

Smooth muscle proliferation in the hilum of superficial lymph nodes

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Summary. A retrospective survey to study hilar smooth muscle proliferation was performed on 410 superficial lymph nodes from 130 patients. Smooth muscle proliferation of variable degree was found in a total of 32 patients, affecting both inguinal and axillary nodes. A slight predominance of inguinal lesions was noted, and a higher proportion of nodes from male patients was affected. The smooth muscle proliferation was not age related nor was it associated with metastatic carcinoma. An association between smooth muscle proliferation and prominent hilar vascularity was found. In individual cases where several nodes had been removed, there was a tendency for more than one node to show smooth muscle proliferation, suggesting that there is a locally acting diffusible aetiological agent. We think the smooth muscle proliferation we have described is of vascular origin, and that it may reflect a previous inflammatory reaction.

Key words: Lymph nodes – Hilum – Smooth muscle – Axilla – Groin

Introduction

The presence of smooth muscle within the capsule and hilum of the normal lymph node has long been a matter of debate. Furuta (1948) studied serial sections of normal lymph nodes and found smooth muscle fibres within the fibrous connective tissue capsule, but did not demonstrate smooth muscle fibres in the hilum, other than those fibres which were present in the blood and lymphatic vessels. However, Folse et al. (1975) found smooth muscle to be distributed evenly throughout the capsule and in the capsular part of the hilar region of normal lymph nodes removed during surgery and at post-mortem. An unusual proliferation of smooth muscle with fibrosis in the hilar region of an axillary lymph node, which had been removed at mastectomy, was reported by Lott and Davies (1983). That case prompted this study, the aim of which was to determine the frequency of such lesions and their clinical associations in an attempt to elucidate their nature.

Materials and methods

Two groups of histological sections of lymph nodes were selected retrospectively from the files of the Departments of Histopathology of Southmead Hospital and the Bristol Royal Infirmary. The tissues were received in the period 1981–1984 for diagnostic purposes.

Group 1. "Normal" or reactive lymph nodes from groin and axilla

A total of 76 nodes from 57 cases in which axillary or inguinal lymph nodes, classified as normal or showing only non-specific reactive changes, was reviewed. Clinical indications leading to the removal of these nodes were varied: some were incidental findings, and were excised during operations for hernia repairs or varicose vein ligations and others had been removed specifically for the investigation of lymphadenopathy. Nodes were excluded if the hilar region was not displayed in the plane of section (Hartveit 1984). Thus 7 individual cases were removed from further study as none of the nodes from these cases fulfilled this criterion. This group therefore comprised the remaining 66 nodes from 50 cases (Table 1).

Group 2. Axillary lymph nodes from patients with breast carcinoma

A total of 579 nodes from 93 cases in which lymph nodes had been excised at the time of mastectomy was reviewed. The nodes were all from women with breast carcinoma (predominantly invasive ductal or infiltrating lobular types). Thirteen cases and 235 individual nodes were excluded, as in Group 1, if the hilar region was not shown in the plane of section. Group 2 therefore comprised 344 nodes from 80 cases (Table 1).

Both groups were examined in the same manner; preliminary examination of each node was performed on haematoxylin and eosin-stained sections prepared from formalin-fixed paraffin embedded material, initially using a dissecting microscope at a magnification of X10. Nodes possibly showing hilar smooth muscle changes were then re-examined under higher magnification. The presence of smooth muscle was assessed using light microscopy. Smooth muscle cells all possessed elongated cytoplasmic processes which were deeply eosinophilic; their nuclei were oval and blunt-ended. Distinction between smooth muscle cells and collagen fibres was facilitated in some instances by a modified Massons blue trichrome stain (Lillie 1977). Additionally, Millers elastic stain (1971) was also used in selected cases.

