

Patterns of Axillary Lymph Node Metastasis from Breast Cancer in Egyptian Patients

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ABSTRACT

Background: Although axillary lymph node metastasis is one of the most important determinants of breast carcinoma prognosis and adjuvant therapy, the patterns of axillary lymph node metastasis from breast cancer remain unclear.

Materials and methods: Fifty female patients with operable invasive breast cancer underwent complete axillary lymph node dissection (ALND), as part of their therapy. Forty-six patients underwent modified radical mastectomy, three underwent radical mastectomy and one underwent breast conserving surgery. The number of positive nodes, as well as their levels were recorded. Special group of lymph nodes at the cords of the brachial plexus, named brachial lymph nodes (BLN), were resected separately. Detailed pathological study of the tumor and detected nodes were done.

Results: Thirty-seven patients (74%) were premenopausal and 26% were postmenopausal. The median age of the studied group was 45 years. Tumor was found in the upper outer quadrant in 50% of the cases. Invasive duct carcinoma was the commonest histopathological type (84%). Patients with stage II constituted 84% of the total sample, while stage III were 16%. The median number of nodes identified in the dissection was 18.5 lymph nodes. A total of 41 patients (82%) showed pathologic involvement of lymph nodes, 46% had 1 to 3 positive nodes and 24% had 4 to 9 positive nodes. The frequency of lymph node metastasis was 80% at level I, 34% at level II, 20% at level III and 4% at BLN. Brachial nodes were detected in 22 patients (44%). Their number ranged from 1 to 4 with a mean of 1.86. Only two patients (4%) had positive BLN associated with lymph node metastases at all levels of the axilla.

Conclusion: In Egypt, we are still dealing with relatively advanced cases of breast cancer. Complete ALND is advised in all patients with invasive breast cancer. BLND is specially recommended in patients with clinically positive axillary lymph nodes.

Key Words: *Axilla - Breast neoplasm - Axillary lymph*

nodes - Prognosis - Risk factors.

INTRODUCTION

Breast cancer is the commonest cancer among women worldwide. It accounts for 33% of all female cancers at the National Cancer Institute, Cairo University [6].

Treatment of the axilla by surgery with or without radiotherapy remains an integral part of the management of patients with invasive breast cancer. In general, the standard treatment of the axilla involves axillary lymph node dissection (ALND) in which surgical clearance of axillary nodes with a minimum of level I & II is performed. ALND is an effective staging procedure and is essential for local control of the disease in the axilla. The ability of a level I/II dissection to provide adequate regional control in a group of patients, who already have a 32% rate of pretreatment level III nodal metastases, is of great concern. A less complete axillary procedure is associated with a higher rate of axillary failure [1,26]. Level III dissection is probably superior to radiotherapy in preventing axillary relapse which is a miserable condition that is difficult to treat [9,11].

With increased emphasis on mammographic screening and early detection, the incidence of node positive breast cancer is decreasing. Today, in western series, only 30% to 40% of all invasive breast cancers are node positive [15]. Hence, the clinical staging of regional lymphatics and the emergence of intraoperative lymphatic mapping and sentinel lymphadenectomy

to obviate complete axillary lymph node dissection in patients with breast carcinoma is currently receiving much attention in the medical literature for early breast cancer [4,32]. The value of axillary dissection is to provide accurate prognostic information as well as excellent local control and to improve the survival rate in the node positive group [17].

In addition, nodal status has been one of the most important determining factors in recommending adjuvant chemotherapy for patients with breast carcinoma [5]. It was suggested that improved survival is associated with a more complete axillary lymph node dissection in patients with stage I breast cancer [25]. For proper diagnosis, the surgeon should provide the pathologist with a specimen containing at least 10 lymph nodes [3]. There is a 25-30% error in the clinical staging of the axilla, that is 25% of palpable nodes will be uninvolved on histological analysis, while 30% of axilla with no palpable nodes will be involved. As a consequence, axillary dissection has been the standard method to evaluate axillary node involvement [24].

However, variations in axillary anatomy have not been described in most texts of operative surgery or anatomy [16]. So, come the importance of determining the potentially involved groups of axillary lymph nodes in patients with invasive breast cancer.

