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Clinicopathologic Characteristics of Malignant Non-Hematopoietic Tumors First Presented as an Axillary Mass with Emphasis on Occult Breast Carcinoma

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Abstract

Background: Non-hematopoietic malignancies first presented as an axillary mass constitute a unique clinical presentation. We investigated the incidence of various types of malignancies and aimed to define clinicopathologic variables that may assist in the diagnosis, with focus on occult breast carcinoma (OBC).

Design: We reviewed the pathology reports of cases with non-hematopoietic malignancies of the axillary region in our institution between 2000 and 2016. We included patients who presented first with axillary mass and with absence of a known primary. We recorded patients' age and gender, tumor characteristics including size, histologic type, number of positive lymph nodes, and the clinical management. Then we focused on BC which were divided into occult BC (OBC) or primary BC (PBC).

Results: There were 100 cases that met our criteria (28 melanoma, 7 sarcoma and 65 carcinoma). For carcinoma cases, there were 42 BC (19 OBC, 17 PBC, and 6 possible OBC), 17 non-BC, and 6 carcinoma of unknown primary (CUP). Tumors found incidentally were more likely to be of breast primary ($p=0.01$). Larger tumor size (in mm) favored melanoma or sarcoma over BC, non-BC carcinoma or CUP with median and range 61 (15,180), 60 (23,80), 30 (15,75), 31 (17,90), 26 (20,55), respectively ($p<0.001$). There were no differences in the histopathologic findings or clinical presentation.

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Conclusions: More than half of the patients with axillary malignancy have a tumor of non-breast origin. Therefore, clinical and pathologic studies are warranted to identify the primary site.

Keywords

axilla; occult breast carcinoma; melanoma; sarcoma; first presentation

INTRODUCTION:

The axillary region is an area in the body located between the arm and the lateral chest wall. It contains various tissue types including lymphoid tissue [axillary lymph nodes (ALN)], accessory breast tissue, skin adnexa with apocrine glands, and soft tissue including angiomatous, lepromatous, fibrous, muscular, chondro-osseous, and neuronal (1). Lymphadenopathy accounts for more than 80% of the axillary masses. The most frequent diagnosis is nonspecific benign lymphadenopathy. When a malignant tumor is encountered, it usually involves the ALNs (lymphoma or metastatic tumor from breast or non-breast) (2, 3).

When a non-hematopoietic malignancy is discovered in the axillary region with no readily known primary site, the first suspicion would be mammary origin, particularly in women. The literature does not offer any data about the incidence of mammary carcinoma (with primary breast tumor or without) vs. tumors from other sites. Occult breast carcinoma (OBC) is defined as mammary carcinoma involving the axillary lymph node with unidentifiable primary breast tumor using all the clinical and pathologic means including physical examination, imaging [(mammography, ultrasound and magnetic resonance imaging (MRI)] or pathologic examination of the mastectomy specimen (4). The literature describes both metastatic malignant melanoma of unknown primary (MUP) and carcinoma of unknown primary (CUP). However, it does not treat the axilla as a discrete entity (5).

The aims of this study are: 1) Evaluate the incidence of various types of non-hematopoietic malignancies first presented as axillary mass whether detected incidentally or as a chief complaint; 2) Examine the clinical and pathologic differences between various types of tumors; and 3) Focus on BC cases, particularly OBC and study the clinical presentation, the incidence, and the clinical management.

MATERIAL AND METHODS:

Case Selection:

The cases were identified at Roswell Park Cancer Institute through a computer-based search in PowerPath between 2000 and 2016 [under Institutional Review Board (IRB) #BDR 037113]. The cases were found using these keywords, “axillary lymph node”, “axilla”, “carcinoma”, “melanoma”, “sarcoma”, and “metastatic”. A total of one hundred cases fulfilling the inclusion criteria were found. The conditions were that: 1) the patient presented first with an axillary mass, through self-detection or incidentally found during imaging for unrelated reason; and 2) the patient had no prior history of malignancy unless proven to be unrelated to the axillary tumor. For melanoma patients, the skin examination and/or biopsy

should be negative for the primary site. Cases with prior presentation of a regressed pigmented lesion (n=8) were excluded.

