ISSN: 2634 - 680X

Journal of Clinical Case Studies Reviews & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Metaplastic Carcinoma of the Breast, Spindle Cell Type: A Case Report

Angelie Grace V Alvarez

Department Of Pathology, Corazon Locsin Montelibano Memorial Regional Hospital, Bacolod City, Negros Occidental, Philippines

ABSTRACT

Metaplastic breast carcinoma accounts for less than 1% of all breast malignancies. This subtype is the most aggressive triple negative breast cancer and remains therapeutically challenging to treat, highly unresponsive to chemotherapy. Here we present a case of a 54 year old female presenting as a non-tender, left breast mass. Core needle biopsy reports atypical cells present, suggestive of malignancy: considerations are Malignant Phyllodes tumor and Invasive Ductal Carcinoma. Subsequently she underwent a modified radical mastectomy (MRM). Microscopic examination revealed spindle cell neoplasm without epithelial component. On immunohistochemically examination, the tumor cells were positive for Cytokeratin and Smooth Muscle Actin and negative for S-100, ER (Estrogen receptors), PR (progesterone receptors) and Her2/Neu.

***Corresponding author**

Angelie Grace V. Alvarez, MD, Department Of Pathology, Corazon Locsin Montelibano Memorial Regional Hospital, Bacolod City, Negros Occidental, Philippines. E-mail: gialvarez86@gmail.com

Received: September 13, 2019; **Accepted:** September 20, 2019, **Published:** October 14, 2019

Introduction

The reported incidence of Metaplastic Breast Carcinoma (MBC) is 0.2% of all breast cancers MBC is generally considered to be high grade, representing a morphologically heterogeneous group of invasive breast cancers in which a variable portion of the glandular epithelial cells comprising the tumor have undergone transformation into an alternate cell type, either a non-glandular epithelial cell type or a mesenchymal cell type [1, 2]. The 2012 WHO Classification of Tumors of the Breast divided MBC into subtypes based upon the morphologic components of the tumors. It includes various categories such as sarcomatoid carcinoma/ carcinosarcoma, spindle cell carcinoma, carcinoma with osteoclast like giant cells, squamous cell carcinoma and others [1].

We report a case of metaplastic carcinoma of the breast entirely composed of spindle cells in a 54-year-old female. MBC was not officially recognized as a distinct histologic entity until 2000, and research on this disease process has been limited due to its rarity and the variety of tumor types included in this diagnosis. In most cases, breast sarcomas are firm and well-circumscribed with gross cysts. The age range at time of presentation varies in the literature from the 2nd to the 9th decade. The youngest patient who has been previously published is 14 years old [3]. MBC more commonly presents as a large, unilateral, rapidly growing mass, generally greater than 2cm [4]. Majority of cases contained greater than 80% spindle cell component. Most metaplastic carcinomas are negative for hormone receptors (estrogen, progesterone) and Her2/Neu. Patients with metaplastic carcinomas have poor outcome with a high risk of recurrence after surgery, although it presents more commonly as node-negative disease [5]. The systemic treatment for this tumor remains unclear. MBC has consistently shown a suboptimal response to standard chemotherapy regimens and few options are available. The absence of hormone receptors and Her2/Neu oncoprotein expression also limit oncological treatment options.

Case Report

This is a case of a 54-year-old female who presented with a left breast mass five years prior to admission. Clinical examination revealed a nodular mass occupying the entire left breast. The mass was approximately 11 cm in maximum diameter, slightly movable with unremarkable overlying skin. She had no concomitant diseases at the time of presentation. She is non-alcoholic and she was a nonsmoker. She has a second-degree family medical history of breast cancer. The patient is married and already in postmenopausal stage. She had her menarche at 12 years of age with regular monthly periods. Her past medical history was not significant. Her biochemical and hematology laboratory "work-up" was within normal limits. There was no significant axillary or cervical lymphadenopathy. The other breast was normal. An initial clinical diagnosis of breast carcinoma to consider Malignant Phyllodes tumor vs. Invasive ductal Carcinoma was made. On radiologic examination, an irregular ill-defined density was seen superimposed at the left breast (Figure 1). Other chest structures are unremarkable. A decision to perform core needle biopsy followed by excision was done. Patient underwent unilateral mastectomy of the left breast with Axillary lymph node dissection three months later. We conducted an intraoperative frozen section of the mass, showing presence of atypical cells suggestive of malignancy. The case merits presentation because of its rarity and its difficulty to diagnose especially that the tumor is composed

mainly of sarcomata's elements. Our case was lost to follow-up after surgery. No oncologic treatment was documented in the outpatient department records.