Cases showing smooth muscle proliferation in the nodal hilum were defined as those in which there was more than one focus of extravascular smooth muscle cells. This excluded a few cases in which it appeared that vessels, cut obliquely, might account for the presence of smooth muscle fibres, although no vessel wall or lumen was visible in the actual plane of section. Cases with significant smooth muscle proliferation were then further divided into those showing only moderate changes and those with marked smooth muscle proliferation. Cases where smooth muscle was present in several scattered foci but did not form the predominant tissue within the hilum were classified as showing moderate smooth muscle proliferation. Cases with marked proliferation included only those where smooth muscle fibres formed a large part of the hilar tissue. In each individual case, agreement concerning the degree of smooth muscle proliferation was reached between the two observers (JLC and JDD).

An assessment of the hilar vascularity was also made, subdividing the cases with smooth muscle proliferation into those with a highly vascular hilum, and those with only a few vessels

Table 1. Clinical groups and lymph nodes examined

	Number of cases	Mean age (range) years	Number of nodes with hilum	Mean number with hilum per case (range)
"Normal" or reactive nodes	50	45(1–71)	66	1.32(1–9)
Breast carcinoma	80	61(35–75)	344	4.3(1–12)

present. The vessels examined when making this assessment were small and medium sized muscular arteries, muscular veins and venules, excluding capillaries. The degree of vascularity in each case was assessed independently of the extent of smooth muscle proliferation.

The results were analysed by non-parametric statistical methods, using the Exact Test (Siegel 1956).

Results

Examination of the nodes from the 130 cases, as described above, revealed 32 cases (25%) with hilar smooth muscle proliferation from both groups of lymph nodes.

Morphology

The hilar changes showed varied patterns. In some, the smooth muscle fibres were densely interwoven within fibrous tissue and were adjacent to the node itself, often hugging the hilar nodal capsule (Fig. 1). In the majority, however, the smooth muscle fibres formed a loose network extending out in all directions within the hilar adipose tissue (Fig. 2). The smooth muscle frequently surrounded individual islands of fat cells (Fig. 2). Despite the random arrangements in the core of the hilum, the fibres often ran parallel to the capsule or to hilar blood vessels. In some cases, smooth muscle formed a large proportion of the hilar tissue (Fig. 1), but despite this, the general architecture of the nodes was well preserved (Fig. 3).

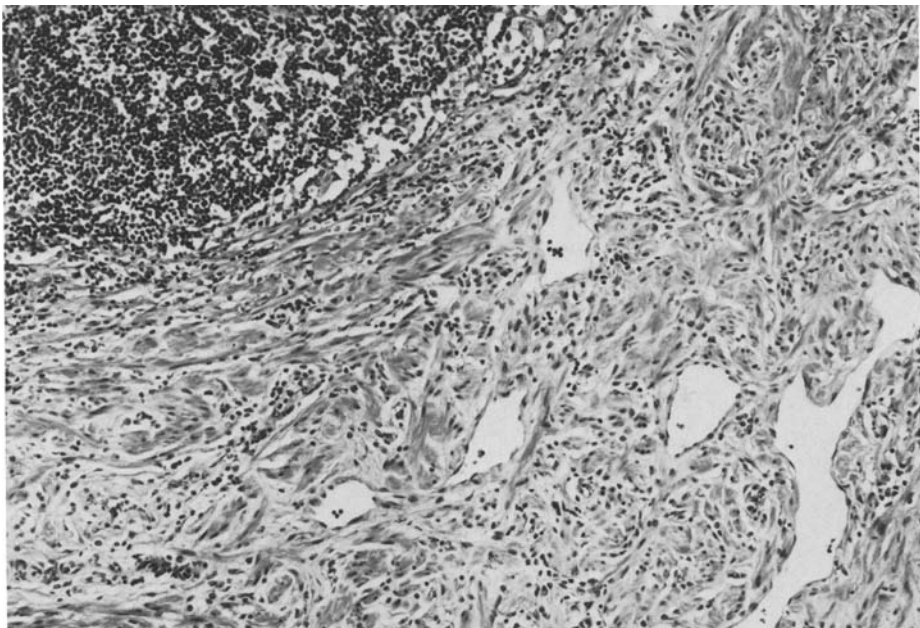


Fig. 1. Hilum of inguinal lymph node with smooth muscle proliferation within fibrous tissue, adjacent to lymphoid tissue. Haematoxylin and Eosin $\times 156$