Clinical and Pathologic Work-Up and Decision Tree:

There were two layers of the level of evidence for the site of origin: layer 1, clinical (physical exam and/or imaging); and layer 2, pathology [histomorphology with or without immunohistochemistry (IHC)] (Figure 1). When the clinical evidence was clear, the site of origin was decided (e.i. breast mass for BC). However, when the IHC was strongly against it, the diagnosis was based on the latter (e.i. the axillary mass is BC proven by IHC and the lung mass biopsy proven to be lung primary). The IHC evidence was considered strong when the panel included at least a single specific IHC stain such as TTF-1 for lung and thyroid, CDX-2 for gastrointestinal, PAX8 for Mullerian, or typical cytokeratin 20 staining pattern for Merkel cell carcinoma (6, 7). When there was no clinical evidence of the primary site through physical examination or imaging, we relied on histomorphologic and IHC findings. The tumor was considered melanoma when it had the proper histomorphology and had positive IHC specific stains (any mixture of S100, MART-1, HMB45, MITF, SOX10 and Melan A) (8). The tumor was considered Merkel cell carcinoma when the tumor had the proper histomorphology and showed the typical cytokeratin 20 staining pattern (6). The difference between carcinoma and sarcoma was based on the histomorphology (spindle cell neoplasm with or without matrix production such as chondroid or osteoid), while carcinoma is comprised of epithelioid cells and demonstrates expression of at least one keratin marker (AE1/3, HMW-CK, CAM 5.2, CK7) or EMA. One exception was synovial sarcoma that occasionally had biphasic morphology, epithelioid and spindle (9). In carcinoma cases, we relied on the histomorphology and IHC findings to define the primary site. The tumor was considered breast primary if the tumor had mammary histomorphology along with at least one positive marker including CK7, estrogen receptor (ER), progesterone receptor (PR), GATA3, Gross cystic disease fluid protein 15 (GCDFP-15) or mammaglobin and lacked markers normally not expressed in mammary carcinoma such as CK20 and TTF1; otherwise it was labeled as CUP. The location of the tumor played a role in the decision tree. If the location was skin based, the differential diagnosis was breast vs. skin adnexal primary neoplasm. When the tumor was not skin based, it was considered breast primary. In order to classify a tumor as OBC, MRI and/or the surgical resection (wide local excision or mastectomy) should be negative. If MRI and surgical resection were not performed, the tumor was considered possible OBC.

Other Clinical, Imaging, and Pathologic Features:

The patients' age and gender were extracted from the medical records. The clinical presentation was considered as self-detected when the patient complained of a self-palpated axillary mass, axillary or shoulder pain and/or paresthesia, constitutional symptoms, and/or skin ulceration. It was considered incidental when the tumor was detected by routine physical exam, or imaging either as a routine procedure or for staging/follow-up for other unrelated disease. Medical history of cancer including the type and site was also obtained, and cases proven to be related to the prior cancer were excluded from the study. The following findings were recorded for all cases: ALN dissection procedure (ALND, performed vs. not performed), number of positive ALN, largest tumor size, and type of

involved tissue (lymph node vs. soft tissue). The tumor size was measured pathologically when the tumor was resected; otherwise, the clinical measurement was recorded. When the patient was treated in the neoadjuvant setting, we used the size of metastasis as clinically measured prior to therapy onset. The clinical staging parameters were also recorded (i.e. visceral or bone involvement).

For BC, the cases were divided into PBC, OBC or possible OBC (see above). For statistical analysis only PBC vs. OBC were compared to each other. In addition to the abovementioned variables, the following variables were also recorded, histologic subtype (no special type vs. special type), surgical procedure [tumor removal (through wide local excision or mastectomy) vs. no removal], chemotherapy (CT), radiation therapy (RT) and hormonal therapy (HT).

For melanoma, we excluded all cases with prior history of overt melanoma (skin or mucosal) or regressed pigmented lesion. Then, we reviewed the pathology record looking for any biopsied pigmented skin lesion that was taken in an attempt to locate the primary site (n=7).

