Short Report

Study of axillary lymph node asymmetry in a female population

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ABSTRACT

We analysed a large series of axillary lymph nodes, with and without metastases following radical mastectomy for breast cancer. We found left/right asymmetry in numbers of lymph nodes, and also asymmetry of lymph node dimensions, which could have been the caused by tumoral antigenic stimulation. The distribution of hyperplastic node patterns differed significantly.

Key words: Mastectomy; breast cancer; hyperplasia; tumoral antigenic stimulation; histopathological changes.

INTRODUCTION

A lymph node (LN) is the terminal organ of efferent lymphatic vessels; it drains extracellular fluid and collects antigens from tissue deposition sites. Its function is the initiation and modulation of immune responses. LNs are scattered throughout the body, usually in groups, as in the axilla or the groin. Reactive LNs are very small round and reniform structures; when they are palpable, it usually means that there has been some enlargement through immunological stimulation (van der Valk & Meijer, 1977).

Asymmetry in LN numbers between the right and left sides has been described in various sites, including the axillary group (Sapin, 1980; Luscietti, 1980). This asymmetry was more evident in male subjects than in female ones, according to Sapin (1980), contradicting earlier findings (Misnik, 1979). Moreover, great variability in the number and size of LNs has been described in various regional groups (Sapin, 1989).

In this study, we analysed a large series of axillary LNs obtained from specimens following radical mastectomy for breast carcinoma. We focused particularly on LN number, LN dimension and on the type of hyperplasia.

MATERIALS AND METHODS

Axillary LNs were obtained from 240 radical mastectomies (120 right and 120 left). All subjects were women; their mean age was 56.3 (range 21–77, S.D. 6.3) y. LNs were accurately isolated by dissection from the axillary fat, then formalin-fixed and paraffin-embedded along their major axis. Sections were stained with H&E (5 sections) and PAS (5 sections); metastatic involvement was excluded using human cytokeratin (DAKO, cat. no. N1589, monoclonal, 1:50) immunostaining (LSAB2 kit peroxidase, DAKO, Cat. No. K0677) in uncertain cases. In the absence of metastasis, we registered the length of the LN grouping them in 6 dimensional categories (< 2 mm, 2 to < 5 mm, 5 to < 7 mm, 7 to < 10 mm, 10 to < 15 mm, and 15+ mm), and the type of hyperplasia (simple, follicular, paracortical, sinusoidal or medullary, or mixed; Fig.). Standard statistical analyses were applied to calculate means and standard deviations. A one way analysis of variance was used to determine the presence of significant differences within the data. Differences between the means were regarded as significant when a value of $P < 0.05$ was obtained.

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Fig. 1. The classic lymph node and the different types of hyperplasia. (*A*) Classic type. (*B–E*) Simple hyperplasia. (*B*) Follicular; (*C*) paracortical; (*D*) sinusoidal; (*E*) medullary. (*F–P*) Mixed hyperplasia (*F*) medullary + sinusoidal; (*G*) medullary + follicular; (*H*) paracortical + follicular; (*I*) follicular + sinusoidal; (*J*) paracortical + medullary; (*K*) paracortical + sinusoidal; (*L*) paracortical + follicular + medullary; (*M*) medullary + paracortical + sinusoidal; (*N*) paracortical + follicular + sinusoidal; (*O*) medullary + follicular + sinusoidal; (*P*) follicular + paracortical + sinusoidal + medullary.

RESULTS

We isolated 5961 LNs, 3135 (52.6%) from the right side, finding an average of 24.5 LNs for each case (S.D. 2.0), with a mean of 26.1 LNs (S.D. 2.2) in the right side and a mean of 23.6 (S.D. 1.7) in the left side.

Altogether 1250 of 5961 (22.5%) presented focal to massive metastasis, mainly (699, 53.5%) in the right side. The remaining 4711 (73.5%), 2526 (53.6%) of which were isolated from the right side, presented different dimensions and types of hyperplasia. Most of the lymph nodes (1837, 39%) ranged in size from 2 to 5 mm, with a few nodes larger than 15 mm (190,

Table 1. *Distribution of HMG LNs by dimensional category*

Size	Right (n = 2426; 53.6%)	Left (n = 2285; 46.4%)	Total (n = 4711; 100%)
< 2 mm	659 (61.1%)	420 (38.9%)	1079 (22.9%)
2 < 5 mm	1038 (56.5%)	799 (43.5%)	1837 (39%)
5 < 7 mm	374 (49.3%)	384 (50.7%)	758 (16.1%)
7 < 10 mm	250 (44.2%)	315 (45.8%)	565 (12%)
10 < 15 mm	125 (44.3%)	157 (45.7%)	282 (6%)
> 15 mm	80 (42.1%)	111 (47.9%)	190 (4%)

Table 2. *Distribution of OHG LNs by dimensional category*

Size	Right (n = 570; 57.2%)	Left (n = 426; 42.6%)	Total (n = 996; 100%)
< 2 mm	136 (62.4%)	82 (37.6%)	218 (21.9%)
2 < 5 mm	265 (59.3%)	181 (40.7%)	447 (44.9%)
5 < 7 mm	99 (54.7%)	82 (45.3%)	181 (18.2%)
7 < 10 mm	48 (48.5%)	51 (51.5%)	99 (9.9%)
10 < 15 mm	15 (42.9%)	20 (57.1%)	35 (3.5%)
> 15 mm	7 (36.8%)	9 (63.2%)	16 (1.6%)

Table 3. *Distribution of HMG LNs by type of hyperplasia*

Simple hyperplasia	Total (n = 1480, 31.4%)	Right	Left
F	663	362	301
P	508	260	248
S	223	129	94
M	86	44	42
Mixed hyperplasia	Total (n = 3231, 68.6%)		
F+P	716	351	365
F+S	519	269	250
F+P+S	450	242	208
F+P+M	406	206	200
P+S	348	175	173
P+S+M	331	157	174
F+S+M	198	99	99
F+M	72	40	32
F+P+S+M	69	36	33
P+M	66	32	34
S+M	56	26	30

F, follicular; P, paracortical; S, sinusoidal; M, medullary.

