Transposition, apotheosis and benign metamorphosis-lymph node

Keywords: neoplastic tissue, tumour, proliferative lesions, lymph node, resembling structures, thyroid follicles

Introduction

Ectopic foci of non neoplastic tissue situated in the lymph node are designated as benign inclusions. A sequel to a metastatic process induces the epithelial cells in a lymph node which may be clinically significant on account of the probable impact in the determination of tumour staging and the employment of subsequent therapeutic options. Therefore, a distinction from the benign proliferative lesions in the lymph node (vascular proliferations, T lymphocyte clusters, hamartomas, viral infections or angiomomas) is a pre-requisite. Intramural locations may be prefered and the inclusions may elucidate as epithelial cysts or duct resembling structures. The pathogenesis of benign lymphoid inclusions comprises of:

1. Transference of dissociated epithelium as a form of benign metastasis.
2. Evolving heterotopias.

The cells may be derived from the paramesonephric ducts, salivary gland tissue, breast tissue, thyroid follicles, squamous epithelium or mesothelial incorporation. Paramesonephric duct like configurations and inclusions are preferentially located in pelvic lymph nodes and may simulate the uterine tube epithelium. Breast tissue inclusions are chiefly constituted of ectopic mammary glands and ducts of diverse morphology and unknown aetiology. Thyroid inclusions may be incorporated in the cervical and axillary lymph nodes. Mesothelial inclusions appear particularly in the mediastinal lymph nodes of the patients with pleural and pericardial effusions. The occurrence of melanocytic cells discovered in the lymph nodes are attributed to the faulty migration of neural crest cells or they may arise as benign metastasis of existing dermal nevi. The diagnosis of benign inclusions is necessitated in order to exclude adenocarcinomatous metastasis in patients presenting with benign nodal proliferations. The existence of benign inclusions was initially recounted by Reis et al. in 1897. These are defined as tubular spaces corresponding to cysts, appearing in lymph nodes of patients who may undergo surgical interventions for malignant tumours of the uterus, cervix and vulva. Inclusions may as well arise in non malignant disease processes and may be situated in locales extraneous to the pelvic cavity such as in the lumbar, mediastinal, parotid, submandibular, jugular, hepatic and iliac lymph nodes. Brooks et al divided the inclusions in three sub-categories, epithelial, neovolamanoctic and decidual.

Clinical exponents

1. The benign epithelial inclusions may be discerned coincidentally and may typically lack specific symptoms. The diagnostic significance of the benign inclusions is considerable as they may be misinterpreted for metastatic malignant processes which may result in the employment of extensive and expensive investigative and therapeutic options (Table 1).

Table 1 Selective sites of benign lymph node inclusions

<table>
<thead>
<tr>
<th>Tissues favoring heterotopia</th>
<th>Implicated lymph nodes</th>
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<tbody>
<tr>
<td>Mammary gland tissue</td>
<td>Axillary nodes</td>
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<td>Aggregates of nevus cells</td>
<td>Axillary nodes</td>
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<tr>
<td>Blue nevus</td>
<td>Axillary nodes</td>
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<tr>
<td>Squamous Epithelium</td>
<td>Cervical &amp; peri-pancreatic nodes</td>
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<td>Salivary Gland Tissue</td>
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<td>Thyroid Follicles</td>
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<td>Decidual Tissue</td>
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<td>Paramesonephric Epithelium</td>
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<tr>
<td>Intestinal Glands</td>
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<td>Mesothelial Cells</td>
<td>Mediastinal and Retroperitoneal nodes</td>
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</tbody>
</table>

Adapted from: Pantanowitz & Upton 2003.

2. Inclusions of the lymph node situated in the intramural locations may be configured in cysts or as innumerable duct replicating formations. The epithelial cells articulating the inclusions may arise from the paramesonephric ducts, salivary glands, breast tissue, thyroid follicular epithelium, squamous epithelium and the mesothelium.

3. Lymph node inclusions of paramesonephricus sub-type may especially emerge in the pelvic lymph nodes and infrequently in the axillary lymph nodes. The concurrence with adenocarcinoma of the mammary glands is debatable.

4. Ectopic breast tissue is more prevalent in the sentinel lymph nodes, in contrast to adjunctive axillary nodes, on account of an obligatory embryologic connection.

5. Decidual inclusions are elucidated in the paramesonephric processes and may originate from submesothelial cells secondary to a hormonal trigger.

