



## Core needle biopsy is effective in the initial diagnosis of mediastinal lymphoma

PIER LUIGI ZINZANI, GABRIELA CORNELI,\* ALESSANDRA CANCELLIERI,<sup>o</sup> MASSIMO MAGAGNOLI, NICOLA LACAVA,\* FILIPPO GHERLINZONI, MAURIZIO BENDANDI, PATRIZIA ALBERTINI, GIUSEPPE BARUZZI,<sup>o</sup> SANTE TURA, MAURIZIO BOARON\*

Institute of Hematology and Medical Oncology "Seràgnoli", University of Bologna; \*Division of Thoracic Surgery, Maggiore Hospital, Bologna; <sup>o</sup>Department of Pathology, Maggiore Hospital, Bologna, Italy

### ABSTRACT

**Background and Objective.** With the development and refinement of guidance modalities for percutaneous biopsies, many investigators have reported studies supporting the role of guided core needle biopsy in the diagnosis of mediastinal lymphoma. The aims of this report are to evaluate the efficacy of findings at core needle biopsy of mediastinal masses on patient care and define the key determinants of clinical success.

**Design and Methods.** Fluoroscopy-guided (in 75 patients) and computed tomography-guided (in 8 patients) core needle biopsies were performed in 83 patients with mediastinal lymphoma: all but one of the patients were at first diagnosis. All the biopsies were performed using a Menghini needle (from 1.2 mm to 1.8 mm). In the vast majority of cases the 1.8 mm gauge was employed.

**Results.** The overall sensitivity for the diagnosis of lymphoma was 81% (67/83 cases). In the remaining 16 patients the lymphoma diagnosis was reached either by mediastinoscopy (11 cases) or anterior mediastinotomy (3 cases) or core needle biopsy of the lung (1 case); one patient was treated directly after the needle biopsy had been unsuccessful because he needed rapid therapy. In 77/82 (93%) patients it was possible to assess the specific histotype. There was no operative mortality; all the biopsies were performed on an outpatient basis.

**Interpretation and Conclusions.** Our data indicate that core needle biopsy should be considered as an effective and safe procedure in the diagnosis of patients with mediastinal lymphoma with the possibility of determining the tumor subtype and subsequent specific treatment.

©1999, Ferrata Storti Foundation

Key words: core needle biopsy, mediastinal lymphoma, specific treatment, diagnosis

Correspondence: Pier Luigi Zinzani, M.D., Istituto di Ematologia e Oncologia Medica "Seràgnoli", Policlinico S.Orsola, Via Massarenti 9, 40138 Bologna, Italy.  
Phone: international +39-051-390413 - Fax: international +39.051.6364037.

The mediastinum is commonly involved by lymphoma, either at the time of diagnosis or on relapse.<sup>1</sup> Hodgkin's disease (HD) and in particular aggressive non-Hodgkin's lymphomas (NHL) are often localized in the anterior mediastinal and hilar lymph nodes without superficial lymph nodes.<sup>2-4</sup> Differential diagnosis of anterior mediastinal and hilar adenopathy must include secondary pulmonary neoplasms, thymomas, sarcoidosis, teratomas and germ cell tumors. For this specific clinical presentation, expensive, invasive and potentially dangerous surgical procedures have in recent years been substituted in a few specialist centers by core needle biopsy. This particular technique with fluoroscopic, ultrasonographic or computed tomographic (CT) guidance allows sufficient tissue to be taken for accurate histologic and immunohistochemical evaluation, thereby obviating the need for mediastinoscopy, mediastinotomy, thoracoscopy, or open chest surgery.<sup>5-10</sup> On the basis of previous experiences,<sup>11-19</sup> cutting needles have been employed, since histology is more reliable than cytology. The advantage of CT guidance is that the whole mediastinum is visualized, allowing accurate planning of the biopsy of deep or small lesions and lesions with extensive necrotic areas. Fluoroscopic guidance makes the procedure simpler, faster, less expensive, and feasible in an endoscopy room. X-ray exposure both for the patient and operator is minimal even when there are masses of considerable size.