For sarcoma cases, the diagnosis was based on histomorphology when typical and/or absence of any specific IHC marker (i.e. keratin or melanoma markers). Moreover, the possibility of metaplastic BC arising from ectopic breast tissue was considered. In order to qualify for metaplastic BC, the tumor should express at least one keratin marker or has coexistent ductal carcinoma in situ per World Health Organization (WHO) criteria (10).

RESULTS:

Overall:

Figure 2 shows the distribution of the axillary tumors based on the histologic subtype and the site of origin. Table 1 shows the distribution of the diagnoses correlating with clinicopathologic variables. The site of origin correlated with gender ($p<0.001$), type of involved tissue (lymph node vs. soft tissue) (<0.001), and the initial presentation (incidental vs. patient complaint) ($p=0.01$). Patients with carcinoma or melanoma were more likely to undergo completion of ALND than patients with sarcoma ($p<0.001$).

There were nine patients with history of malignancy in whom the axillary tumor was proven to be unrelated by IHC. Three additional patients had concurrent malignancy in other organ that was proven unrelated to the axillary tumor (Table 2).

Clinical Presentation and Physical Examination:

The tumor was symptomatic in 86 patients (self-detected mass in 81, axillary swelling or pain in 3, 1 with respiratory symptoms, and 1 with abdominal pain). In 14 patients, the tumor was detected incidentally, one of which was detected during physical examination. The following additional complains were reported by patients: pain and/or paresthesia in 16, constitutional symptoms in 5, skin ulceration in 2, and one for each patient with pruritic rash, supraclavicular lymphadenopathy, inguinal mass or fever. The rest of the patients (n=71) did not have any additional symptoms.

Imaging:

Imaging and clinical examination identified the primary site in 34 patients (17 BC and 17 non-BC). Staging work-up identified 9 patients in whom the tumor was found in the viscera and/or bone (4 BC, 2 melanoma, and 3 non-BC). Three more patients with BC had concurrent primary carcinoma of other sites (kidney renal cell carcinoma with typical histomorphology, lung adenocarcinoma with TTF1+, and colon adenocarcinoma with CDX-2+).

Pathology:

The tissue was initially obtained via fine needle aspiration in 5 patients, core biopsy in 46, ALND in 8, excision in 40, and skin punch biopsy in one case. When the imaging studies and the clinical examinations were negative, histomorphology and IHC were able to identify the type of the tumor in 60 cases (28 melanoma, 7 sarcoma, 19 OBC, 6 possible OBC). Both clinical/imaging evaluation and pathologic examination (histomorphology and IHC) were unable to identify the site of origin in 6 carcinoma cases (Figure 2).

Breast carcinoma:

The total number of patients who had PBC was 17 and OBC 19, while 6 patients had possible OBC. Although all OBC cases had c-and/or p-T-stage 0, there was no statistically significant difference in the AJCC stage between PBC and OBC. Only 4 of OBC women had surgical excision/mastectomy, while 13 of 17 PBC women had surgical removal of tumor ($p<0.001$) (Table 3).

Mammography/ultrasound imaging was performed in 32 women. Among women who had PBC ($n=17$), imaging was able to detect a mass in the breast in 7 (41.2%) patients. MRI was performed on 30 women. Among women who had negative initial imaging results or mammography/ultrasound was not performed and subsequently underwent MRI ($n=27$), MRI was able to detect tumor in the breast in 7 (25.9%) women. However, two women who had negative mammography/US and MRI had PBC discovered by surgical excision and 1 woman had her PBC discovered by surgical excision but did not undergo MRI (Figure 3).

There was no difference in the rate of CT or RT between the two groups. As expected, however, the patients with PBC underwent breast surgical procedure more often than OBC ($p=0.002$). The 5-year OS rate for OBC and PBC was 89.5% and 84.2%, respectively.

Five tumors were triple negative and 6 were HER2+. Adjuvant CT was given for 10 women and neoadjuvant CT for 3, while 3 had no CT at all. HT was given to all women with ER+ except for a single woman whose status was unknown. The median and range of follow up time was 82 (2 to 184) months. Four women died due to disease after 47, 55, 88, and 147 months from diagnosis, respectively (Table 4).

