BRIEF COMMUNICATION

VIDEO-ASSISTED THORACOSCOPIC SURGERY FOR THE DIAGNOSIS OF PATIENTS WITH HILAR AND MEDIASTINAL LYMPHADENOPATHY

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Abstract: In areas where tuberculosis (TB) is rare, cases of hilar and mediastinal lymphadenopathy are often attributed to the diagnosis of sarcoidosis or a malignant process. However, these manifestations have been only sparsely reported in countries with high rates of TB. The role of simultaneous lung biopsy in the differential diagnosis of these patients using a thoracoscopic approach is also undetermined. In this prospective study, 15 adult patients with hilar and mediastinal lymphadenopathy were evaluated using video-assisted thoracoscopy during the period from May 1995 through September 1999. Biopsy of the hilar and mediastinal lymph nodes was undertaken in all 15 patients, and a wedge biopsy of the lungs was performed whenever frozen section of the nodes disclosed granulomatous inflammation. The final diagnoses included sarcoidosis (10 patients), TB (2), metastatic small cell carcinoma (2), and reactive lymphoid hyperplasia (1). No morbidity or mortality was associated with the operation. In patients with sarcoidosis and TB, most of the lymph node biopsy specimens disclosed extensive hyaline fibrosis. Lung biopsy specimens presented small non-necrotizing granulomas with multinucleated giant cells even in the absence of demonstrable parenchymal lesions. In the two patients with TB, identification of acid-fast bacilli and growth of \textit{Mycobacterium tuberculosis} occurred only in lung specimens and not in specimens from lymph nodes. Video-assisted thoracoscopic surgery is a safe, simple, and effective procedure for the diagnosis of patients with hilar and mediastinal lymphadenopathy. Our results suggest that for a better differentiation between TB and sarcoidosis, an additional lung biopsy could be undertaken to provide specimens for microscopic examination and culture.

Adult patients with hilar and mediastinal lymphadenopathy who have negative findings on sputum and other non-invasive examinations present a diagnostic challenge. Although numerous investigators have suggested that sarcoidosis is the most common cause of this presentation, its differentiation from tuberculosis (TB) remains very difficult, especially in areas of high TB prevalence such as Taiwan. Mediastinoscopy has been widely used with satisfactory diagnostic results in Western Europe and the USA, where sarcoidosis is highly prevalent [1]. However, problems still exist with this procedure. First, the involved nodes are sometimes difficult to approach so that mediastinotomy or thoracotomy is warranted. Second, studies of the lymph nodes are occasionally inconclusive and additional lung biopsy, therefore, needs to be done. Third, TB is very common and sarcoidosis is extremely rare in Taiwan, making the diagnosis of sarcoidosis a challenging task. With the recent advancements and the expanded application of video-assisted thoracoscopic surgery (VATS), most minor therapeutic or diagnostic thoracic procedures might be performed using this technique [2]. This prospective study was conducted to investigate the safety and efficacy of VATS, as well as the value of additional lung...
biopsy, in the diagnosis and management of patients with hilar and mediastinal lymphadenopathy.

Patients and Methods

From May 1995 to September 1999, 15 patients were selected to undergo thoracoscopic diagnostic procedures based on the following criteria: presence of hilar and mediastinal lymphadenopathy with or without pulmonary infiltrates on chest radiography (Fig. 1) or computerized tomography (CT) of the thorax; negative sputum examinations for bacteria, fungi, and tuberculous bacilli; no obvious endobronchial abnormality on fiberoptic bronchoscopy; negative cultures and cytologic examinations of bronchoalveolar lavage fluid; no demonstrable lymphadenopathy on physical examination or by sonography; no evidence of extrathoracic malignancies or associated skin lesions. The presence of pulmonary infiltrates and the definite location of hilar and mediastinal lymphadenopathy were determined by pulmonologists and radiologists.