This study reports our experience with the application of fluoroscopy-guided core needle biopsies of the mediastinum for the diagnosis and management of lymphoma.

### Design and Methods

From 1985 to 1997, 260 patients presented with clinically primary anterior mediastinal masses. Of these masses, 208 were  $\geq 4$  cm and closer than 3 cm to the chest wall and underwent core needle biopsy; the majority of them were large lesions. The remaining 52 underwent other diagnostic procedures such as mediastinoscopy, mediastinotomy, video-thoracoscopy or primary resection depending on the site,

dimensions, and clinical diagnosis. Out of 214 core needle biopsies performed on 208 patients, a diagnosis of lymphoma was made in 83 outpatients (44 females, 39 males; median age 35 yrs, range 1-79 yrs). Patients not deemed suitable for biopsy on the basis of coagulopathy, inability to cooperate, or anatomic and vascular appearance as noted on the chest X-ray and CT scan were excluded. Informed consent was obtained from all patients. All but one of the patients had no known prior malignancy. The remaining patient had a history of previously diagnosed NHL.

All biopsies were taken from anterior mediastinal masses that were >4 cm in size, <3 cm from the chest wall, and easily observed using two plane fluoroscopy. CT was employed mainly for fine needle aspiration of small and deep mediastinal lesions, and specifically in 8 patients of this series. Most of the lesions were large or bulky masses, often adherent to the chest wall.

### Biopsy technique

All the biopsies were performed by Menghini needle. All patients had been investigated by CT scan before the biopsy. Conditions necessary to perform the biopsy were prothrombin activity >50% and platelet count >70,000/ $\mu$ L. Severe respiratory insufficiency and previous pneumonectomy when the residual lung had to be passed through were considered the only contraindications. Superior vena cava syndrome in the presence of a large mediastinal mass was considered a formal indication.

Premedication was atropine (0.5 mg) only. The procedures were performed in an operating room under local anesthetic, except in the case of children who received general anesthesia. We routinely employ a 1.8 mm disposable Menghini needle (Hepafix,® B Braun, Melsunge, Germany), fitted with a homemade blunt steel obturator, which is exchanged for the original one when the needle has reached the lesion. Smaller bore (mm 1.2, 1.4, 1.6) Menghini needles were occasionally utilized in the pediatric age group, in conditions of poor coagulation, and when a ventilated lung had to be deeply penetrated. A rotating C arm X-ray apparatus was utilized for a two plane approach. After the procedure, the patients were kept under observation for about 4 hours and were discharged if asymptomatic after a chest X-ray had excluded any complication. Most patients, however, spent their first post-operative night in the hospitals from which they had been referred to our department.

### Histologic preparations

All the specimens were formalin-fixed and paraffin embedded, after which 3-mm thick sections were cut and stained with hematoxylin and eosin (H&E). Additional sections were obtained for histochemical study or immunophenotypic analysis, which was performed according to the avidin-biotin-peroxidase complex method and by applying a panel of anti-

bodies including the key-markers listed in the REAL classification.<sup>20</sup>

### Results

Diagnostic tissue was obtained first time in 64/83 (77%) biopsies. Four biopsies were repeated once. In 3 cases, the second biopsy produced a true positive result. Core needle biopsy showed an overall sensitivity for the diagnosis of lymphoma in 67/83 (81%) cases. As regards the remaining 16 patients, in 3 (4%) cases the procedure yielded a specimen that was *consistent with or suspicious of* lymphoma, and in 13 (15%) patients the material was considered non-diagnostic. Three main reasons for unsatisfactory biopsy were necrosis, limited cellularity, or sampling outside the lesion.

In 67 patients in whom core needle biopsy was the diagnostic procedure, there were 45 cases of NHL and 22 cases of HD. Moreover, a diagnosis was achieved in all patients but one (82/83, 99%): the latter was the only patient with a previous diagnosis of NHL, and needed rapid treatment because of his poor performance status (he was treated *exjuvantibus* according to the NHL therapeutic approach, and obtained a good response). In the other 15 patients in whom needle biopsies had been unsuccessful a definitive pathologic diagnosis was reached either by mediastinoscopy (11 cases) or anterior mediastinotomy (3 cases) or, in 1 case, by a lung core needle biopsy. Table 1 summarizes the different and sequential surgical techniques utilized to obtain the pathologic diagnosis.