Other tumors:

All patients with melanoma received thorough skin and mucosal examination looking for the primary melanoma site. Pigmented lesion was identified in 7 patients, none of which revealed melanoma (4 patients with melanocytic nevus, and one for each of the following,

tattoo, basal cell carcinoma, and capillary hemangioma). There were seven sarcomas (three pleomorphic sarcoma not otherwise specified, and 1 of each of chondrosarcoma, osteosarcoma, malignant peripheral nerve sheath tumor and synovial sarcoma. The most common site of origin for carcinoma after breast was lung, followed by Merkel cell carcinoma (Figure 2).

DISCUSSION:

To our knowledge, this is the first study to thoroughly evaluate this rare clinical entity of non-hematopoietic malignancy first discovered in the axillary region. The general purpose of the study is to serve as a reference when a clinician or a pathologist faces such clinical situation and to present the diagnostic possibilities one should consider during clinical evaluation and management. We also aimed to evaluate the clinical and pathologic finding of OBC in order to expand further the current knowledge of this rare entity.

There were a few clinical and pathologic variables that could assist the clinical team in narrowing down the primary site of the tumor including patient's gender, the size of tumor, the clinical presentation, and the type of involved tissue (LN vs. soft tissue). As expected, women were more likely to have breast primary carcinoma than men. The male to female ratio for melanoma patients was 2:1, consistent with a previous meta-analysis report (5). Smaller metastasis size was more consistent with carcinoma. Within the carcinoma groups (OBC, PBC, or non-BC), the size was not statistically different. The median size of the LN in OBC was 30-mm, consistent with the Institute Curie study (4). Generally, both melanoma and sarcoma tend to be clinically more aggressive than carcinoma. However, this finding may not be that useful as the range of the size of melanoma is quite wide (15-mm to 180-mm). That may explain why these tumors are larger at time of presentation than carcinoma. Conversely, when the tumor is found incidentally, it is more likely to be breast primary. That could be explained by the fact that breast is not a visceral organ, therefore, does not create clinical symptoms or signs, other than presenting as a palpable mass. When the tumor involves the soft tissue rather than the lymph node, it is more likely to be sarcoma. That could be explained by the fact that in most patients sarcoma is more likely to arise from the normal pre-existing soft tissue elements in the axillary region, while other malignancies present as true metastases to the axillary lymph nodes.

History of malignancy in itself could be misleading, as 9% of the patients had metastatic disease in the axilla that was different from their prior malignancy. Moreover, additional 3% of the patients had incidentally discovered concurrent but different malignancy elsewhere in the body while being evaluated for potential primary for the neoplasm found in the axilla. However, the rate of this type of clinical presentation is in reality smaller, as the cases with metastatic carcinoma that were consistent with the prior cancer were excluded from this study. We conclude that although clinical history is an important piece of the puzzle, the pathologist should be careful during histopathologic evaluation and perform, if necessary, a panel of IHC when the histomorphology does not fit with the prior or concurrent malignancy from potential primary sites. Indeed, it is imperious to underline that this should be dealt with on a case by case basis.

We found that melanoma is the second most common non-hematopoietic malignancy involving the axillary region after BC. We were very stringent in our criteria to include only melanoma cases with no prior history or with unidentifiable primary skin or mucosal sites during evaluation for potential primary in occult cases. Therefore, most cases were examined by a short panel of IHC due to the high suspicion of melanoma on histology.

The most common site of origin for carcinoma after breast was lung, followed by Merkel cell carcinoma. The pathologist should be aware of the increased incidence of Merkel cell carcinoma in this setting, as the differential diagnosis includes metastatic neuroendocrine carcinoma from other organs, particularly lung. In these cases, the characteristic pattern of perinuclear dot staining for cytokeratin 20 seen in Merkel cell carcinoma (6) is very useful in the differential diagnosis, as it is only very rarely seen in metastatic small cell carcinoma.