The aim of this work is to highlight the pattern of axillary node metastases in Egyptian patients with breast cancer. Moreover, we have to detect any variations in the sites of lymph node groups to be involved as well as the nodal bearing tissue in the pad of fat anterior and above the cords of brachial plexus (brachial nodes).

PATIENTS AND METHODS

The present prospective study was conducted on fifty female patients with operable primary breast cancer treated in the department of surgery, National Cancer Institute, Cairo University, between December 1998 and April 2000.

After admission, all patients were subjected to full history, thorough clinical examination, preoperative investigations including CBC, liver function tests, kidney function tests, blood sugar test, as well as mammography. Metastatic work up in the form of chest X-ray, abdominal

sonography and bone scanning were done. According to the international TNM staging system, all patients had operable breast cancer T1, T2, T3; any N, M0 were included in the study. Patients with locally advanced and metastatic breast cancer were excluded from the start. All patients were candidates to surgery either radical mastectomy, modified radical mastectomy or breast conserving surgery.

Forty-six patients underwent modified radical mastectomy, three underwent radical mastectomy and one patient underwent breast-conserving surgery. The specimens were examined pathologically and the tissues removed were assessed regarding the site and size of the tumor. The tissues removed were preserved in formaldehyde and then dissected meticulously for detection of the total number of lymph nodes in the axilla. The breast tissues processed were routinely embedded in paraffin. Sections were prepared and stained by Hematoxylin and Eosin, examined microscopically for histological type and grade of the tumor. Different cut sections were taken from different lymph nodes detected and were prepared and examined for the presence or absence of metastatic deposits and the presence of capsular invasion. The number of positive nodes, as well as their level, was recorded.

The brachial nodes were defined in this work as the pad of fat containing lymph nodes anterior and above the cords of the brachial plexus, behind the insertion of the pectoralis minor muscle and medial to coracobrachialis muscle. This pad of fat, which was taken separately, was examined carefully to detect the presence of any lymph nodes. These nodes were examined microscopically and any positive nodes were reported. Routine postoperative care was adopted and all the patients had uneventful postoperative periods. Follow-up of all patients especially for arm edema was done for a minimum of one year.

RESULTS

The present study was conducted on fifty female patients with primary breast cancer. Their age ranged from 29 to 70 years with a median age of 45 years and a mean of 47 years. The highest frequency of age was found between 41 and 50 years (44%). Thirty-seven patients (74%) were premenopausal (below 50 years)

and thirteen patients (26%) were postmenopausal (above 50 years).

The tumor site was found more commonly in the upper outer quadrant of the breast (in 50% of cases), followed by the retro-areolar region (in 18% of cases), then the other quadrants.

As regards surgical staging, about 80% of the tumors were T2, while T3 constituted 18% of cases and T1 were only in 2%. The tumor size ranged from 1 to 10 cm with a median tumor size of 4 cm.

As regards the pathological typing, invasive duct carcinoma was the commonest histopathological type (84%) Pathological staging revealed that patients with stage II constituted 84% of the total sample, while those with stage III were 16%.

The number of the examined lymph nodes in the 50 patients ranged from 10 to 30 lymph nodes with a median of 18.5 lymph nodes. The brachial nodes were detected in 22 patients of the fifty cases (44%). Their number ranged from one to four lymph nodes with a mean of 1.86. However, only two patients of the total study (4%) had been proved to have positive brachial lymph nodes (Figs. 1&2). There were associated lymph node metastases in all levels of the axillary lymph nodes in these two patients. In both of them, the tumor was T2 (4 cm each), both were premenopausal and the tumors were invasive duct carcinoma on histopathological study.

Among the 50 patients, 41 patients showed pathologic involvement of lymph nodes (82%), 46% had one to three positive nodes and 24% had four to nine positive lymph nodes. The rest (9 patients constituting 18%) had no lymph node deposits.

In positive lymph node patients, the incidence of positive nodes at different levels of the axilla is shown in Table (1). Capsular invasion was evident in 22/41 patients with positive axillary lymph nodes.

The frequency of lymph node metastases in each level is shown in Table (2). Level I showed the highest frequency (80%).

The present results show that level I axillary lymph nodes were especially affected, whatever

the tumor site in the breast, as shown in Table (3).

It was also observed that, as the tumor size increased, more lymph node levels were involved (Table 4).