The final histopathologic subtypes in the 82 patients are listed in Table 2. The majority of NHL patients had diffuse mediastinal large B-cell tumors (36/52, 67%). All the cases of HD were nodular sclerosis subtype. The tissue samples allowed a refined diagnosis in 77/82 (93%), while in the remaining 5 they were sufficient to recognize the existence of lymphomatous involvement (5 NHL high grade) but not the histologic subtype. Of the 5 unclassified NHL patients, 3 were given a NHL diagnosis from core needle biopsy and 2 from anterior mediastinotomy, respectively. Nevertheless the diagnostic data on these 5 patients were sufficient to define a specific

**Table 1. Histologic diagnosis with core needle biopsy and subsequent mediastinoscopy/anterior mediastinotomy in patients with mediastinal lymphoma.**

	No. of patients	Core needle (first time)	Mediastinoscopy/anterior mediastinotomy (second time)	Total
HD	30	22 (74%)	8 (26%)	30 (100%)
NHL	53	45 (85%)	7 (13%)	52 (98%)

**Table 2. Immunohistochemical diagnosis by core needle biopsy or mediastinoscopy/mini-thoracotomy in 82 patients.**

Histologic subtype	No. of patients
HD:	
Nodular sclerosis	30
NHL	
Diffuse mediastinal large B-cell	36
Lymphoblastic	7
Anaplastic large cell	2
Diffuse large B-cell	1
MALT-type	1
Unclassified	
High grade	5

therapeutic approach.

No death was recorded in this series. In only six (7%) of the 83 patients did complications arise. Three patients developed pneumothorax, one of which required drainage. Two patients had minor hemothorax which required no treatment. Transient blood staining of the sputum was not considered a complication. One patient had transitory hypotension due to the vago-vagal reflex and acute pain probably referable to a minimal pneumothorax. Patients were seen on a weekly basis in the outpatient clinic for 1 month. One patient developed immediate superior vena cava syndrome due to intra-lesional hemorrhage which led to a critical caval compression; this complication resolved spontaneously in 48 hours. No delayed complications were observed.

## Discussion

The particularly high overall accuracy of radiologically guided percutaneous biopsy in the diagnostic phase of patients with mediastinal lymphoma<sup>11-19</sup> has opened interesting new possibilities in diagnosis-specific treatment concepts. The role of guided fine-needle biopsy in the definitive tissue diagnosis of epithelial neoplasms (and especially metastatic ones) is well established. However, its use in primary evaluation of mediastinal lymphomas has, as yet, been somewhat limited.

In our study, the diagnostic success with only core needle biopsy was 81%. All these cases of mediastinal lymphoma were specifically treated according to the results from the core needle biopsy alone, and did not require any other surgical biopsy. In addition, specific classification of histologic subtype of these NHL and HD core needle biopsy specimens was possible by means of immunohistochemical techniques in 64/67 (96%) patients. For the 15 patients with non-diagnostic core needle biopsy results, the lymphoma diagnosis was obtained utilizing more invasive techniques such as mediastinoscopy (11 cases), anterior mediastinotomy (3 cases), and lung core

needle biopsy (1 case). The remaining patient was treated directly with NHL regimens after the first non-diagnostic core needle biopsy since his poor clinical condition after relapsed NHL made waiting unadvisable. The overall diagnostic success rate was 99% with 93% of histologic subtypes defined.