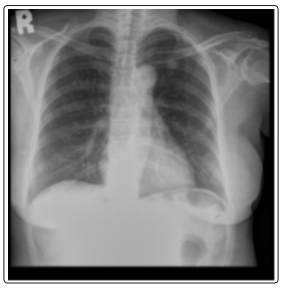

Figure 1: An ill-defined density is superimposed at left breast

Gross Findings

Grossly, the mass measuring 11 cm in length, 10 cm in width and 6 cm in height, is located 0.1 cm from the basal surgical margin. Cut section revealed a pale tan, firm and fibrotic, unencapsulated tumor. There were no necrotic areas, areas of hemorrhage or calcification (Figure 2).

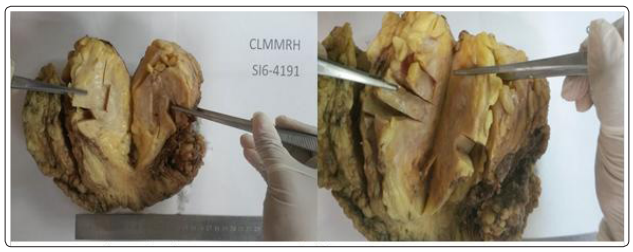

Figure 2: A-B) Grossly, the cut section revealed firm, pale tan mass measuring 10 x 11 x 6 cm located 0.1 cm from the basal margin. There were no areas of hemorrhage or calcification

Histopathologic Findings

Microscopically, hematoxylin and eosin (HE) stained sections of core needle biopsy reveal presence of atypical cells suggestive of malignancy. The nuclei are round to oval with marked hyperchromasia (Figure 3A). On frozen section, tumor cells have variable nuclear atypia surrounded by occasional hyperchromatic stromal cells interspersed with neoplastic cells that resemble lipoblasts, which are highly pleomorphic, some are of signet-ring cell type (Figure 3B). On histologic sections, the degree of differentiation is highly variable consisting of mature adipocytes and cells resembling small lipoblasts. Poorly cohesive pleomorphic cells and spindle cells with elongated nuclei and pale eosinophilic cytoplasm are seen. No glandular/epithelial or heterologous elements identified (Figure 4 A-D).

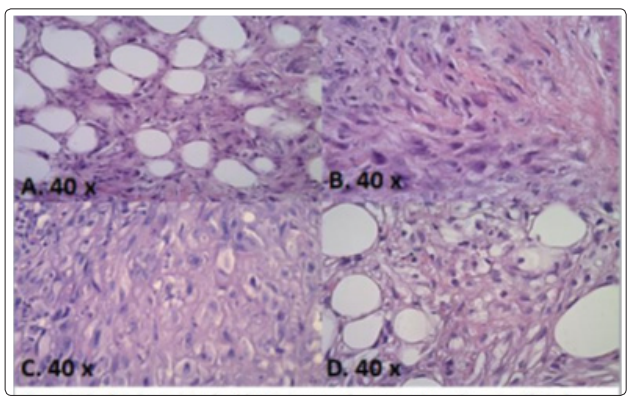

Figure 3: A) Core needle biopsy of the breast mass show adipocytes and presence of atypical cells with pleomorphic, hyperchromatic nuclei in desmoplastic stroma. B) Frozen section of the breast mass show pleomorphic round to ovoid cells with hyperchromatic nuclei.

Surgical margins were tumor negative. Lymph/vascular invasion or perineural invasion were absent and no metastatic deposits were seen in all ten lymph nodes.

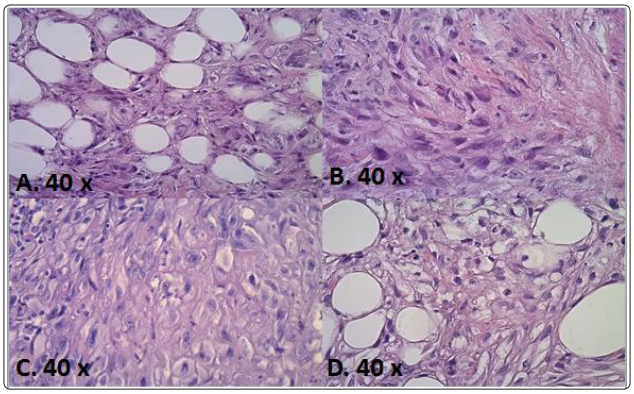

Figure 4: A) Isolated signet ring lipoblasts interspersed among mature adipocytes. B) Single crescent-shaped hyperchromatic nuclei are compressed at the periphery of the cell. C) Spindle cells with elongated nuclei and pale eosinophilic cytoplasm. D) Mitotic figures are readily indentified

