed in the upper outer quadrant, without speculation, calcification or architectural distortion which describe the character of most primary carcinomas. However, benign lesions (such as fibroadenoma) can come into sight in a similar way on mammography.<sup>3,4</sup>

In this case report, the history, physical examination, laboratory findings, imaging studies, and pathological findings of breast choriocarcinoma in a 41-year old woman are described and previous literatures about choriocarcinoma in the breast are reviewed.

**Case Report**

A 41-year-old woman with history of severe dyspnea and cough for three months and hemoptysis for 5 days was referred to oncology department at Sayed-Al-Shohada University Hospital in Isfahan (IRAN). Past medical history revealed two full term pregnancies. The latest full term pregnancy happened six month

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ago and she had one molar pregnancy, four years ago. Breast palpation revealed multiple, firm, non-tender masses with different sizes in the right and left breasts without any nipple retraction. Palpation of the right axillary fossa showed three non-tender masses with 1.5×1.5 cm in size. In laboratory data, the serum  $\beta$ hCG level was markedly high, 35200 mIU/mL (normal range <5 mIU /ml).

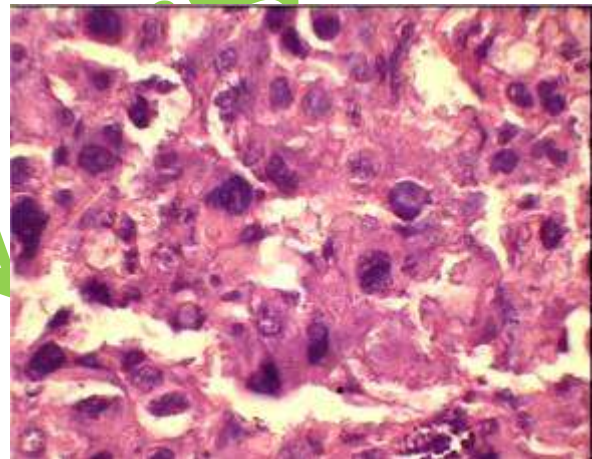
### Imaging studies

Chest X-ray revealed multiple round/oval shaped parenchymal lesions with different sizes and well-defined borders at both lungs with normal size of the heart (Figure 1). Mammograms showed multiple lobulated and high-density masses in both breasts without calcification. Abdominopelvic sonography revealed a round and hypoechoic lesion in the right lobe of the liver. Similar lesions in both kidneys were also recognized. Spleen, pancreas, and para-aortic area were normal. Also, trans-vaginal sonography was recommended for evaluation of ovaries, uterus, and bladder, but due to patient's poor general condition, it was not done.

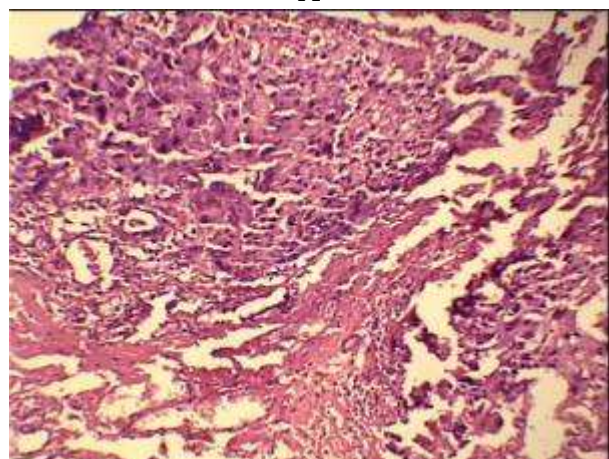


**Figure 1.** Round/oval shape parenchymal lesions with different sizes and well-defined borders at both lungs.

The patient underwent excisional biopsy from one of the right breast masses. Grossly, the tumor was 3×3×2 cm with extensive necrosis and hemorrhage in the lesion. Histologically, the tumor made up of proliferation of large sized cells with high nucleus/cytoplasm ratio and increased nuclear chromatin. A hemorrhagic and necrotic background was seen. Multinucleated giant cells resembled syncytiotrophoblastic and cytotrophoblastic cells were seen (Figure 2). This finding was similar to choriocarcinoma originating from genital tract. No intraductal carcinoma or other subtypes of breast carcinoma were identified in the periphery of the tumor. No lymphovascular invasion was also identified.



A



B

**Figure 2.** A- High nucleus-cytoplasm ratio (N/C) and increased nuclear chromatin. B- Multinucleated giant cells resembling syncytiotrophoblastic and cytotrophoblastic cells.