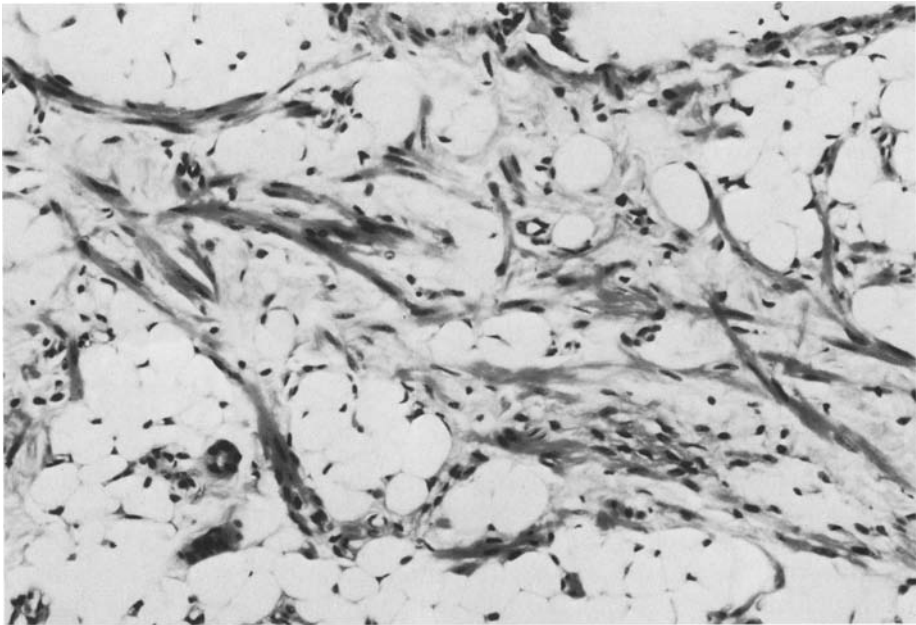


Fig. 2. Axillary lymph node showing the haphazard arrangement of smooth muscle fibres within adipose tissue of the hilum, with a tendency to surround individual fat cells. Haematoxylin and Eosin $\times 250$



Fig. 3. Superficial lymph node showing marked smooth muscle proliferation occupying most of the hilar region. The node itself shows preservation of the normal architecture. Haematoxylin and Eosin $\times 23$

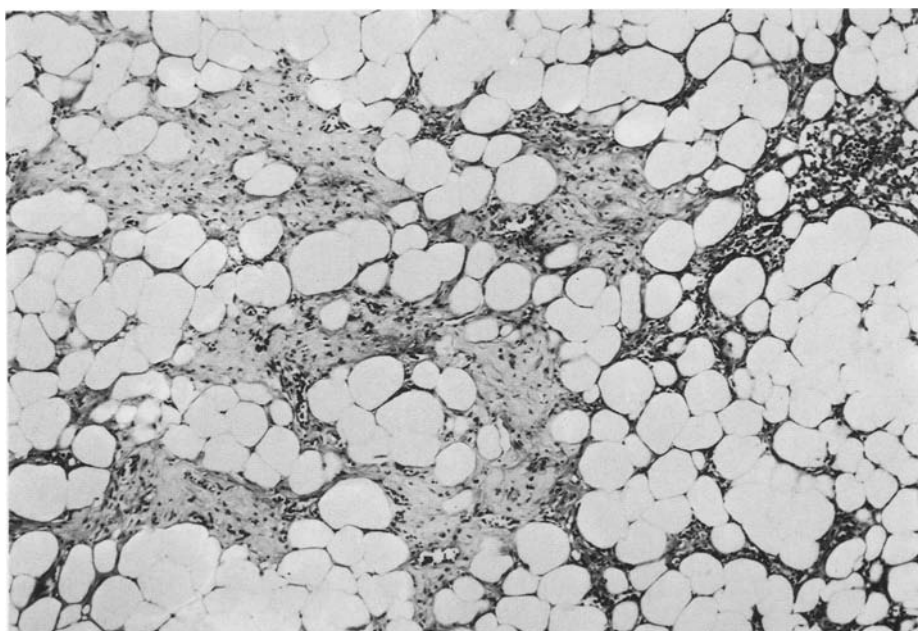


Fig. 4. Lymph node hilum in which areas of fibrosis lie within the adipose tissue. No smooth muscle proliferation is present. Haematoxylin and Eosin $\times 98$