Immunohistochemically studies show tumor cells with diffuse and strong cytoplasmic staining for Cytokeratin and Smooth Muscle Actin (Figure 5). Negative staining for S-100, ER, PR and Her2/Neu was demonstrated (Figure 6).

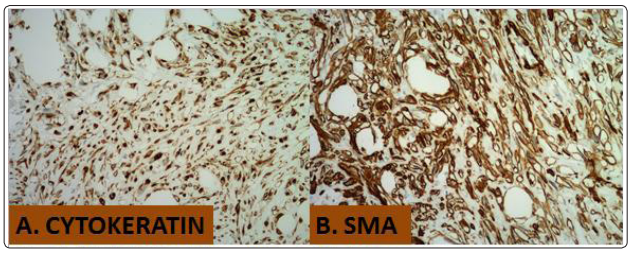

Figure 5: Pancytokeratin [CK AE1/AE3](A) and Smooth Muscle Actin (B) show diffuse and strong positive cytoplasmic staining.

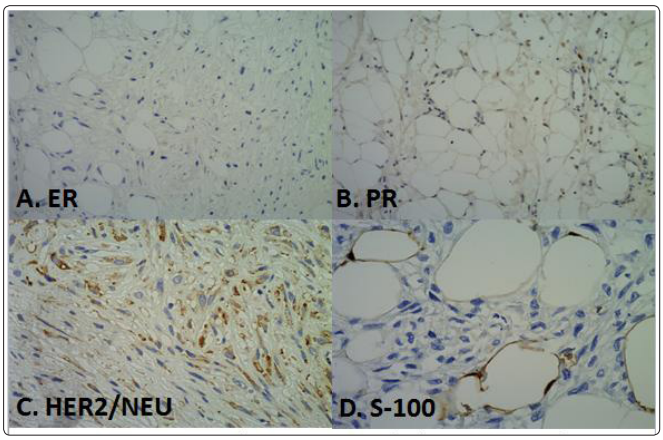

Figure 6: Tumor cells show no nuclear staining for ER & PR (A-B). Her2/Neu show no cytoplasmic membrane staining (C). S-100 is positive for mature adipocytes and negative in tumor cells (D).

Discussion

In 1974, Huvos et al. first introduced the term metaplastic carcinoma [6]. It encompasses a group of neoplasms characterized by differentiation of the neoplastic epithelium into squamous

cells with intermixed nonepithelial elements including spindle cells, bone, cartilage, myxoid stroma, and anaplastic stroma with giant cells [7]. The World Health Organization (WHO) classifies MBC into (1) epithelial type and (2) mixed type. Epithelial-type MBC is classified into (1) squamous cell carcinoma, (2) adenocarcinoma with spindle cell differentiation, and (3) adenosquamous carcinoma. Mixed type MBC is classified into (1) carcinoma with chondroid metaplasia, (2) carcinoma with osseous metaplasia, and (3) carcinosarcoma [8]. See Table 1 for an outlined description of these classifications according to the WHO.

Table 1: World Health Organization histologic classification of metaplastic breast cancer

Epithelial type metaplastic breast cancer	Histologic features
Squamous cell carcinoma	Infiltrating squamous carcinoma with polygonal cells, eosinophilic cytoplasm and possible keratin pearl formation.
Adenocarcinoma with spindle cell differentiation	Poorly cohesive sheets of predominant spindle cell morphology; resembles a low grade sarcoma.
Adenosquamous carcinoma	Glands display varying degrees of squamous differentiation, characterized by pavement-like architecture, prominent intercellular bridges and, to a lesser extent, keratin formation.
Mixed-type metaplastic breast cancer	Histologic features
Carcinoma with chondroid metaplasia	Immunoreactive for S-100, patchy for cytokeratin while being negative for smooth muscle antigen.
Carcinoma with osseous metaplasia	Infiltrating carcinoma with osseous differentiation of the mesenchymal component.
Carcinosarcoma	Infiltrating carcinoma with a malignant mesenchymal component.

