Benign lymph node inclusions mimicking metastatic carcinoma

Although previously well recognised, Fisher et al have highlighted the importance of differentiating between metastatic carcinoma and benign intranodal epithelial inclusions.1 I describe three further cases encountered recently in which immunocytochemical analysis provided valuable evidence to help clarify the nature of intranodal inclusions. In each case the differentiation was clinically critical in that no other nodes were involved.

Case 1
A 66 year old woman had a mass in the left breast detected by screening. A localisation biopsy specimen showed a grade 1 ductal carcinoma and a diffusely infiltrating lobular carcinoma. She underwent mastectomy: there was residual invasive lobular carcinoma and multiquadrant foci of invasive lobular carcinoma up to 7 mm diameter. The original tumour was estimated at 200 mm diameter and there was pagetoid spread of lobular carcinoma in ducts and extensive vascular invasion. Three of 12 axillary lymph nodes contained groups of small cells in the capsule. Initially thought to be metastatic lobular carcinoma, immunocytochemistry was performed to look for lesser degrees of spread to the lymph nodes in the same slide. Immunocytochemistry was performed on the breast tumour and the lymph nodes for HMFG-2 AE1/AE3, CAM 5.2, and S100. The lobular carcinoma stained strongly positively for AE1/AE3, CAM 5.2, and HMFG 2, and weakly for S100. Cells in the lymph node stained strongly for S100 but were otherwise negative, indicating that they were benign naevus cells. Interestingly, there were numerous S100 positive cells scattered through the lymph node parenchyma.

Case 2
A 65 year old woman had a cytologically malignant lump detected by screening in the left breast. She underwent mastectomy and histological examination showed a 14 mm lobular carcinoma. One of 17 axillary lymph nodes contained a suspicious focus of sclerosis and scattered histiocyte-like cells with clear cytoplasm. Periodic acid Schiff stain showed intracytoplasmic mucin, and immunocytochemical staining showed positivity for HMFG-2 and CAM 5.2 and was negative for carcinoembryonic antigen (CEA) in both intranodal cells and the original carcinoma, confirming metastatic lobular carcinoma (fig 1).

Case 3
A 26 year old woman had bilateral papillary serous cystadenomas of the ovaries of borderline malignancy excised. No unequivocal stromal invasion was seen, but tumour was present on the surface of the left ovary. The right external iliac lymph node was excised. Histological analysis showed a single large lymph node in which there were multiple subcapsular epithelial structures, some of which showed papillary structure with psammoma body formation. These were thought to be benign inclusions of multinucleated epithelium (fig 2). In an attempt to demonstrate disparity in immunocytochemical profile to support this diagnosis immunocytochemistry was performed on both ovarian tumours and the lymph node for CEA, vimentin, HMFG-2, S100, CAM 5.2 and AE1/AE3. The immunocytochemical markers were similar in the ovarian tumours and inclusions except that CA125 showed delicate membrane staining in both ovarian tumours but the epithelial structures in the lymph nodes did not stain.

In each of the cases described the lymph node diagnosis made the difference between lymph node positive and lymph node negative, with subsequent implications for clinical management. The cases illustrate the use of immunocytochemistry to support or refute a morphologically based opinion. The first case showed that many cell inclusions can line up in a pseudo-Indian file looking remarkably like metastatic lobular...

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I read with interest the paper by...

Four of the six letters to the Editor in the April issue of the Journal begin with the statement "I (we) read with interest the paper by ..." (IRWITTPB). One might have assumed that the preparation of a letter was sufficient evidence of an interest, stimulated in turn by reading the relevant paper. So why are they telling us of their interest?

Clearly many writers have information which supplements or clarifies an aspect of a paper or which corrects an error but there may be some additional factor, some intensity of interest which stimulates the letter, so, if subjective feelings are to be included, why stop at the bland "interest"? Why not indicate the author's true feelings and begin, for example, with, "We read with mounting indignation the flawed paper by ..." or "We were devastated to see in print a study almost identical to our soon-to-be-completed study", or "We were dumbfounded to find that our paper was not cited by ..." The "interest" of other writers might be a code concealing lyrical, cynical or even machiavellian approaches.

I looked over the most recent 16 issues of the Journal and found that almost 40% (22 of 56) of letters began with IRWITTPB or its variants (one writer was very interested, another fascinated; one simply said he very much enjoyed the paper). A warning to IRWITTPB writers is the response to one letter, [they] may have read our article "with interest", but clearly they have not read it with "great care". The prevalence of IRWITTPB indicates that rather than hiding an undisclosed intensity of interest, it has become a cliché to introduce a letter and, as such, should be discouraged... or is anyone interested?

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**Figure 1.** Case 2: suspicious area in an axillary lymph node (a) haematoxylin and eosin; (b) immunocytochemistry of same area showing numerous single HMFG-2 positive cells (metastatic lobular carcinoma).