It is of the utmost importance to know the exact diagnosis of a mediastinal tumor so that the patient receives the appropriate treatment. The most common neoformations in the anterior mediastinum are lymphomas, thymomas and metastases of lung cancer. The last are usually identified by the presence of the primary tumor eventually verified by fine needle aspiration. Thymomas can be suspected based on the imaging but they should be primarily resected only in the presence of myasthenia, as the imaging diagnosis is not reliable. In our experience of 65 thymomas, 39 were needle biopsied, 12 had myasthenia and out of the 14 we operated on based upon a clinical diagnosis, 2 were lymphomas. This experience emphasizes the need for a definite diagnosis before resecting an anterior mediastinal mass. Often there may be an urgent need to start treatment immediately because of severe respiratory or circulatory problems. The superior vena cava syndrome is a frequent complication of extensive anterior mediastinal masses. It is an oncologic emergency as patients are usually dyspneic and orthopneic. The general anesthesia which is required for mini-invasive surgical sampling procedures is risky as positive pressure ventilation further jeopardizes atrial filling. In all these patients we have obtained the diagnosis, in a very short time, without major complications sometimes even being obliged to perform the biopsy with the patient in a semi-setting position. We are persuaded that the advantages of needle biopsy in these patients are considerable. If appropriately trained cytologists are available, fine needle aspiration may be sufficient for the diagnosis of a solid tumor. On the other hand, for lymphoma patients cytology alone may be insufficient to differentiate between the different lymphoma subgroups. Many centers are still reluctant to use core needle biopsy for mediastinal masses because of the theoretical risk of serious complications and unsatisfactory sampling. For this reason, surgical procedures such as thoracotomy, video-assisted thoracoscopy, and mediastinoscopy are still extensively utilized.

Core needle biopsy is the least traumatic invasive sampling technique. When a large lesion is close to the chest wall the risk of puncture is usually minimal, regardless of the caliber of needles. We chose the Menghini needles because of the optimal external/internal diameter ratio, and because of previous experience of tissue tearing, which could be dangerous in the mediastinum, during withdrawal of *sleigh needles*. Concerning the guidance, we have employed the fluoroscopic approach since 1974.<sup>14</sup> Indeed, even when CT became available at the beginning of the eighties,

we tended to use it almost only for core or fine needle biopsies of small and deep mediastinal masses, and occasionally in cases of large lesions close to the chest wall in order to avoid extensive necrotic areas. Fluoroscopic guidance is easier, faster, less expensive and allows the operator to work in a fully equipped operating room and to take the biopsy under direct control with minimal X-ray exposure. Ultrasound guidance can be usefully employed when the lesion is close to the chest wall.

Risks, morbidity and limitations of the core needle procedure must be compared with those of mediastinoscopy, mediastinotomy, and video-assisted thoracoscopy. These more commonly employed techniques can be more risky,<sup>21,22</sup> are usually performed under general anesthesia, and are much more expensive. There are definite indications for fluoroscopy core needle biopsy in patients with NHL and HD in the mediastinum: to establish accurately and efficiently the diagnosis of masses not initially known to be lymphomatous prior to a surgical technique with a specific treatment possibility in accordance with the subtype classification. We believe it should be possible to employ this very simple, fast and economic technique on a large scale. It can also be performed on outpatients, avoiding more complex and expensive procedures in a large percentage of cases. Above all, this technique obviates risks and discomfort for the patient. For guiding the biopsy, fluoroscopy is less costly and time consuming, and is widely available.

#### Contributions and Acknowledgments

PLZ, MB and AC were the principal investigators involved in the conception of the study, its design, and the writing of the paper. MM, GC and FG helped the principal investigators (PLZ, MB and AC) with the data analysis interpretation. NL, MB and PA collected the study data. GB and ST critically revised the paper and gave the final approval for its publication.

#### Funding

This research was partially supported by "AIL 30 ore per la vita" funds.

#### Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

#### Manuscript processing

Manuscript received December 16, 1998; accepted March 17, 1999.