Adapted from Tavassoli FA, Devilee P: World Health Organization classification of tumors: tumors of the breast and female genital organs. Pathology and genetics of tumors of the digestive system. In World Health Organization Classification of Tumors. Lyon, France: IARC Press; 2003: 37-41.

Tse et al. classified MBC into three groups: epithelial-only carcinoma, biphasic epithelial and sarcomatoid carcinoma, and monophasic spindle cell carcinoma. A total of 34 metaplastic carcinomas were included in the report. 24 cases are metaplastic carcinoma with a sarcomatoid or spindle cell component, with 14 (58%) of the 24 cases being biphasic and 10 (42%) of the 14 cases being monophasic [9]. Most metaplastic carcinomas are sporadic, but there may be a slight propensity for metaplastic spindle cell carcinoma to arise from pre-existing lesions, including papillomas, complex sclerosing lesions and nipple adenomas [10].

The clinical presentation of our case has several similarities from other Metaplastic Spindle Cell Breast Carcinomas. Our reported case presented as a unilateral left breast mass. In literature, the most frequent presentation was a unilateral, rapidly enlarging breast mass. A study by Abdul Hameed et al revealed 1 out of 7 cases with right laterality and one case which is bilateral. 5 out of 7 cases presented on the left, similar to our current case [11]. The median age at diagnosis, tumor size range, lymph node involvement, hormonal profile, Her2/neu status and outcome are equally diverse.

According to a study by Park et al, all Metaplastic Breast carcinoma cases were females. Their mean age at diagnosis was 49 years (range 28-68 years old). [5] Similarly, other studies revealed age range at diagnosis as young as 14 years to as old as 90 years with mean age of 52 years [3,11-14]. Our case presented in a 54-year-old female in her postmenopausal stage, which is consistent with the literature.

According to various case reports of Metaplastic Breast Carcinoma specifically the Spindle Cell subtype with a total of 59 cases, the mean age is 60, which ranges from 27 to 96 years old, with more patients in the premenopausal and postmenopausal stage [4,15-17].

Most case reports of Metaplastic Breast Carcinoma suggest a fairly large tumor size. In a study by different authors, the median tumor size of metaplastic breast carcinomas was 6.64 cm ranging from 2.5 to 18cm [3,11,18]. In our case, the tumor size was 10 x 11 x 6 cm, which was consistent with the literature. Several studies of Metaplastic Breast Carcinoma, Spindle Cell subtype present with sizes ranging from 1.5 to 20 cm with mean tumor size of 4.65 whereas smaller tumor sizes have also been reported with metaplastic carcinoma of the breast but data are sparse [4,15,16]. In a study carried out in Nottingham, England the mean tumor size was reported 1.6 cm ranging from 0.7 - 2.4cm [10].

In literature, among the histologic classification of Metaplastic Breast Carcinoma, the most common subtype is the spindle cell type, which demonstrates cells forming poorly cohesive sheets of predominant spindle cell morphology. The spindle cell component can be challenging to differentiate as it often resembles a low-grade sarcoma or a reactive process such as granulation tissue [19]. Khan et al. collected 19 cases of Spindle cell carcinoma of the breast from a 15year period. Four of the tumors were intermediate grade and fifteen were high grade. Six of the tumors contained the usual infiltrating ductal component of conventional carcinoma [15]. In our case, the tumor is predominantly comprised of spindle cells and cells resembling lipoblasts, without associated squamous or glandular component. However, lipoblastic features present in our case was not observed in any of the Metaplastic Breast carcinoma subtypes. This makes our case of Metaplastic Breast Carcinoma, Spindle cell subtype unusual.

Immunohistochemistry has an important role in the pathology of breast disease. IHC evaluates overexpression of the receptor protein at the surface of the cells. A pancytokeratin (CK) panel is used to distinguish Metaplastic CA from Phyllodes tumors (PT), primary sarcomas, and fibromatoses. Cytokeratin (AE1/AE3) remains the most widely used and the most sensitive marker for defining the metaplastic spindle cells, particularly the monophasic subtype. Smooth muscle actin (SMA) has long been used as a myoepithelial marker in breast pathology diagnosis as a sensitive marker of myoepithelial differentiation. In our case, the tumor was found to be positive for Cytokeratin and Smooth Muscle Actin (Figure 5) showing diffuse and strong cytoplasmic staining. S-100 is known to have a wide distribution in human tissues, including, neurons, Schwan cells, melanocytes, myoepithelial cells and various epithelia (especially in the breast, salivary glands, sweat glands and female genital system). Representative sections from our case show positive staining for mature adipocytes and negative S-100 in tumor cells (Figure 6).

