Value of lung biopsy in pulmonary diseases in children

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ABSTRACT

Purpose: Open lung biopsy (OLB) is claimed to be a sensitive tool for the diagnosis of interstitial lung disease. It is reported to be associated with significant morbidity and mortality.

Aim: Evaluate whether lung biopsy helped us to make a specific diagnosis, it had resulted in change in therapy and assessment of its morbidity and mortality.

Materials and Methods: This was a retrospective analysis of 91 lung biopsies performed in 83 patients between January 2000 and December 2003. These children were allocated to three groups: a. Primary pulmonary pathology (22), b. Immunocompromised (49) i. Primary immunodeficiency (10), ii. Postchemotherapy and BMT (39), c. Pulmonary metastases from solid tumors (20)

Results: A specific diagnosis was reached in 87/91 children (95%), but this resulted in a change in therapy (excluding lung meet) in only 23/71 (32%). It is lower in those postchemo/BMT 8/39 (20.6%). Postoperative morbidity occurred in 11/91 (12%) but procedure-related morbidity was only (3.2%). Death within a month of the biopsy occurred in six children (6.5%), with one (1.1%) procedure-related.

Conclusion: 1. OLB is a safe procedure at our institution. 2. OLB is a sensitive tool to determine the specific cause of pulmonary infiltrate. 3. Change in therapy expected to be only in 32% of patients and even lower in postchemotherapy and BMT children.

KEY WORDS: Interstitial lung disease, open lung biopsy, thoracoscopy

INTRODUCTION

A child who presents with severe respiratory distress with diffuse infiltrates seen on the chest radiograph is often a diagnostic challenge. Empirical therapy is frequently begun with a combination of antibiotics, antifungal therapy with or without steroids, based on the clinical picture and the radiologic abnormalities. However, when there is no improvement in clinical or radiologic findings, definitive diagnosis is required. Less invasive procedures such as bronchoscopy and bronchoalveolar lavage may be helpful in diagnosing infectious causes, but not so in noninfectious causes and in some fungal infections, when a lung biopsy may be essential. Lung biopsy is considered to be the gold standard for the diagnosis of parenchymal lung disease. Recent advances in imaging techniques viz, high resolution computerized tomography have helped in accurate localization of pulmonary lesions. The improvements in pediatric anesthesia and the emergence of video-assisted thoracoscopic surgery have decreased the morbidity of lung biopsy. Nevertheless, lung biopsy is still an invasive procedure associated with significant morbidity and mortality, especially in immunocompromised children.

Our aim of this review is to evaluate the yield of lung biopsy done at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia (KFSH and RC), to make a specific diagnosis in both immunocompetent and immunocompromised child, whether open lung biopsy (OLB) resulted in change in therapy, to assess morbidity and mortality of the procedure and develops strategies or find alternative to OLB.

MATERIALS AND METHODS

A retrospective review of 91 lung biopsies in 83 children was performed at KFSH and RC, with the age range between 3 months to 15 years (median = 7.37 years),
in the period between January 2000 and December 2002. The data collected demographic information, primary diagnosis, prebiopsy therapy, indication for OLB, pathological and microbiological diagnosis, type of surgical procedure, modification of therapy postbiopsy and morbidity and mortality of the procedure (within 30 days). Children were grouped into three groups:

Group I: Primary pulmonary pathology children (22)

Group II: Immunocompromised children (49):
- Primary immunodeficiency (ID) (10)
- Postchemotherapy and BMT (39)

Group III: Pulmonary metastasis from solid tumor (20)

In Group I, all children are immunocompetent with no underlying immunodeficiency or malignancy. Indication for OLB in this group primarily prolonged respiratory distress with significant radiological abnormalities with or without oxygen dependency.

Group II are those congenital primary immunodeficiency common variable ID (2), bare lymphocytic syndrome (2), severe combined ID (scid) (3), chronic granulometous disease, Chediak Higashi syndrome (1).

The primary indication of OLB in this group is recurrent chest infection with persistent or worsening radiological signs.

Group II b, are those children who was on chemotherapy and those postbone marrow transplant (BMT): AML (12), ALL (16), lymphoma (2) and post BMT (9). Those patients usually had routine computed tomography (CT) scan of chest if they develop fever or chest symptoms or shows sign of sepsis.

Group III (20) those patient suggestive of pulmonary metastatic lesion to solid tumor.

Both Group I and II patients started first on emperic treatment before OLB, in the form of antibiotic, antifungal or steroids according to prebiopsy clinical and radiological diagnosis. Group III, all sent for biopsy based on suspecting metastasic lesion radiologically, either persistent lesions despite chemotherapy or lesions appeared during remission of solid tumors. These lesions should be three or less, to quality for OLB.