In some lymph nodes there were scattered areas of fibrosis. These foci differed from the smooth muscle proliferation in the lack of smooth muscle cells and individual fibrous trabeculae had a spiculate appearance (Fig. 4). The modified Masson's blue trichrome stain demonstrated the smooth muscle cytoplasm well, and was useful in excluding cases where collagenous bands superficially simulated smooth muscle bundles. In cases where the smooth muscle was closely interwoven within fibrous tissue, the blue trichrome helped to display the smooth muscle component.

The hilar of the nodes showing marked smooth muscle proliferation were generally well vascularised, both in terms of blood vessels and number of vessels (Fig. 5) – see also below. Miller's elastic stain showed fine elastic fibres, arranged haphazardly within the sites of smooth muscle proliferation.

Group 1. "Normal" or reactive lymph nodes from groin and axilla

Of the 50 cases of normal or reactive nodes, 31 were from the inguinal region, 19 from the axilla. The mean number of nodes with a sectioned hilum per case was 1.32 (range 1–9). Thirty of the 50 cases were male, 20 were female. Smooth muscle proliferation was identified in 14 of 31 (45%) cases from the inguinal regions, and 4 of 19 (21%) from the axilla, making an overall total of 18 (36%). More detailed examination subdivided these 18 cases into 8 showing marked hilar smooth muscle proliferation and 10 showing significant but less marked (moderate) changes (Fig. 6). The

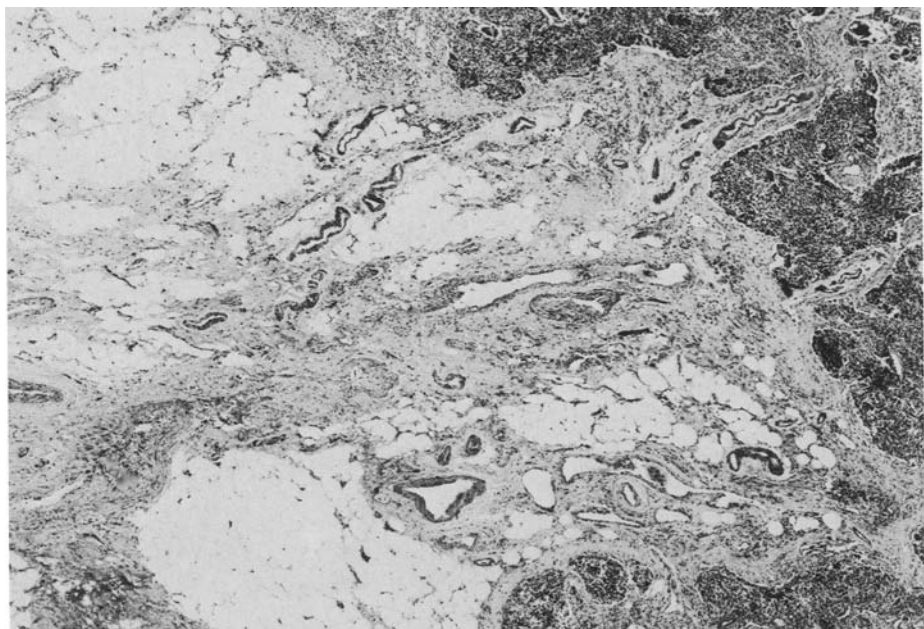


Fig. 5. Lymph node hilum within which there is smooth muscle proliferation. Numerous blood vessels are also present. Haematoxylin and Eosin $\times 23$

