

Intramammary lymph nodes in breast cancer

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Abstract

Introduction: Intramammary lymph node (IMLN) in breast cancer is under estimated. Pathological aspects were not commonly reported. Its impact on breast cancer management is controversial.

Methods: We report four cases of primary breast cancer presenting with IMLN treated at the radiation oncology department of Salah Azaiez Institut. We analyze the clinical profile, the prognostic significance and the appropriate management through a literature research.

Results: The mean age at the time of diagnosis was 59 years and they were all women. IMLN were seen on mammography and ultrasonography in three cases. IMLN was discovered incidentally during histopathology assessment in the fourth case. They were located in the same quadrant as the tumor in three cases. Three patients had metastasis within the IMLN and with capsula infraction in one case. Two of them had additional metastases in the axillary nodes. One patient had eight positive IMLN with negative axillary node. Three patients had a mastectomy while one patient had breast conservation surgery. They all had adjuvant chemotherapy and radiotherapy. One patient was lost from follow-up. The three others were disease free at last follow-up.

Conclusion: The incidence of IMLN, in breast cancer, is variable and their existence is not commonly assessed. Whether IMLN should be considered as an in-transit node in breast draining system is still controversial. Further studies on lymphatic mapping would answer to this question. IMLN involvement should be considered as a poor prognostic factor that requires an adequate adjuvant treatment.

Introduction

Intramammary lymph node (IMLN) is an anatomical variant that can be a site of regional dissemination of breast cancer. Most of the published studies are either case reports or retrospective series of sentinel-lymph-node technique in selective patients or pathological series in which a pathological protocol was used to search for IMLN on mastectomy pieces. According to the latter two types of series, IMLN is prevalent in 1-50% [1, 2]. A large proportion of these IMLNs were discovered incidentally on pathology. This implies that IMLN can

be invisible by routine imaging and thus can be missed in patients who receive a conservative treatment without sentinel lymph-node technique. The choice of the loco-regional treatment when an IMLN is discovered either preoperatively or during surgery is not a consensus because of the rarity of these cases.

In this study, we will present the epidemiological, anatomical and pathological aspects of IMLN through four case-reports and a literature research.

Methods

We report four cases of primary breast cancer having IMLNs discovered either by imaging methods or incidentally on pathology, treated at Salah Azaiez Institute. The clinical and pathological characteristics of the primary tumor were recorded. For each patient, clinical stage at presentation was classified according to the 2002 American Joint Committee on Cancer Staging System. Primary tumor treatment features were also recorded: type of surgical treatment, neoadjuvant or adjuvant systemic therapy use, radiation-therapy use and treatment outcome.

Results

The mean age at the time of initial diagnosis was 59 years (range from 41 to 70). The mean primary tumor size was 26 mm (range from 25 to 30 mm); 3 were T2 tumors, and one was T4d tumor. Tumors were invasive ductal carcinoma in three cases and the fourth was invasive lobular carcinoma. The pathological grade of the primary tumor was grade 3 in 3 cases and grade 2 in one case. Hormone receptor status was available for 3 patients and was positive in once. IMLNs were seen on mammography and ultrasonography in three cases and were incidentally discovered on histopathologic assessment in one case. The IMLN was located in the superior and external quadrant in 3 cases and in the inferior internal quadrant in the other case. Tumors were located in the same quadrant as IMLN in three cases. None of the patients had a sentinel lymph node biopsy. Three patients had metastasis within the IMLN and with capsula infraction in one case. Of the 3 patients with IMLN metastasis, 2 had additional disease in the axillary nodes (3N+/17N and 9N+/6R+/16) while 1 patient had an isolated metastasis in IMLN with no axillary node involvement and the fourth patient was axillary

and IMLN negative. Three patients had mastectomy while one patient had breast conservation surgery (IMLN negative). All patients had adjuvant chemotherapy and radiotherapy. One patient had endocrine therapy. One patient lost from follow-up. The three others were disease free after a median follow up of 48 months (range from 12 to 84) (Table1).

Table 1: Patient characteristics

	Case 1	Case 2	Case 3	Case 4
Age	65	61	70	41
Quadrant of IMLN	IIQ	SEQ	SEQ	SEQ
Quadrant of the tumor	SIQ	SEQ	SEQ	SEQ
Mammography & US	-	+	+	+
TNM	T2 N0 M0	T2 N1 M0	T2 N0 M0	T4d N1 M0
Type of surgery	Radical	Conservative	Radical	Radical
Histological type	DIC	DIC	LIC	DIC
pSize (mm)	25	30	30	30 & 15
SBR	3	3	2	3
IMLN status	8N+	N-	1N+/1R+*	1N+
Axillary status	8N-	19N-	3N+	9N+
Hormone receptors	Unknown	-	+	-
Chemotherapy	Yes	Yes	Yes	Yes*
Radiotherapy	50Gy	64Gy	50Gy	64Gy
Hormonal therapy	No	No	Yes	No

US: ultrasonography; DCI: invasive ductal carcinoma; LIC: lobular invasive carcinoma; SEQ: superior and external quadrant; SIQ: superior and medial quadrant; IIQ: inferior and medial quadrant; pSize: pathological size; 1N+/1R+: a positive IMLN with capsular rupture; Yes*: this patient had chemotherapy before surgery

Discussion

By definition, IMLNs are completely surrounded by breast tissue, and must be distinguished from low-lying axillary lymph nodes of level one of Berg. The 7th edition of the American Joint Committee on Cancer staging system does not consider IMLNs in breast cancer classification [3].