4%) (Table 1). The types of hyperplasia are reported in Table 3.

We did not register LN metastasis in 52 (21.4%) of the 240 cases (28 of which were in the right side, 53.8%), and we kept the data from this group (only hyperglasia group, OHG) separate, so that we could subsequently compare these data with the global data (from the hyperplasia and metastasis group, HMG).

996 hyperplastic LNs were in the OHG (mean 19.2 from each case, S.D. 1.8), 570 of which (57.2%) were from the right side (Table 2). We found a mean of 20.3 LNs in the right side (S.D. 2.1), while the mean of LNs in the left side was 17.8 (S.D. 1.5). The types of hyperplasia in this group are reported in Table 4.

Table 4. *Distribution of OHG LNs by type of hyperplasia*

Simple hyperplasia	Total (n = 334; 33.5%)	Right	Left
F	164	96	68
P	101	64	37
S	41	25	16
M	28	16	12
Mixed hyperplasia	Total (n = 662, 66.5%)		
F+P	127	75	52
F+P+S	99	54	45
F+S	96	53	43
F+P+M	61	37	24
P+S	59	32	27
P+S+M	49	26	23
F+S+M	44	22	22
F+M	39	22	17
F+P+S+M	36	18	18
P+M	28	15	14
S+M	24	15	9

F, follicular; P, paracortical; S, sinusoidal; M, medullary.

When we compared the numbers of right-sided LNs in the OHG and HMG, we found no statistically significant difference. By contrast, the differences in LN numbers between the right and left sides was significant ($P < 0.05$) in both the OHG and the HMG.

Tables 1 and 2 show that more LNs, in both the HMG and the OHG, were in the 2 to 5 mm size category. This confirms our earlier findings in a smaller group of normal and metastatic LNs (Cappello et al. 2000). In addition, 61.9% of LNs in the HMG and 66.8% of LNs in the OHG were smaller than 5 mm ($P < 0.05$). Right-sided LNs were smaller than left-sided ones in both the HMG and the OHG ($P < 0.05$).

Tables 3 and 4 show the hyperplastic distribution in the HMG and the OHG. Mixed hyperplasia was frequently seen in both groups (68.6% in the HMG and 65.9% in the OHG), but no statistical difference between the groups was found. The most frequent pattern found in the HMG was the mixed hyperplasia of follicular and paracortical components, while the OHG showed a relative prevalence of a simple follicle hyperplasia, with no statistically significant difference between right- and left-sided LNs in either groups (Tables 3, 4). Finally, the distribution of the hyperplastic pattern was similar in both the HMG and the OHG, and this distribution did not vary when we made separate analyses of right-sided LNs, left-sided LNs and the global data.

DISCUSSION

LNs have a crucial function for individual survival, due to antigen uptake and processing. This role makes them complex and highly adaptable organs (Robb-Smith, 1947). LNs are small, bean-shaped, encapsulated structures, usually not clinically detectable within adipose or areolar tissue (van der Valk, 1997). They enlarge following a reactive stimulation (Marshall, 1956), but generally they do not exceed 1 cm in diameter. A diameter of more than 3 cm is uncommon, and often indicative of malignancy (Dorfman & Warnke, 1974). Histologically, a LN has 4 compartments: (1) follicles, sometimes with germinal centers; (2) paracortex; (3) sinuses; (4) medullary cords. Various antigen stimuli can lead to enlargement of one or more compartments. The former event is called 'simple hyperplasia', the latter 'mixed hyperplasia' (Cottier et al. 1972).

As shown in the Figure, we identified 4 types of simple hyperplasia and 10 types of mixed hyperplasia. Our results confirmed the existence of an asymmetric LN distribution, with 53.6% of the HMG and 54.3% of the OHG on the right side. Most nodes were less than 5 mm in diameter and found more often in the OHG (66.8%) than in the HMG (61.9%). Tumoral antigenic stimulation of *viciniori* metastatic LNs could be a possible additional hyperplastic stimulus, as described in the literature (Rappaport 1966, Schnitzer, 1985).

Right-sided LNs, although more numerous, were generally smaller than the ones in the left and we suggest that this represents a more pronounced left 'compensatory type' LN hyperplasia.

Finally, we evaluated the type of hyperplasia in each LN, finding that: (1) the more common hyperplastic type in both the MHG and the OHG was the 'mixed type'; (2) the most common pattern was the mixed type, in both the HMG and the OHG, with hyperplasia of follicular and paracortical components; (3) the most common pattern referred to the simple type in both the HMG and the OHG was the follicular hyperplasia; (4) unlike in the HMG, the most common hyperplastic feature in the OHG was the follicular pattern, 'simple type'; (5) no statistically significant difference regarding the distribution of the different type and pattern of hyperplasia in both groups and in both sides was present.

In conclusion, this work has identified an asymmetry in distribution of axillary LNs in women, with left-sided LNs fewer in number but larger in size than the right-sided ones. Our results show the great variability of LN anatomy.

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