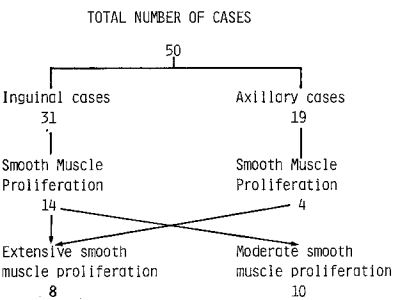
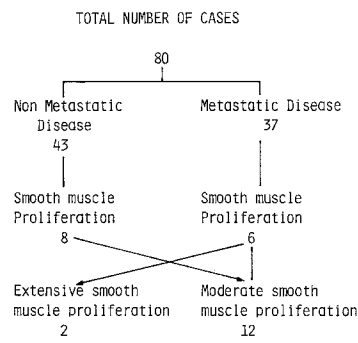


Fig. 6. Flow diagram showing the number of inguinal and axillary cases with hilar smooth muscle proliferation in the normal/reactive group of nodes (Group 1), and the degree of hilar change in each identified case

clinical indications leading to the removal of the nodes did not appear to be related to the presence of smooth muscle proliferation. Some nodes with smooth muscle proliferation had been incidental findings at varicose vein ligation operations (3 cases), herniorrhaphy (3 cases), and arterial bypass operations (2 cases). Others also showing smooth muscle proliferation, had been removed specifically for the investigation of lymphadenopathy (10 cases).

There was an increased proportion of inguinal nodes with smooth muscle proliferation (14 cases: 45%), as compared with axillary nodes (4 cases: 21%), and although the total number of inguinal nodes examined exceeded the total axillary nodes in this group, this difference in proportions almost

Fig. 7. Flow diagram showing the number of nodes with smooth muscle proliferation in mastectomy cases (Group 2) with and without lymph nodal metastatic disease, and the degree of hilar change in each identified case



reached 5% statistical significance, ($p=0.06$. Exact Test). However, the 8 cases with marked proliferation were equally distributed between inguinal and axillary cases. Significantly more lymph nodes from males were found to show smooth muscle proliferation (50%) compared with female cases (15%): ($p= <0.01$. Exact Test).

Group 2. Axillary lymph nodes from patients with breast carcinoma

Of the 80 mastectomy cases, 37 (46%) had metastatic carcinoma involving one or more lymph nodes. The mean number of nodes with a hilum in the plane of section per case was 4.3 (range 1–12). Review of 344 nodes was performed, from which 14 cases (17.5%) were found to show smooth muscle proliferation. Six of these 14 (42%) had metastatic disease, showing no significant difference in this respect between cases with and without muscle proliferation. However, all the individual nodes showing smooth muscle proliferation from these cases were free of metastatic deposits. Detailed examination further divided the 14 cases into two with marked smooth muscle proliferation and 12 with only moderate smooth muscle proliferation, (Fig. 7).

Groups 1 and 2. Multiple node involvement, age distribution and hilar vascularity

When one node showed smooth muscle proliferation, there was a tendency for other lymph nodes from the same patient to be similarly affected. This was a trend seen in both Groups 1 and 2. The number of nodes per case in the mastectomy patients was very variable (range 1–12). Thirty of 62 nodes (48%) were affected in the 14 cases with smooth muscle proliferation, compared with an overall proportion of 9% (30 out of 344). Four of the 18 cases with smooth muscle proliferation from Group 1 had more than one node available for examination. In three cases, 2 nodes had been removed and in each case both nodes showed hilar smooth muscle proliferation. The fourth patient had had nine nodes removed, 5 of which showed smooth muscle proliferation. In cases with more than one node affected,

Table 2. Contingency table to show the relationship between the degree of smooth muscle proliferation and hilar vascularity in superficial lymph nodes

	Highly vascular hilum	"Normally" vascularised hilum
Cases with marked smooth muscle proliferation	9	1
Cases with moderate smooth muscle proliferation	9	13

Exact test $p=0.01$

the degree of smooth muscle proliferation of each node fell into the same category, either moderate or marked.

In both Groups 1 and 2 there was no difference in either the mean age or the age range between those cases with hilar smooth muscle proliferation (mean 51.1 years; range 20–75), and those with no hilar change (mean 55.8 years; range 1–80).