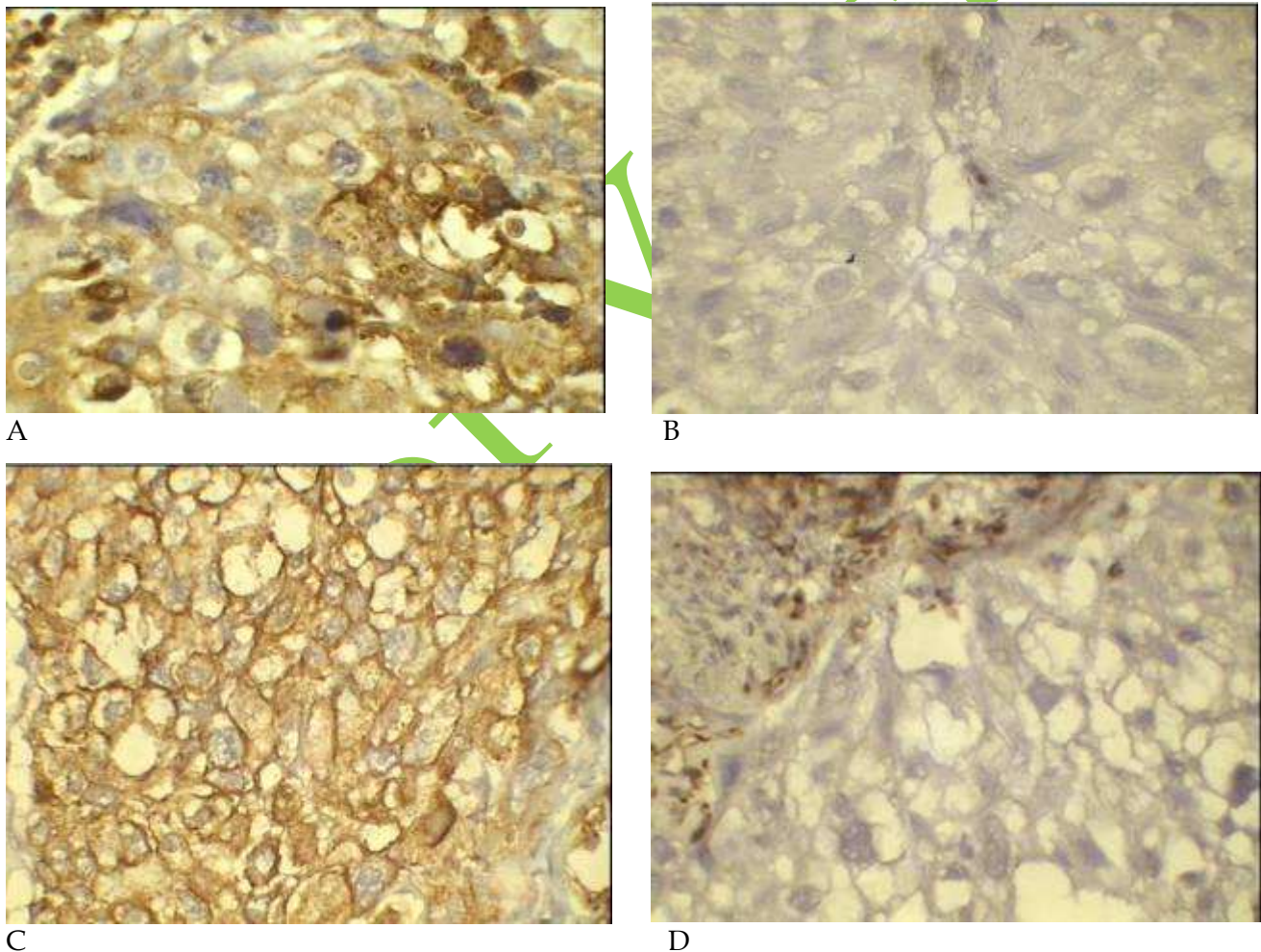
Immunohistochemical (IHC) findings were as follow: for the confirming of tissue diagnosis, IHC study was performed on paraffin embedded tissue block by avidin-biotin method. IHC with CK7, CK20, CEA, BHCG, and vimentin revealed positive CK7, negative CK20, negative CEA, positive  $\beta$ HCG, and vimentin was negative in neoplastic cells but positive in stromal cells (Figure 3). According to the finding of IHC study, the diagnosis of choriocarcinoma was confirmed.

Combination chemotherapy of etoposide, methotrexate, dactinomycin and cyclophosphamide, oncovin (EMA-CO) was prescribed

for the patient but unfortunately she died one month later due to multiple metastases to the lung, liver, and kidneys.