Carter et al. studied 29 cases of Spindle Cell Carcinoma of the breast from a 10 year period. All cases contained greater than 80% spindle cell component. The cases showed a range of nuclear grade (7 low, 9 intermediate, and 13 high). Definitive axillary lymph node involvement was seen in only 1 of 20 cases (5%) that had axillary lymph node biopsies, and this patient had a tumor with 20% grade 3 invasive ductal component. The authors report that all cases were negative for ER, PR and Her2/Neu [4].

As in the present case, the majority of MBCs is triple negative for estrogen receptors (ER), progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2) expression (Figure 6). The absence of the predominant glandular epithelial component may explain the rarity of ER/PR expression. Taken together with the pathologic features described above, this immunohistochemical profile supports the diagnosis of metaplastic carcinoma with spindle cell differentiation.

One hundred cases of spindle cell carcinoma were examined by Wargotz et al. in 1988. Lower rate of nodal metastasis are seen in purely spindled/sarcomatoid tumors, as demonstrated in our reported case. Out of 47 patients with axillary dissection, only 6% had lymph node metastases. Distant metastases developed in 30 patients, and 29 (97%) of these died of their disease [20]. In the study by Khan et al, axillary lymph node involvement was seen in 6 of 15 cases (40%) that underwent a lymph node dissection [15]. In a study by Tse et al. 25 cases had known histologically proven axillary status at the time of surgery, 14 (56%) patients showed positive axillary lymph node metastases [9].

The incidence of stage IV disease at presentation for MBC is high. In one single institution study by Park et al, 10.3% of patients with MBC had stage IV disease at presentation. The incidence of distant metastasis cases in MBC were reported as 3.3-13.2% [5]. In a study by Carter et al. eleven patients (46%) developed metastatic disease, most commonly to the lung, followed by bone, pleura, mediastinum, liver and brain. Median survival for these patients was 11.5 months [4]. Our case was lost to follow-up after surgery. No oncologic treatment was documented in the out-patient department records. A study conducted by Wargotz et al. showed median follow-up was 63.5 months. Six patients (32%) had local recurrence, 5 of whom went on to have metastatic disease. Overall, 11 patients (58%) developed metastatic disease, with the lung being the most common site, followed by bone and liver. Eleven patients (58%) died of breast cancer. The median survival was 18 months [11].

Although the response of MBC to systemic chemotherapy has been consistently poor, neoadjuvant chemotherapy can still be minimally effective at reducing tumor burden and preventing progression of disease. Chen et al. reported an 83% progression rate in patients who received neoadjuvant chemotherapy [20].

Conclusion

Metaplastic breast carcinoma (MBC) is a rare subtype of invasive breast cancer that tends to have a variety of distinct histologic designations, as well as an aggressive clinical presentation. The clinical behavior is as diverse as the histology. Most of the cases in literature presented with advanced clinical stages. Despite the larger tumor size, MBC presents with axillary nodal involvement less frequently with lower potential for lymph node metastasis. Most metaplastic cancers are estrogen receptor (ER), progesterone receptor (PR) and Her2-neu negative with fewer therapeutic options. They have characteristics that result in a worse overall prognosis compared to other triple negative breast carcinoma. However, in a small study on the prognosis of metaplastic carcinoma, patients with non-triple negative metaplastic carcinoma had poorer prognosis than those with triple negative breast Cancer [21].

Due to the low response rate with chemotherapy, surgical intervention should be the first step in management of patients with operable tumors, regardless of tumor size. The disease tends to recur locally and frequently metastasizes to the lung. Radical local and adjuvant treatment by radical mastectomy followed by radiation and chemotherapy is recommended for the aggressive presentation of this case. Patients with metaplastic carcinoma who receive adjuvant chemotherapy have demonstrated a better survival rate than those who do not. However, due to the small number of cases that occur, it is difficult to perform further cohort randomized controlled trials. The prognosis reported in the literature is quite variable. Tumor size at diagnosis has been postulated as the single most useful prognostic indicator and the mesenchymal elements involved, may also have some importance in prognosis. Relative data in this aspect need to be accumulated in the future. Further studies are warranted to explore potential therapeutic agents for metaplastic carcinomas.