In a small proportion of cases (6%) the primary site of the tumor was not identified, these being designated as CUP cases. The improved ability of discovering the primary site is owed to the advancement of sophisticated imaging diagnosis and IHC over the last two decades (11). In our study population, the primary site was identified by clinical examination and imaging in 34% of cases, while IHC was helpful in 60% of cases. We reckon that the percentage of CUP may have been even smaller had molecular profiling been performed in the remaining cases. Nevertheless, these patients are currently treated based on the molecular profile of the metastatic disease and presence of targetable genes (12, 13).

The differential diagnosis of spindle cell malignant neoplasm in the axillary region is primary sarcoma of the axillary region versus metastasis from breast primary sarcoma, malignant Phyllodes tumor or sarcomatoid metaplastic carcinoma. Primary sarcoma diagnosis is in this setting a diagnosis of exclusion after careful clinical and imaging examination of breast masses. It is recognized that metaplastic carcinoma may arise from ectopic breast tissue present in the axillary region (14). In order to make a diagnosis of metaplastic carcinoma, at least one of the following two features should coexist: ductal carcinoma in situ or IHC expression of epithelial markers (10). In cases of malignant phyllodes tumor with sarcomatous component metastasizing to the axilla, the diagnosis is established after examination of the concurrent breast lesion. However, in our study, all sarcoma cases were found to be primary neoplasms arising from structures present in the axillary region. Although the number of cases is very small (n=7), there was no apparent predilection to a type of sarcoma. The remote possibility of sarcomas as part of phyllodes arising from accessory breast tissue was excluded based on the absence of epithelial component in all our axillary sarcoma cases.

It is difficult to compare our results with the published literature regarding OBC, as the imaging quality of US and mammography has improved significantly over the last two decades, and MRI is consistently used nowadays in the evaluation of patients with BC. In this study, we designated cases as OBC only when MRI was negative and/or pathologic examination of the breast resection specimens, if resection was performed, was negative for breast malignancies. In a meta-analysis of 7 published studies, MRI was found to have 90% sensitivity and 31% specificity in detecting non-palpable BC (15). The authors concluded that the high sensitivity of MRI makes it a good tool to identify OBC. In this study we

included only patients who presented with axillary mass. There was no uniform systematic approach in the patient population (e.g. MRI was not always preceded by ultrasound or mammography or MRI was not performed at all). Nonetheless, in our study population MRI was able to detect BC in 4 of 25 (16%) mammography/US-negative breasts and 3 of 10 (30%) breasts without preceding mammography/US. At the same time, MRI failed to identify BC in 2 of 17 (11.8%) cases (Figure 3).

We did not find a specific biomarker profile unique to OBC. The distribution of ER/PR/HER2 expression was not different from PBC and these were not different from the general population, findings consistent with previous studies (16). We could not compare OBC vs. PBC in terms of the clinical outcome and survival, as BC is biologically diverse and our cohort is too small.

In terms of the volume of the disease in the axilla, we found that the median number of involved lymph nodes was 2 with a median size of 30 mm. 18.8% of cases were stage pN3. The overall volume of the axillary disease was slightly less than the reported studies particularly the rate of pN3 which was previously reported to be around 50% (16–18). That could be explained by the fact that 2 patients did not undergo ALND procedure. The other possibility is that our study population was treated after year 2000 when imaging was much better in detecting the primary tumor. In the group of PBC, the median number of involved LN was 6.5 and the rate of pN3 was 28.6%. Some of these cases could have been misclassified as OBC prior to the year 2000.

Finally we conclude that non-hematopoietic malignancy first presenting with axillary involvement should be classified and evaluated as a unique clinical and pathologic entity. Although BC (occult or non-occult) is the most common tumor in women, other cancers should be considered in both men and women presenting with axillary metastatic disease. It is thus recommended that clinical oncologists obtain a comprehensive clinical history and perform the proper imaging work-up of these patients. For the pathologists, one should not assume that the tumor is BC without proper histologic and IHC evaluation. These patients should benefit from multidisciplinary evaluation within an academic center where direct collaboration between oncologist and pathologist will yield an accurate diagnosis with less effort and cost.

