Mediastinal lymph node metastases in lung cancer: is size a valid criterion?

Few surgical procedures are so demoralising to the patient, disappointing to the referring physician, or frustrating for the surgeon as a thoracotomy for inoperable carcinoma of the bronchus. It is axiomatic that surgery is curative only when the disease is extirpated in its entirety. Despite major advances in the non-surgical management of other malignancies, carcinoma of the bronchus in all its manifestations remains stubbornly resistant to adjuvant treatment. Attitudes to staging and surgical intervention vary widely, reflecting the personality and philosophy of the clinicians concerned. The divergence of opinion stems from the desire to reconcile the conflict between two mutually exclusive arguments. On the one hand, patients should be exposed to the hazards and discomfort of surgery only when the procedure is curative. On the other, all patients with potentially curable lesions should be offered the benefits of surgery.

Advances in diagnostic hardware, such as computed tomography, magnetic resonance imaging, and ultrafast computed tomography, offer images with ever increasing detail. Their failure to provide a presurgical clinical assessment of tumour and node (T and N) stage dramatically superior to that produced by conventional radiology has been disappointing. Curable patients will be denied the benefits of surgery if abnormalities detected by staging investigations are accepted without histological confirmation. When the results of screening are equivocal the patient must be given the benefit of the doubt.

The waters are muddied still further by the current debate on the implications of N2 disease. Carlens described the technique of mediastinoscopy in 1959, and this was followed shortly afterwards by Chamberlain’s description of anterior mediastinotomy. These procedures quickly gained popular support because of their low morbidity and high accuracy in assessing metastasis to the superior mediastinum. In the prestaging era the incidence of thoracotomy without resection was as high as 25%. The average incidence in the United Kingdom remains unacceptably high at 16% (United Kingdom Thoracic Surgical Register, 1988). In thoracic surgical units that follow stringent preoperative staging protocols with strict operative criteria, however, rates of less than 5% are commonly achieved. Selection criteria should never be absolute. There is an ever present danger that by applying these criteria too assiduously some patients will have been denied optimal treatment.

If all patients who are operable by other criteria are offered routine mediastinoscopy 70% will be found normal. In patients with normal results from imaging the strike rate falls even lower. Specificity is 100%, but the incidence of false negatives is about 9%; these are due to either sampling error or, more commonly, metastatic disease in inaccessible lymph node stations. When there are gross abnormalities within the mediastinum and the procedure is performed largely for diagnosis rather than staging, the incidence of positive biopsy findings rises to over 60%. A positive result from mediastinoscopy is a relative but not absolute contraindication to further surgery: patients with single station N2 disease in ipsilateral nodes can still benefit from surgical intervention.

An enormous volume of work has been published establishing the relation between lymph node size and metastatic infiltration. The sensitivity of computed tomography ranges from 24% to 96% and specificity from 46% to 97%. As the size of lymph nodes increases, sensitivity decreases and specificity increases. It is accepted that the inability of current non-invasive techniques to detect the presence of micrometastases guarantees some false negatives. A consensus view has emerged as a result of these debates. Most thoracic units perform routine mediastinoscopy only in those patients with demonstrable lymphadenopathy. The work of Kerr et al published in this issue (p 337) challenges present dogma. The authors present an analysis of mediastinal lymph node metastases in patients with lung cancer. They draw the following conclusions: (1) lymph nodes greater than 15 mm in diameter are as likely to be benign as malignant; (2) regardless of what size criteria are applied, about 20% of lymph nodes are likely to be malignant; (3) there is an association between acute pulmonary inflammation and benign lymphadenopathy. Their findings, if accurate, will have far reaching effects on the management of lung cancer. It must be emphasised that this paper is not a study assessing the ability of computed tomography to stage N2 disease but a pathological assessment of mediastinal lymph nodes. It should stand or fall on its own merits.

Little or no information has been given about the author’s selection criteria for the 60 patients included. Four patients were excluded after a positive result from mediastinoscopy. Twelve of the 60 were found at exploration to have unresectable tumours. Is this figure representative of the authors’ normal staging policies, or for the purposes of this study were routine, more rigid, standards relaxed?

The lymphatic drainage of the lung was well described in a monograph by Nohl-Oser in 1972. To standardise the staging of patients with mediastinal lymph node metastases regional lymph nodes have been allocated numbered positions or stations according to their anatomical site. In their study Kerr et al state that all accessible lymph nodes were removed in their entirety; 168 lymph nodes were submitted for examination from 54 thoracotomies. This represents a mere three, perhaps four, nodes per patient. There are at least nine mediastinal and still more intrapulmonary stations, all of which are accessible at thoracotomy. Despite assurances to the contrary, a complete mediastinal dissection cannot have been performed. The failure to include so many presumably normal lymph nodes from the analysis must bias the results.

No attempt is made by the authors to compare clinical staging with pathological staging. A 15 mm diameter lymph node visible on the computed tomogram and the same lymph node after fixation are unlikely to be equivalent. This point, however, becomes less important because the authors’ basic thesis maintains that size is no longer relevant. In this study only 38 (24%) of the nodes are less than 1 cm in diameter. Where have all the normal sized lymph nodes gone?

The authors introduce a new variable into what is already a very complex equation, establishing a relation between acute pulmonary parenchymal inflammation and mediastinal lymphadenopathy. Normal lymph nodes, however, are not spherical structures. The geometry of a reactive lymph node is usually maintained. In these circumstances nodes may measure 4 or even 6 cm in their maximum dimension, whereas the transverse diameter (shown on cross sectional imaging) is maintained within or around
normal limits. This merely strengthens the arguments for giving patients the benefit of the doubt—offering support for those who routinely use frozen section for the analysis of mediastinal lymph nodes at the time of thoracotomy.

The thesis expressed by the authors is compelling and worthy of careful consideration. They challenge clinicians to re-examine their views on an enormous volume of published material suggesting that the size of mediastinal lymph nodes is a valid means of predicting metastatic disease. There is clearly a need to address the shortcomings of this study and establish this relationship more precisely.

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