The relation between histopathological types of the tumor and the level of axillary lymph node metastasis was not obvious in this study (Table 5).

It seems that the tumor size and site were more important in determining the level(s) of axillary lymph nodes to be affected.

As regards the relation between the tumor grade and the levels involved, no conclusions could be done because most of the tumors in this work were grade II, only four tumors were of grade III as shown in Table (6).

Follow-up of the cases for a minimum of one year revealed that none of them developed arm edema in spite of brachial node dissection in conjunction with axillary clearance to level III nodes.

Table (1): Incidence of positive nodes in different levels of axillary lymph nodes (41 patients with positive nodes).

Level of positive axillary lymph nodes	No. of cases	Percent (%)
Level I alone	23	56.1
Level I & II	8	19.5
Level I, II & III	9	22
Level III alone	1	2.4
Total	41	100

Table (2): Frequency of positive nodes in each level of axillary lymph nodes (50 patients).

Axillary lymph nodes metastasis	No. of cases	Percent (%)
Negative axillary L.N. metastasis	9	18
Level I	40	80
Level II	17	34
Level III	10	20
Brachial L.N. metastasis	2	4

Table (3): Relation between tumor site and level of positive axillary lymph nodes.

Tumor site	Total No. of cases in each group	Level I		Level II		Level III		Brachial L.N.	
		No.	%	No.	%	No.	%	No.	%
U.O.Q.	25	19	76	8	32	6	24	1	4
U.I.Q.	7	6	85.7	1	14.3	-	-	-	-
L.I.Q.	5	5	100	1	20	-	-	-	-
L.O.Q.	2	1	50	1	50	-	-	-	-
Retroareolar region	9	7	77.8	4	44.4	4	44.4	1	11.1
Multicentric tumor	2	2	100	2	100	-	-	-	-

U.O.Q.: Upper outer quadrant.
 U.I.Q.: Upper inner quadrant.
 L.O.Q.: Lower outer quadrant.
 L.I.Q.: Lower inner quadrant.

Table (4): Relation between tumor size and level of positive axillary lymph nodes.

Tumor size	Total No. of cases	Level I		Level II		Level III		Brachial L.N.	
		No.	%	No.	%	No.	%	No.	%
T1 (< 2 cm)	1	1	100	1	100	-	-	-	-
T2 (2-5 cm)	40	31	77.5	12	30	8	20	2	5
T3 (> 5 cm)	9	8	88.9	4	44.4	2	22.2	-	-

Table (5): Relation between tumor histology and level of positive axillary lymph nodes.

Tumor histology	Total No. of cases	Level I		Level II		Level III		Brachial L.N.	
		No.	%	No.	%	No.	%	No.	%
Invasive duct ca.	42	33	78.6	11	26.2	7	16.7	2	4.8
Invasive lobular ca.	5	4	80	3	60	2	40	-	-
Combined duct & lobular ca.	1	1	100	1	100	1	100	-	-
Multicentric invasive duct ca.	1	1	100	1	100	-	-	-	-
Multicentric invasive lobular ca.	1	1	100	1	100	-	-	-	-

Table (6): Relation between tumor grade and level of positive axillary lymph nodes.

Tumor grade	Total No. of cases (50 patients)	Level I		Level II		Level III		Brachial L.N.	
		No.	%	No.	%	No.	%	No.	%
G I	0	-	-	-	-	-	-	-	-
G II	46	38	82.6	17	37	10	21.7	2	4.4
G III	4	2	50	-	-	-	-	-	-

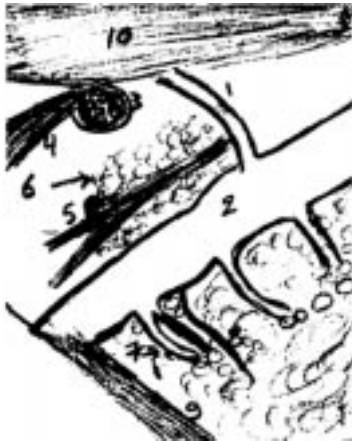


Fig. (1): Diagrammatic scheme of the brachial lymph nodes. 1- Cephalic vein. 2- Axillary vein. 3- Insertion of pectoralis minor muscle (cut). 4- Corachobrachialis muscle. 5- Cords of brachial plexus. 6- Pad of fat containing brachial lymph nodes. 7- Subcapsular vessels. 8- Nerve to latissimus dorsi muscle. 9- Latissimus dorsi muscle. 10- Pectoralis major muscle (retracted).