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Figure 1:
Decision tree. * A single case with IHC proven melanoma in the axilla with imaging showing lung mass. The lung mass stains as lung primary; OBC, occult breast carcinoma, MRI, Magnetic Resonance Imaging

Figure 2:
Schematic figure showing the distribution of diagnoses based on the histologic subtype and site of origin. BC, breast carcinoma; OBC, occult breast carcinoma; PBC, primary breast carcinoma; CUP, carcinoma of unknown primary

Figure 3:
Distribution of BC cases based on the way of detection; grayed cells = PBC; n, number; ND, not done

Table 1:

Clinicopathologic characteristics of the cases distributed based on the diagnosis

		Breast Ca	Carcinoma other	CUP	Melanoma	Sarcoma	P value
Gender	Male	1(2.4)	10(58.8)	3(50)	19(67.9)	2(28.6)	<0.001
	Female	41(97.6)	7(41.2)	3(50)	9(32.1)	5(71.4)	
Age	Median (range)	58.5(32,81)	59(50,85)	66(44,75)	57.5(38,79)	76(23,82)	0.244
Involved tissue	Lymph Node	40(95.2)	16(94.1)	4(80)	26(96.3)	0(0)	<0.001
	Soft tissue	2(4.8)	1(5.9)	1(20)	1(3.7)	7(100)	
No. lymph nodes	Median (range)	3.5(1,26)	2(0,19)	0(0,23)	3(0,49)	NA	0.303
Size	Median (range)	30(15,75)	31(17,90)	26(20,55)	61(15,180)	60(23,80)	<0.001
Initial clinical presentation	Patient complain	32(76.2)	16(94.1)	4(66.7)	28(100)	6(85.7)	0.010
	Incidental	10(23.8)	1(5.9)	2(33.3)	0(0)	1(14.3)	
Therapy	ALND-yes	32(78)	9(52.9)	4(66.7)	24(85.7)	0(0)	<0.001
	ALND-No	9(22)	8(47.1)	2(33.3)	4(14.3)	7(100)	

Tumors of unknown primary and cases with differential diagnosis BC vs. skin adnexal (n=6) were excluded; BC, breast cancer, CUP, carcinoma of unknown primary; ALND, axillary lymph node dissection; NA, Not Applicable

Table 2:

Cases with concurrent or history of malignancy unrelated to the current axillary tumor

History of malignancy	Final diagnosis of the axillary tumor
Renal cell carcinoma	Breast carcinoma (non-occult)
Thyroid papillary carcinoma	Breast carcinoma (possibly occult)
Melanoma	Breast carcinoma (possibly occult)
Colon adenocarcinoma	Breast carcinoma (occult)
Lung non-small cell carcinoma	Breast carcinoma (occult)
Prostate adenocarcinoma	Melanoma
Laryngeal carcinoma	Melanoma
Prostate adenocarcinoma and Urothelial carcinoma	Lung non-small cell carcinoma
Prostate adenocarcinoma	Lung non-small cell carcinoma
Prostate adenocarcinoma and Colon adenocarcinoma	Sarcoma-NOS
Non-Hodgkin Lymphoma	Carcinoma of Unknown Primary (breast vs. skin adnexal)
Concurrent malignancy	Tumor of the axilla
Kidney-Renal cell carcinoma	Breast carcinoma (non-occult)
Lung non-small cell carcinoma	Breast carcinoma (possibly occult)
Colon-Adenocarcinoma	Breast carcinoma (occult)

Table 3:

Clinicopathologic characteristics of BC cases distributed based on the clinical type of the tumor (occult, possible occult, or primary)