References

1. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ (2012) WHO classification of tumors of the breast. World Health Organization classification of tumours. 4th ed. Lyon: IARC Press 48-52.
2. Ellis, IO, Schnitt SJ, Sastre-Garau X, et al. Invasive breast carcinoma. In: Tavassoli FA, Devilee P, eds. Tumours of the Breast and Female Genital Organs. Lyon: IARC Press; 2003: 13-59.
3. Al Sayed AD, El Weshi AN, Tulbah AM, Rahal MM, Ezzat AA (2006) Metaplastic carcinoma of the breast clinical presentation, treatment results and prognostic factors. Acta Oncol 45: 188-195.
4. Carter MR. Hornick JL. Lester S. Fletcher CD (2006) Spindle cell (sarcomatoid) carcinoma of the breast: a clinicopathologic and immunohistochemical analysis of 29 cases. American Journal of Surgical Pathology 30: 3009.
5. Park HS, Park S, Kim JH, Lee JH, Choi SY, et al. (2010) Clinicopathologic features and outcomes of metaplastic breast carcinoma: comparison with invasive ductal carcinoma of the breast. Yonsei Med J 51: 864-869.
6. Huvos AG, Lucas JC Jr, Foote FW Jr. (1973) Metaplastic breast carcinoma: rare form of mammary cancer. NY State J Med 73: 1078-82.
7. Oberman HA (1987) Metaplastic carcinoma of the breast. Am J Surg Pathol 11: 918-929.
8. Tavassoli FA (1992) Classification of metaplastic carcinomas of the breast. Pathol Annu 27: 89-119.
9. G M Tse, P H Tan, T C Putti, P C W Lui, B Chaiwun, et al. (2006) Metaplastic carcinoma of the breast: a clinicopathological review. J Clin Pathol 9: 1079-1083.
10. Denley H1, Pinder SE, Tan PH, Sim CS, Brown R, et al. (2000) Metaplastic carcinoma of the breast arising within complex sclerosing lesion: a report of five cases. Histopathology 36: 203-209.
11. Abdul Hameed Baloch, Shakeela Daud, Jameela Shuja, Adeel Ahmad, Fateh Ali, et al. (2014) Metaplastic Carcinoma of the Breast: A Clinical Study of 7 Cases from Balochistan 3: 1-5.
12. D. Rayson, A. A. Adjei, V. J. Suman, L. E. Wold ,J. N. Ingle. (1999) Metaplastic breast cancer: Prognosis and response to systemic therapy Annals of Oncology 10: 413-419.
13. Verónica Arce-Grijalva, Teresa Vela-Chávez, Víctor M Pérez-Sánchez, Eva Ruvalcaba-Limón (2007) Metaplastic

carcinoma of the breast: a clinical and pathological study of 40 cases. BMC Cancer 7: A6

14. Brenner RJ, Turner RR, Schiller V, Arndt RD, Giuliano A (1998) Metaplastic Carcinoma of the Breast: Report of Three Cases. Cancer, 82: 1082-1087.
15. Howayda S Abd (2006) Breast spindle cell tumours: about eight cases. Diagnostic Pathology 1: 13.
16. Michio Maemura, Yuichilino, Tetsunari Oyama, Toshiaki Hikino, Takao Yokoee, et al. (1997) Spindle Cell Carcinoma of the Breast. Jpn J Clin Oncol 27: 46-50.
17. Khan HN, Wyld L, Dunne B, Lee AH, Pinder SE, et al. (2003) Spindle cell carcinoma of the breast: a case series of a rare histological subtype. European Journal of Surgical Oncology 29: 6003.
18. Kaufman MW, Marti JR, Gallager H.S, Hoehn J.L (1984) Carcinoma of the Breast with Pseudosarcomatous Metaplasia. Cancer 53: 1908-1917.
19. Luini A, Aguilar M, Gatti G, Fasani R, Botteri E. et al. (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.
20. Wargotz ES. Deos PH. Norris HJ (1989) Metaplastic carcinomas of the breast. II. Spindle cell carcinoma. Human Pathology 20: 73240.
21. Chen IC, Lin CH, Huang CS, Lien HC, Hsu C, et al. (2011) Lack of efficacy to systemic chemotherapy for treatment of metaplastic carcinoma of the breast in the modern era. Breast Cancer Res Treat 130: 345-351.