According to the literature, IMLNs are reported in 1% to 50% of breast cancer patients [2, 4-9]. The highest rates of IMLN were recorded by pathologists [2]. They were metastatic in 24% in Pugliese et al. study and in 27.2% in Intra et al. study [1,10].

The first to publish their results were Egan and McSweeney (initially in 1983 then updated in 1984) [6]. They performed a histological evaluation of mastectomy specimens sectioned into 5 mm-thick sections with a specifically designed protocol to identify IMLN. They found a 26% incidence of IMLNs. Jadusingh detected IMLN in only 7 of 682 specimens (1%) [4]. More recently, Shen et al. reported IMLN involvement in 28% of 130 cases associated with a primary breast malignancy [7]. Guth et al. identified 64 (31%) specimens with IMLNs where 20 were involved, and 44 were negative [11]. Schmidt et al. reported their dissection of cadaver breasts where 7.5% had IMLNs. Half of these nodes were not shown by mammography [12]. Stomper et al. who examined 1500 mammograms, found evidence of IMLNs in 13% [13]. IMLNs with benign features are present in approximately 5% of all patients undergoing mammography according to Gordon and Gilks [14].

The presence of IMLNs may not always be described by the reporting radiologist. Benign IMLN on mammography are typically described as a small nonpalpable mass less than 10 mm in diameter, well circumscribed, more or less lobulated

and characterized by a radiolucent center and a hilar notch, which represents fat in the hilum of the node. On ultrasonographic examination, the mass appears as a solid ovoid node, isoechoic or slightly hypoechoic and an echogenic area representing the hilar fat may be visible.

Deviations or changes during follow-up from the typical characteristic of benign IMLN, such as enlargement (> 1cm) with loss of the lucent centre and hilar notch, usually indicate involvement with metastatic disease as reported by Gunhan-Bilgen et al. [15]. The sensitivity of mammography or ultrasonography in the detection of IMLN metastasis is low: 3 cases in our study were reported as normal [15]. In Hogan et al. study, only 10% of IMLNs were identified on pre-operative imaging and four of them (19%) were described as abnormal [8]. MRI may be useful in diagnosing small IMLN metastasis with 93% sensitivity and 89% specificity using size-based criteria (defining ≥ 5 mm as positive) according to Kinoshita et al. [16]. However, MRI is very expensive compared with mammography and ultrasonography.

IMLN with abnormal radiologic features can be detected but differentiating malignant from benign, such as inflammation or hyperplasia, is impossible by imaging methods only. Therefore, any changes in radiological aspect of IMLN should be considered and a core biopsy using guide wire localization or fine needle aspiration has to be performed [17].

In the absence of systematic research of IMLN by imaging methods, their real frequency and their anatomical aspects are not well established. IMLN can be solitary or multiple, unilateral or bilateral. It is more frequently located in the upper outer quadrants which correlate with our cases [6, 12]. However, they may be located in all quadrants of the breast. According to Upponi et al. half of positive IMLN were located in the same quadrant as the primary tumor [17]. Egan and McSweeney found that IMLNs were located in all quadrants of the breast but were more likely to be positive in the same quadrant as the tumor [6]. IMLN was located in the same quadrant of the tumor in 3 of our cases and situated in a different quadrant than the tumor in one case. IMLN was involved in the latter case.

Some authors found that 72% to 81% of patients who had IMLN metastasis also had axillary lymph node involvement [7-9, 11]. Therefore, on the basis of the strong association of axillary metastases and positive IMLN, when a metastatic IMLN is encountered complete axillary lymph node dissection is recommended. The impact of the IMLN sentinel technique is controversial. IMLN was detected by sentinel technique in several studies [1, 7, 11, 18-21]. However the significance of this node remains unclear. Some authors consider it as in transit node in the classical lymphatic drainage of the mammary gland [19]. Others do not agree with this hypothesis and mandate an axillary-sentinel node to assess the axillary-node status [1, 18, 20, 21]. In our cases no patient had axillary invasion with a negative IMLN which is in favor of the first hypothesis. However, we cannot make any conclusion because of the small number of our cases.

Metastatic disease to the IMLN may significantly affect prognosis and it is an independent predictor of poor outcome in patients with breast carcinoma according to Shen et al. [7]. Guth et al. concluded that IMLN metastases are a marker for disease severity and that it may influence the choice of adjuvant therapy [11]. The benefit of systemic adjuvant therapy is difficult to assess. Nevertheless, IMLN need to be considered.

In cases of breast conservation surgery, a positive IMLN does not mandate a mastectomy as long as both the primary tumor and the IMLN can be resected with an adequate cosmetic result [22]. It shouldn't be considered as a multifocal disease. One of our cases, who had a small tumor at diagnosis, received a radical surgery because of a high number of IMLN which were all involved. For patients undergoing planned mastectomy, the pathologist have to be warned.

Conclusion

The incidence of IMLN, in breast cancer, is variable and their existence is not commonly assessed. Whether IMLN should be considered as an in-transit node in breast draining system is still controversial. Further studies on lymphatic mapping would answer to this question. IMLN involvement should be considered as a poor prognostic factor that requires an adequate adjuvant treatment.

Conflict of interest: Any**References**

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