### Discussion

The first report that described breast carcinoma with choriocarcinomatous features was published by Saigo and Rosen; it was not an ordinary report about breast carcinoma and happened in a 55-years-old woman. The 2.5 cm tumor was grossly hemorrhagic in part. It was consisted of areas of moderately differentiated infiltrating ductal carcinoma admixed with areas strongly looked like choriocarcinoma.<sup>12</sup>



**Figure 3.** A- immunohistochemistry (IHC) showed some tumor cells positive for  $\beta$  human chorionic gonadotropin ( $\beta$ HCG) antibody. B- IHC negative for carcinoembryonic antigen (CEA). C- IHC showed some tumor cells positive for cytokeratin 7 (CK7) antibody. D- IHC showed vimentin negative in tumor cells but positive for stromal cells.

Choriocarcinomatous differentiation with multinucleated syncytiotrophoblastic-like giant cells has been described in non-gestational carcinomas arising in many organ systems including urinary bladder, stomach, and colon but is extremely rare in breast tumors.<sup>4,6</sup> Few case reports of breast carcinoma with choriocarcinomatous features are reported till now.<sup>1-11</sup> In these cases, the median age at the time of diagnosis was 54.5-years. Most tumors were located in the right breast (8 patients). Median size of tumors was 4.3 cm. Most patients had metastasis to axillary lymph nodes (6 patients) and all cases were positive for  $\beta$ HCG antibody in IHC studies (8 patients); 8 patients had invasive ductal carcinoma or other subtypes of breast carcinoma at the periphery of choriocarcinomatous component.<sup>3,6</sup>

It is not uncommon to watch carefully gently elevated serum levels of HCG in patients with breast carcinoma. The source of this hormone production is not exactly clear but is presumed to be the breast tumor itself. It has also been shown that 12% to 60% of patients with breast carcinoma show weak tumor immunostaining for subunits of HCG too. The accurate pathophysiologic role and clinical significance of HCG expression in breast tumors stay unclear. Some speculated that HCG may have a role in synthesis and secretion of estrogen and progesterone.<sup>6</sup> High levels of serum  $\beta$ HCG and also strongly positive  $\beta$ HCG antibody in IHC study are extremely rare in usual breast carcinoma. These findings were explained in metastatic choriocarcinoma to the breast or breast carcinoma with choriocarcinomatous features. Several theories are existed to express the mechanism of the unusual choriocarcinomatous pattern of differentiation in breast tumors that one of them is "metaplastic" process in the primary tumor leading to partial or complete overgrowth and representation as choriocarcinoma.<sup>6</sup>

In brief, most of the reported cases of choriocarcinoma of the breast had poor prognosis and associated with metastasis to other organs. Therefore, rapid staging studies and treatment

is necessary for these patients. Erhan and colleagues reported that half of their cases had disease-free survival up to 2 and 4 years.<sup>3</sup> Complete history, physical examination, pathological and IHC studies, imaging and lab examinations are necessary to distinct metastasis choriocarcinoma to the breast (extramammary origin) and breast carcinoma with choriocarcinomatous features (with breast origin). Existing of gestational trophoblastic disease and breast carcinoma in past medical history suggests metastatic choriocarcinoma and breast carcinoma with choriocarcinomatous features, separately. Most cases of breast carcinoma with choriocarcinomatous features have aggressive clinical features and are associated with other organs such as metastatic choriocarcinoma to the breast. That seems there is no differentiation between the two terms in point of view of clinical features.

Presence of invasive ductal carcinoma or other subtypes of breast carcinoma at the periphery of choriocarcinomatous component suggests breast carcinoma with choriocarcinomatous features; therefore, pathological studies on complete excisional biopsy of tumor and evaluation of free margins to find subtypes of breast carcinoma are necessary for correct diagnosis.

IHC study ( $\beta$ HCG antibody) is necessary to confirm the choriocarcinomatous diagnosis in the breast. Metaplasia of gastrointestinal adenocarcinoma to choriocarcinoma is not rare; therefore, evaluation of CEA is recommended to distinct metastasis to the breast from gastrointestinal tract or other origins. Evaluation of  $\beta$ HCG is a fundamental study in all tumors suspicious of choriocarcinoma. It is not uncommon to observe gently elevated serum levels of HCG in breast carcinoma patients but in usual breast carcinoma, high levels of BHCG are extremely rare. Imaging studies such as ultrasonography and CT scan for finding the origin of metastasis to the breast are very useful. On the other hand, these studies could be used for finding the concurrent metastasis in other organs.

## Conflict of Interests

Authors have no conflict of interests.

## Authors' Contributions

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