6. Lymph node inclusions of mammary gland origin may be composed of deformed mammary gland ducts with divergent morphology and a dual cell population comprising of luminal cuboidal /columnar epithelial cells and basal cells depicting myoepithelial differentiation (Figure 1).
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may also display identical epithelium lined cystic inclusions. A
demarcation from a metastatic well differentiated squamous cell
carcinoma with superimposed cystic change may be mandated.⁵

3. **Thyroid follicles Inclusions:** Capsular or sub-capsular location
of inclusions of non-pathogenic thyroid tissue in the mid-
cervical lymph nodes may be elucidated in concordance with a
normal thyroid gland.⁶ Distinctive colloid follicles lined by
a low cuboidal epithelium lacking autophagy may be exemplified.
Configurations such as papillae or psammoma bodies may be
absent. Follicles may be detected in the peripheral sinus.⁴

4. **Decidual reaction:** Pelvic lymph nodes usually delineate a
decidual reaction which may simulate a malignant metastasis.
It may occur in the stromal cells of co-existent conditions
such as the Endometriosis. The adjucutive stromal cells or the
hormonally susceptive cells are implicated in the genesis of the
anomaly.⁵

5. **Mullerian type epithelium:** Glandular inclusions inter-
lined by cuboidal cells simulating a mullerian or coelomic
epithelium may be located in the pelvic lymph nodes. The
inclusions may resemble the peritoneal lesions denominated as
“endosalpingiosis”. Metastasis from a low grade ovarian
neoplasm which may extend in the peripheral sinus, lesions
which form papillae, the emergence of psammoma bodies or
cellular proliferations configurating small, laminated layers are
the conditions which require a distinction from the inclusions of
mullerian type epithelium. Nodal endometriosis may accompany
the glandular inclusions with an encompassing endometrial type
stroma.⁴

6. **Nevus cells:** Nevus inclusions may articulate as a sinus,
trabaculae, nests, cords, linear strands or may be incorporated in
the capsule. The cells are monomorphic with an indistinct border,
pink cytoplasm, round to oval nuclei, indistinct nucleoli
and contain granules of melanin. Sporadic cell clusters may be
up-to 2.1mm in magnitude. Mitosis is usually absent, in contrast
to a malignant melanoma which may display metastasis in the
marginal sinus. The nevus inclusions may be immune reactive for
S 100 protein, tyrosinase, melanin and non reactive for immune
markers such as melan A, HMB45 and Ki67. In contrast, the
malignant melanoma appears reactive for S100 protein, melan
A, HMB45 and Ki67. On ultra-structural examination, the nevus
inclusions display uniform cells with random aggregates of
cytoplasmic fibrils, mature melanosomes and dispersed
nuclear chromatin.⁴ The axillary, cervical or inguinal lymph
nodes may be implicated, however conventional nevus cells may
be also be enunciated in the capsule of axillary lymph nodes , in
the absence of an involved parenchyma.⁵

7. **Mesothelial cells:** Lymph nodes may infrequently delineate
mesothelial cell aggregates accompanied by an absence of a
malignant mesothelioma, from which a demarcation is required.⁵
Mesothelial windows may also be depicted as mediastinal cysts,
situated in the sub-capsular spaces. The cellular configuration is
that of a uniform tall, columnar epithelium with a low nucleo-
cytoplasmic ratio, a distinct basement membrane and an absence
of mitosis. The cells hypothetically arise from the pleural
mesothelium.⁴

8. **Mammary Inclusions:** Axillary lymph nodes may frequently
depict the ectopic mammary tissue. Inclusions of the breast
tissue are demonstrated as mammary ducts in the subcapsular
region. The cellular components described are the epithelium,
myoepithelium and apocrine cells. Cystic spaces lined with low,
uniform cuboidal epithelium lacking mitosis, hyperplasia or
hyperchromasia may be evidenced.⁴ A singular layer of cuboidal
epithelium interlining the tubules (hobnail appearance) or
epithelial inclusions situated within or beneath the lymph node
capsule may also be elucidated. A distinction is required from a
metastatic breast carcinoma. The inclusions may delineate three
categories i) glandular structures only ii) squamous cysts only
iii) a combination of glandular and squamous epithelium.⁵

To surmise, an extensive morphological evaluation may be
mandated for a substantial and definitive prognostic delineation of
the benign lymph node inclusions as an immunohistochemical or bio-
molecular investigation may not categorically define a non-malignant
tissue metamorphosis or the transformation into a neoplasm.

**Acknowledgements**

None.

**Conflict of interest**

The author declares that there is none of the conflicts.

**References**

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2. Brooks J, Li Volsi VA, Pietra GG, et al. Mesothelial cell Inclusions
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8. Image 3 Courtesy: Pathology,ihu.edu.