All patients underwent surgery under general anesthesia with double-lumen tube endotracheal intubation. Thoracoscopic exploration was performed on the side where the lymph nodes could be most easily accessed. After total lung collapse, VATS was performed to identify pulmonary, pleural, or mediastinal pathology. Hilar and mediastinal lymph node biopsies were performed in all 15 patients, and specimens were immediately examined by frozen section during VATS. An additional wedge biopsy of the lung was taken, using endoscopic staplers whenever the frozen section disclosed granulomatous inflammation. The subapical region of the ipsilateral upper lobe was chosen for biopsy because adult-type TB often involves this area. In addition to histopathologic examinations, the specimens were also cultured to determine the presence of aerobic, anaerobic, fungal, and mycobacterial organisms.

Results

There were nine women and six men in this study, with a mean age of 43.3 years (range, 20–64 yr). At the time of enrollment, 11 patients had various symptoms such as cough, fever, hoarseness, body weight loss, and dyspnea on exertion. The distribution of intrathoracic lymphadenopathy detected by radiography and CT of the chest is shown in the Table. Bilateral hilar lymphadenopathy was observed in 12 patients. Eight patients had bilateral mediastinal lymph node involvement and 13 patients had enlarged subcarinal nodes. Diffuse pulmonary infiltrates were noted in four patients for whom fiberoptic bronchoscopy with transbronchial lung biopsy was done but no definite diagnosis could be made.

Fig. 1. Chest radiograph of a 28-year-old woman showing left hilar lymphadenopathy with diffuse pulmonary infiltrates. Thoracoscopic lung biopsy yielded acid-fast bacilli.

Fig. 2. Diagnostic protocol and final results in 15 patients with hilar and mediastinal lymphadenopathy. VATS = video-assisted thoracoscopic surgery; LN = lymph nodes; FS = frozen section; SCC = small cell carcinoma; AFB = acid-fast bacilli; PS = paraffin section.
Table. Distribution of intrathoracic lymphadenopathy on chest radiography and computerized tomography (CT) in 15 patients

<table>
<thead>
<tr>
<th>Hilar lymphadenopathy</th>
<th>Mediastinal lymphadenopathy</th>
<th>Subcarinal lymphadenopathy</th>
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DPI = diffuse pulmonary infiltrates on both radiography and CT.

Thirteen patients underwent thoracoscopic exploration of right-sided adenopathy and two patients underwent a left thoracoscopic lymphadenectomy. The diagnostic protocol and the results are shown in Fig. 2. In 12 patients, granulomatous inflammation of lymph nodes was noted via intraoperative frozen section. On paraffin section, discrete non-necrotizing granulomas were noted in every lymph node biopsy specimen. Most of these nodes revealed effacement of architecture with replacement by extensive hyaline fibrosis and remnants of granulomas. No acid-fast bacilli could be identified by microscopic examination. Cultures of the lymph nodes for tuberculous bacilli were all negative. We took additional lung biopsies in these patients. The largest dimension of these specimens ranged from 1.8 to 3.5 cm (mean, 2.6 cm). Even when the lungs appeared normal by radiography, scattered, well-demarcated, non-necrotizing granulomas with multinucleated giant cells were identified in each lung biopsy specimen. Most strikingly, the presence of acid-fast bacilli and growth of Mycobacterium tuberculosis were demonstrated in the lung specimens of two patients. These two patients underwent anti-TB treatment that resulted in a decrease in the size of the nodes and improvement of their general health. Sarcoidosis was finally diagnosed in the remaining 10 patients because specimens cultured for tuberculous bacilli, bacteria, and fungi yielded no growth. Three of these patients underwent steroid therapy for stage II disease and no medication was given to the others. All of these patients had stationary disease after VATS.