		PBC (n=17)	OBC (n=19)	Possible OBC (n=6)	P-value (PBC vs. OBC)
Age	Median range	57(44,77)	63(32,81)	60.5(45,79)	0.3
Initial clinical presentation	Patient complain	5(29.4) [^]	4(21.1)	1(16.7)	0.71
	Incidental	12(70.6)	15(78.9)	5(83.3)	
Histology	No special type	14(82.4)	18(94.7)	5(83.3)	0.33
	Special type	3(17.6)	1(5.3)	1(16.7)	
Primary tumor size (mm)		12(0 [*] ,48)	0(0,0)	NA	<0.001
T-stage	0	1(6.7)	19(100)	NA	<0.001
	1	11(73.3)	0(0)	NA	
	2	3(20)	0(0)	NA	
No. lymph node	Median (range)	6.5(1,26)	2(1,19)	NA	0.22
N-stage	1	5(35.7)	10(62.5)	NA	0.41
	2	5(35.7)	3(18.75)	NA	
	3	4(28.6)	3(18.75)	NA	
Lymph Node Size	Median (range)	30(15,50)	30(15,65)	36(20,75)	0.85
AJCC stage	2	4(26.7)	10(62.5)	NA	0.06
	3	9(60)	6(37.5)	NA	
	4	2(13.3)	0(0)	NA	
ER/PR	Positive	10(62.5)	10(52.6)	4(66.7)	0.73
	Negative	6(37.5)	9(47.4)	2(33.3)	
HER2	Positive	2(14.3)	6(37.5)	0(0)	0.23
	Negative	12(85.7)	10(62.5)	4(100)	
ALND	Yes	14(82.4)	17(89.5)	1(20)	0.65
	No	3(17.6)	2(10.5)	4(80)	
Breast surgery	Yes	13(76.5)	4(21.1)	0(0)	0.002
	No	4(23.5)	15(78.9)	5(100)	
Chemo	Yes	13(92.9)	13(81.3)	2(40)	0.6
	No	1(7.1)	3(18.7)	3(60)	
RT	Yes	11(78.6)	12(75)	2(40)	1
	No	3(21.4)	4(25)	3(60)	

* One patients treated with neoadjuvant therapy and has no residual invasive carcinoma;

[^] N(%)

Table 4:

Clinicopathologic characteristics of OBC

	age	ER	PR	HER2	LN+ (n)	LN size (mm)	Surgery	Chemo	RT	HT	Status	OS Months
1	32	ER–	PR–	HER2–	19	30	ALND + Mastectomy	Adjuvant	Yes	No	ANED	179
2	75	ER–	PR–	HER+	2	30	ALND	NK	NK	NK	AWD	67
3	70	ER+	PR–	HER2–	1	26	ALND	No	Yes	Yes	ANED	69
4	53	ER–	PR–	HER2–	4	25	ALND	Adjuvant	Yes	No	ANED	184
5	63	ER+	PR+	HER+	10	15	ALND	Neoadjuvant	Yes	Yes	ANED	167
6	70	ER–	PR–	HER2–	15	18	ALND	Adjuvant	Yes	No	DEC	88
7	56	ER–	PR–	HER+	5	60	ALND	Adjuvant	No	No	LFU	6
8	67	ER–	PR–	HER2–	0*	20	WLE	Neoadjuvant	No	No	ANED	124
9	80	ER–	PR–	NK	3	20	ALND	Adjuvant	Yes	No	DEC	147
10	40	ER–	PR–	HER+	9	65	ALND	Adjuvant	Yes	No	LFU	12
11	70	ER+	PR+	HER+	1	33	ALND	Neoadjuvant	Yes	Yes	DEC	47
12	47	ER–	PR–	HER2–	2	15	ALND	NK	NK	NK	LFU	2
13	64	ER+	PR+	NK	3	30	ALND +WLE	Adjuvant	Yes	Yes	ANED	141
14	73	ER+	PR+	NK	ND	30	None	No	No	Yes	DEC	55
15	41	ER+	PR+	HER2–	2	39	ALND + Mastectomy	Adjuvant	Yes	Yes	ANED	129
16	81	ER+	PR–	HER2–	1	50	ALND	No	Yes	Yes	LFU	82
17	53	ER+	PR–	HER+	1	42	ALND	Adjuvant	No	Yes	ANED	96
18	53	ER+	PR–	HER2–	1	45	ALND	Adjuvant	Yes	Yes	ANED	76
19	62	ER+	PR+	HER2–	ND	28	None	NK	NK	NK	LFU	2

* complete response post neoadjuvant therapy; NK, not known; ND, not done; LN, lymph node; ALND, axillary lymph node dissection; WLE, wide local excision; CT, chemotherapy; RT, radiation therapy; HT, hormonal therapy; ANED, alive with no evidence of disease; LFU, Lost to follow-up; AWD, alive with disease; DEC, deceased; OS, overall survival