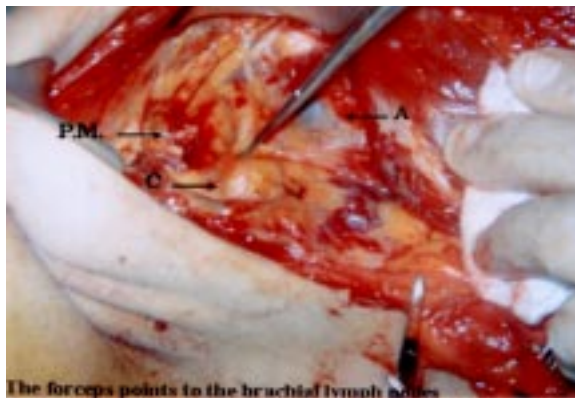


Fig. (2): Axillary dissection of brachial lymph nodes. A: Axillary vein. P.M.: pectoralis minor muscle. C: Cords of brachial plexus. The forceps points to the brachial lymph nodes.

DISCUSSION

Breast cancer is the commonest cancer among women, contributing for 30% of all female cancers. It affects one in 14 women during their life time, almost one every three affected women will die of the disease. Breast cancer constitutes 33% of all female cancers at the National Cancer Institute, Cairo University [6].

In the present work, 50 female patients with operable breast cancer were treated surgically by modified radical mastectomy (46 patients), radical mastectomy (3 patients) or breast conserving surgery (one patient), in a prospective non-randomized study. About 75% of the studied patients were premenopausal with a mean age of 47 years (i.e. one decade younger than

the corresponding age in western countries) [6]. This may explain the more aggressive nature of the disease among Egyptian patients.

Most patients (84%) had stage II disease. The commonest site for breast cancer was the upper outer quadrant that constituted 50% of the studied cases. This observation is confirmed by many authors [6,10,23]. T2 constituted the majority of cases (80%), T3 constituted 18% and T1 were 2%, with a median tumor size of 4 cm. Invasive duct carcinoma was found to constitute 84% of the pathological types in this series of tumors. This is not different from other reports on the common pathological types [6,22,31]. The majority of cases (92%) were grade II, while grade III tumors constituted only 8% of the studied patients, with no grade I cases.

Although the majority of cases (82%) were T1 and T2, only one case underwent conservative mastectomy, as most of them did not fit within the rules adopted in our department for breast conservation. These rules include:

- 1- Tumor size 3 cm or less.
- 2- Tumors that showed evidence of multicentricity in mammography or extensive intraduct component at frozen section study were not included.
- 3- Central tumors were excluded.
- 4- Ptotic breasts as well as huge breasts especially in elderly and obese patients were not included for their poor cosmetic results.
- 5- Patient's preference and written consent were also important factors in patient selection for conservative mastectomy.

There is a great difference between the kind of breast cancer we face and that reported in different series in western countries. This could be revealed if we compare our data with those reported in 1999 by Brenin et al. [2], where patients with clinical T1a tumors were 87% and grade I histology mounted to 92%, while patients with favorable tumor types constituted 91% of cases.

Axillary lymph node status is the most powerful prognostic factor in breast carcinoma. Axillary lymph node dissection is an important procedure in the surgical treatment of breast cancer. It is the gold standard for staging breast cancer and an important tool in the locoregional

control as well as its impact on deciding subsequent adjuvant therapy. However, it is associated with significant morbidity in terms of axillary pain, numbness and lymphedema.

The present study showed that among the 50 patients, 41 showed pathological involvement of lymph nodes (82%). On the other hand, in western countries, due to adopting early detection programs with widespread use of mammographic screening, only 30-40% of all invasive breast cancers are node positive. Therefore, two thirds of their patients have histologically negative nodes [15].

This explains the numerous reports that flooded the medical literature about the intraoperative lymphatic mapping and sentinel lymphadenectomy to avert axillary dissection with its complications in almost two-thirds of the axillary negative patients. However, the difficulty of using prediction models of axillary node involvement should not be underestimated [12,14,18,19,20,28,30].