Metastatic small cell carcinoma was diagnosed by biopsy of mediastinal lymph nodes in two patients. One received chemotherapy and survived 2 years after VATS. The other patient was lost to follow-up and died of multiple metastases 10 months after the diagnosis. Reactive lymphoid hyperplasia was diagnosed in the last patient. No evidence of malignancy or granulomatous inflammation was noted on pathologic examination. Cultures for microorganisms were all negative.

No patient had evidence of pleural involvement during thoracoscopic exploration. An intercostal tube was routinely placed after the thoracoscopic procedure. No patient had persistent air leakage and blood loss was minimal. Surgical incisions were cosmetically satisfactory and patients rarely complained of wound pain. There was no morbidity or mortality associated with the operation. The mean hospital stay was 4.2 days (range, 3–6 d).

Discussion

The management of patients with hilar and mediastinal lymphadenopathy remains a challenge because there are no simple laboratory techniques that can clearly distinguish neoplastic, infectious, and sarcoid origins. Together with a more aggressive attitude and the use of advanced diagnostic approaches by pulmonologists [3, 4], the diagnostic yield among patients with hilar and mediastinal lymphadenopathy has been greatly improved. Nonetheless, surgical intervention is still occasionally indicated to provide a definitive diagnosis when noninvasive examinations are inconclusive. Mediastinoscopy is widely applied for sampling of paratracheal lymph nodes and provides low operative risk and satisfactory results in countries where TB is rare [1]. However, access to adenopathy in the aorticopulmonary window, periazygos, and subcarinal areas is difficult [5]. Furthermore, simultaneous lung biopsy is impossible with this technique. VATS not only provides access to the thoracic cavity and mediastinum by an approach associated with lower morbidity, but also allows large quantities of tissues to be obtained easily and lung or pleural biopsy to be performed simultaneously whenever indicated [6].

Because TB is highly prevalent [7] and sarcoidosis is very rare in Taiwan [8], mycobacterial infection should be very carefully ruled out when sarcoidosis is diagnosed. However, the clinical and radiologic pictures of these two diseases are sometimes indistinguishable. Mikhail et al [9] and Kent et al [10] emphasized that clinical criteria and mediastinal lymph node biopsy are unreliable for the diagnosis of sarcoidosis. In the latter study, only open lung biopsy provided a definitive diagnosis in 53% of patients. In order to obtain both lymph node and lung tissue for cultural and pathologic studies, we chose VATS as the diagnostic approach for patients with hilar and mediastinal lymphadenopathy. In the two patients with
TB, tuberculous bacilli were identified and cultured from lung specimens rather than from lymph nodes. This result might have been caused either by the smaller tissue sample from the lymph nodes or by higher tissue oxygen tension in the lungs, thus making M. tuberculosis more easily localized and cultured through lung biopsy.

Many authors demonstrated that when a sufficiently large volume of tissue is available, the incidence of lung granulomas is nearly 100% in patients with stage 1 sarcoidosis [11]. The operative results of our study agree with this finding. Granulomatous inflammation was demonstrated in every lung specimen in the 12 patients with sarcoidosis and TB even when the lungs appeared normal by radiography. The benefit of additional lung biopsies is twofold. First, a diagnosis can be made using this approach in some TB patients with negative studies of the mediastinal nodes. Second, in the diagnosis of sarcoidosis, the presence of granulomas both in the lungs and lymph nodes confirms the presence of multisystem disease rather than a local sarcoid reaction. Malignancy is also a possible cause of hilar and mediastinal lymphadenopathy. The short recovery period offered by VATS could allow these patients to undergo chemotherapy earlier.

Although the number of cases is very limited, the results of this study indicate that VATS is more than just a supplementary method for mediastinoscopy in the management of patients with hilar and mediastinal lymphadenopathy. In addition to providing a safe, simple, and effective way to access intrathoracic lesions, VATS provides large amounts of specimens for pathologic examination and microbiologic culture. Our results also suggest that a simultaneous lung biopsy should be performed as a routine procedure to further differentiate sarcoidosis from TB, especially in areas of high prevalence of TB.

References