A feature of the hilar smooth muscle proliferation already noted above was the strong association with a well vascularised hilum, found in both the normal or reactive group and the mastectomy group, particularly when the node showed marked smooth muscle change (Table 2). Although some cases with only moderate smooth muscle proliferation were also well vascularised (9 out of 22), a significantly higher proportion of those with marked proliferation was associated with numerous or large blood vessels (9 out of 10), ($p=0.01$, Exact Test).

Discussion

This study has shown that an unexpectedly high proportion of lymph nodes display some degree of hilar smooth muscle proliferation. The variation in the degree of these lesions was marked. In cases without proliferation, no smooth muscle could be detected in the hilum apart from that within or very close to the walls of blood vessels. However, in some cases with smooth muscle proliferation, the hilum of the lymph node consisted almost entirely of muscle, interspersed with numerous blood vessels. The haphazard arrangement of the smooth muscle, often in single fibres, suggested that they were not muscular vessels cut obliquely. As noted before, any case in which we felt this was possible, was regarded as showing no smooth proliferation. In between these extremes, other cases showed definite but patchy smooth muscle amongst the central adipose tissue of the hilum, or adjacent to the capsule. This suggests that there may be a spectrum from normality to marked smooth muscle proliferation.

The case that prompted this study was from a mastectomy specimen, and so initially the possibility that the proliferation of smooth muscle was related to the invasive breast carcinoma was considered. However, our find-

ings indicate that although further cases have been found in axillary nodes received with mastectomy specimens, more have been found in a group of nodes showing either normal features or non-specific inflammatory change. In cases of breast carcinoma, the presence of metastatic lesions within the lymph nodes was not associated with smooth muscle proliferation. Although cases with metastatic disease showed proliferation within some other lymph nodes, no nodes actually containing tumour had evidence of smooth muscle change.

Significantly more males than females showed the smooth muscle lesion. Sex differences have been reported with other smooth muscle lesions. Wile et al. (1981) reported significantly more female than male cases of retroperitoneal leiomyosarcomas, but found more vascular and peripheral leiomyosarcomas in male patients. Peritoneal and pulmonary leiomyomatosis, occurring exclusively in women, is thought to be hormone dependent (Martin 1983). Gastrointestinal leiomyomatous lesions are equally distributed between the sexes (Ashley 1978). The male predominance in our cases of smooth muscle proliferation may, however, be partially explained by the higher number of male inguinal noddes examined compared to female inguinal nodes.

Aging is known to influence the structure of superficial lymph nodes, with a reduction in the cortical tissue with advancing age, accompanied by fatty infiltration or fibrosis of the hilum (Denz 1947; Lusciati et al. 1980). The hilar smooth muscle proliferation found in this study however, does not seem to be age related, as no difference was found in either the mean age or age range between positive and negative cases.

Two cases of scleroderma have been reported in which there was smooth muscle proliferation within lymph nodes (Klug 1975). However, no blood vessels were reported in the area of proliferation in either case. This contrasts with our observations on smooth muscle proliferation in non-sclerodermatous lymph nodes. We found a strong association between marked smooth muscle proliferation and numerous or large muscular blood vessels within the hilum. This suggests that the smooth muscle proliferation may be of vascular origin, rather than capsular.

The tendency for more than one node in each case to show similar smooth muscle proliferation suggests that there is a local aetiological factor. The efferent lymphatics and blood vessels leave the node via the hilum, so any pathological event, such as back pressure, may produce hilar changes. However, we have no evidence for such a situation in our cases.

Another possible local influence is inflammation, which is a known cause of capillary vascular proliferation. In support of this theory, we found a higher incidence of smooth muscle proliferation in inguinal nodes, an area particularly susceptible to repeated infective episodes, compared with axillary nodes. Various chemical mediators are known to be released during an acute inflammatory reaction. It is possible that one such mediator acts as a stimulus to smooth muscle proliferation. The smooth muscle we have identified may, therefore, represent the remnants of a regressed inflammatory reaction.

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