In Egypt, in spite of the increased awareness of cancer and attempts at early detection, we are still facing relatively advanced cases with clinically palpable axillary nodes. The present study showed that 82% of the patients had nodal metastases. Whatever the tumor site in the breast, level I was the commonest to be involved with metastases. However, levels I,II,III were involved with metastases in 22% of patients with positive axillary nodes. In one patient, level III was the only site of axillary lymph node metastasis. Thus, complete axillary lymph node dissection is required for proper staging and for therapeutic potentials. This is in favor with Stewart et al. [26] who reported that a less complete axillary procedure was associated with a higher rate of axillary failure. Moreover, level III dissection is probably superior to radiotherapy in preventing axillary relapse [9]; when it occurs it is a miserable condition that is difficult to treat due to involvement of axillary vessels and cords of the brachial plexus [11,21].

Voss et al. [29] showed a high rate of level III lymph node metastasis, even in well differentiated tumors and until down staging was demonstrated following induction therapy they showed that a level III clearance offers the best prospect for axillary control. Hence, this work cannot agree with the old opinion given by Fisher et al. [8] that lower axillary dissection is

more than adequate.

In our studied cases, the number of axillary lymph nodes in the delivered surgical specimens ranged from 10 to 30 lymph nodes with a mean of 18.9 lymph nodes. Studies have advised that the minimum number of axillary lymph nodes to be examined to accurately determine nodal positivity or negativity should be at least 10 lymph nodes [3].

Iyer et al. [13] showed that the accuracy of the extent of axillary nodal positivity was related to the number of nodes examined. For patients with T1 tumors and 1,2 or 3 positive nodes, the minimum number of nodes examined needed for 90% accuracy is 19,20 & 20 nodes, respectively. For T2 tumors and 1,2 or 3 positive nodes a minimum of 20 nodes is required. These data emphasize how crucial proper axillary clearance is needed in the management of breast cancer.

In their valuable work, Utada et al. [27] showed that when the prognosis of breast cancer was considered from the viewpoint of lymph node metastasis, the location of lymph node metastasis (location number) as described in general rules was an excellent classification. However, we should be aware of possible differences in the prognosis depending on the number of positive nodes, as this is masked by the location number.

Variations in axillary anatomy have not been described in most texts of operative surgery or anatomy [16]. There are a few other lymph nodes associated in an indirect way with the breast [7].

In this work, we investigated what we call the brachial nodes contained within the pad of fat seen anterior and above the cords of the brachial plexus, behind the insertion of the pectoralis minor muscle and medial to the coracobrachialis muscle. One to four lymph nodes were observed in 44% of patients.

In 22 patients with proved brachial nodes, more than 15 axillary nodes were harvested to the pathologist. Moreover, 9% of these 22 patients proved to have positive brachial nodes and all the three levels of axillary nodes in these patients were positive. However, none of these patients developed arm edema during at least one year of follow-up period.

In the standard nodal dissection of breast cancer, we are limited to nodal bearing tissues at the level of the lower border of the axillary vein. Extension of the nodal dissection beyond that level carries the risk of post-dissection arm edema. However, removal of the brachial plexus nodes does not interfere with this concept, as it does not interrupt the lymphatic channels at the upper border of the axillary vein that drain the upper limb. Removal of such nodes prevents local recurrence at the brachial plexus, which is usually beyond resection.

Moreover, the present study showed that the tumor site and size were more important in determining the level(s) of axillary lymph nodes that will be affected with metastasis. This is consistent with what was stated by Iyer [13].

Conclusion:

In Egypt, breast cancer is more aggressive and we are still dealing with relatively advanced cases. Complete axillary lymph node dissection (ALND) is advised in all patients with invasive breast cancer for proper staging and therapeutic purposes. The accuracy of the extent of axillary lymph nodal positivity is influenced by the number of observed positive nodes, tumor size and the number of nodes examined. Under-estimation of the number of positive nodes will result in errors in the assessment of individual risk for loco-regional recurrence, distant lesions, death rate and will adversely impact on treatment.

Brachial lymph node dissection is especially recommended in breast cancer patients with clinically positive axillary lymph nodes. Further studies are recommended on more cases, to do step sectioning every 10 to 20 microns and to apply cytokeratin immunohistochemistry to know the exact incidence of metastases in these nodes.

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