#### References

- Strickler JG, Kurtin PJ. Mediastinal lymphoma. *Semin Diagn Pathol* 1991; 8:2-13.
- Longo DL, Glatstein E, Duffey PL, et al. Alternating MOPP and ABVD chemotherapy plus mantle-field radiation therapy in patients with massive mediastinal Hodgkin's disease. *J Clin Oncol* 1997; 15:3338-46.
- Zinzani PL, Bendandi M, Martelli M, et al. Anaplastic large-cell lymphoma: clinical and prognostic evaluation of 90 adult patients. *J Clin Oncol* 1996; 14:955-62.
- Zinzani PL, Bendandi M, Frezza G, et al. Primary mediastinal B-cell lymphoma with sclerosis: clinical and therapeutic evaluation of 22 patients. *Leuk Lymphoma* 1995; 21:311-6.
- Gobien RP, Skucas J, Paris BS. CT assisted fluoroscopically guided aspiration biopsy of central hilar and mediastinal masses. *Radiology* 1981; 141:443-7.
- Adler OB, Rosenberger A, Peleg H. Fine-needle aspiration biopsy of mediastinal masses: evaluation of 136 experiences. *Am J Radiol* 1983; 140:893-6.
- Ariza MAdG, Aguiran ERA, Atance JLV. Transthoracic aspiration biopsy of pulmonary and mediastinal lesions. *Eur J Radiol* 1991; 12:98-103.
- Herman SJ, Holub RV, Weisbrod GL, Chamberlain DW. Anterior mediastinal masses: utility of transthoracic needle biopsy. *Radiology* 1991; 180:167-70.
- Goralnik CH, O'Connell DM, El Youssef SJ, Haaga JR. CT-guided cutting needle biopsies of selected chest lesions. *Am J Radiol* 1988; 151:903-7.
- Sokolowski JW, Burgher LW, Jones FL, Patterson JR, Selecky PA. Guidelines for percutaneous transthoracic needle biopsy. *Am Rev Respir Dis* 1989; 140:255-6.
- Zafar N, Moinuddin S. Mediastinal needle biopsy. *Cancer* 1995; 76:1065-8.
- Powers C, Silverman J, Geisinger K, Frable W. Fine-needle aspiration biopsy of the mediastinum. *Am J Clin Pathol* 1996; 105:168-73.
- Hughes JH, Katz RL, Fonseca GA, Cabanillas FF. Fine-needle aspiration cytology of mediastinal non-Hodgkin's non-lymphoblastic lymphoma. *Cancer* 1998; 84:26-35.
- Boaron M, Mattioli G, Ravasi G, Zinco L. Needle biopsy of endothoracic neoformations: a five-year experience. *J Surg Oncol* 1978; 10:55-9.
- Chong-Jen Y, Pan-Chyr Y, Dun-Bing C, et al. Evaluation of ultrasonically guided biopsies of mediastinal masses. *Chest* 1991; 100:399-405.
- Andersson T, Lindgren PG, Elvin A. Ultrasound guided tumour biopsy in the anterior mediastinum. An alternative to thoracotomy and mediastinoscopy. *Acta Radiol* 1992; 33:423-7.
- Venuta F, Rendina EA, Pescarmona EO, et al. Ambulatory mediastinal biopsy for hematologic malignancies. *Eur J Cardiothorac Surg* 1997; 11:218-21.
- Rendina EA, Venuta F, De Giacomo T, et al. Comparative merits of thoracoscopy, mediastinoscopy, and mediastinotomy for mediastinal biopsy. *Ann Thorac Surg* 1994; 57:992-5.
- Morrissey B, Adams H, Gibbs AR, Crane MD. Percutaneous needle biopsy of the mediastinum: review of 94 procedures. *Thorax* 1993; 48:632-7.
- Harris NL, Jaffe ES, Stein H, et al. A proposal for an international consensus on the classification of lymphoid neoplasms. *Blood* 1994; 84:1361-92.
- Elia S, Cecere C, Giampaglia F, Ferrante G. Mediastinoscopy vs. anterior mediastinotomy in the diagnosis of mediastinal lymphoma: a randomized trial. *Eur J Cardiothorac Surg* 1992; 6:361-5.
- Porte H, Roumilhac D, Eraldi L, Cordonnier C, Puech P, Wurtz A. The role of mediastinoscopy in the diagnosis of mediastinal lymphadenopathy. *Eur J Cardiothorac Surg* 1998; 13:196-9.