The lung biopsy was performed under general anesthesia by thoracotomy (open lung biopsy - OLB) or by video-assisted thoracoscopic surgery. OLB was performed by a muscle-sparing mini-thoracotomy \( n=56 \) through the 4th/5th intercostals space. Thoracoscopic biopsy \( n=28 \) was performed by using three ports - a 5/10 mm port for a 30° telescope and two other 3.5/5 mm working ports, with \( n=7 \) converted to open. Biopsy was taken using an endo-GIA stapler or rarely with an endo-loop. A chest tube was left in situ for 24 hours in the initial cases. The trend later was to remove the chest tube after re-expansion of the lung on table with positive pressure ventilation, except when there was a risk of persistent air-leak/bleeding from the biopsy site and in ventilated patients.

The biopsy tissue was subjected to regular histopathology, including special studies for acid-fast bacilli; fungus; cytomegalovirus (CMV); pneumocystis carinii and also the specific cultures. Change in therapy was instituted when indicated, based on the pathological/culture results; and the outcome (benefit or otherwise) was analyzed.

RESULTS

In Group I, histological specific diagnosis reached in 21 (95%) with 10 (45%) unexpected diagnosis [Table 1]. However, change in therapy as a result of OLB was in 11 (50%). Two had Nissen fundoplication for lipoid pneumonia [Figure 1], Secondary to GER, one lobectomy, five steroid therapy for hemosiderosis [Figure 2] and sarcoidosis, two anti-tuberculous treatments and one sepha and choquine for streptomycyes.

For Group II a, specific histological diagnosis reached in 10 (100%) and tissue culture was positive in only five (50%) (bacterial-1; mycobacterial-1 [Figure 3]; fungal-1; and those postbonemarrow transplant (BMT): AML (12), ALL (16), lymphoma (2) and post BMT (9). Those patients usually had routine computed tomography (CT) scan of chest if they develop fever or chest symptoms or shows sign of sepsis.

Table 1: Results summary

<table>
<thead>
<tr>
<th>Group</th>
<th>Histological specific diagnosis</th>
<th>Change in therapy</th>
<th>Tissue culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>21 (95)</td>
<td>10 (45)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>IIA</td>
<td>10 (100)</td>
<td>4 (40)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>IIB</td>
<td>38 (97)</td>
<td>8 (20)</td>
<td>8 (20.5)</td>
</tr>
<tr>
<td>III</td>
<td>18 (90)</td>
<td>N/A</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Overall</td>
<td>87/91 (95)</td>
<td>23/71 (32)</td>
<td>17/91 (18.7)</td>
</tr>
</tbody>
</table>

Figures in parentheses are percentage

Figure 1: Lung biopsy in this child found to have: both lipoid pneumonia with tuberculosis
Table 2: Comparison between pre and postbiopsy tissue diagnosis in Group I

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pre-biopsy</th>
<th>Post-biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipoid pneumonia</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Surfactant deficiency</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Idiopathic pulmonary hemosidrosis</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Bronchiolitis obliterans</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Interstitial pneumonia</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Niemann-pick disease</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Nonspecific/undiagnosed RDS</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

DISCUSSION

The causes of persistent and progressive distress in a child are many including interstitial lung disease, infections, chronic aspiration, pulmonary vascular disease, and other rare conditions. A specific diagnosis can frequently be made from the chest X-ray or CT scan appearance of the lung lesions and the appropriate therapy started. This may not be true in children occasionally, where the appearances on the imaging studies are nonspecific.[13] There is also a group of patients who have been started on empiric therapy, but are not responding to this type of treatment where there is in need for other mode of diagnostic tools.

Children postchemotherapy particularly for leukemia and lymphomas and also those children who are postbone marrow transplant as well as other immunocompromised children like primary and secondary immunodeficiency, are at risk of developing a serious pulmonary complications. These children usually have severe and prolonged neutropenia and they will be at risk of developing opportunistic infections. With the widespread use of prophylactic antibiotics, antiviral drugs for CMV and Septran® for pneumocystis carinii, there has been a significant decrease in the incidence of these infections as well as their complications. Some centers even advocate the empiric use of antifungal therapy in the group of neutropenic patients with persistent fever and characteristic lesions of lung infection on CT scans. An optimal and safe means of obtaining lung tissue for diagnosis is debatable, but an open lung biopsy either by thoracotomy or thoracoscopy can be considered to be the best diagnostic tool.[2-5] We found, in our group of patients, it is safe and provide good volume of tissue for diagnostic purposes. Video-assisted thoracoscopic surgery provides a better and wider visibility of the lung tissues.

Our morbidity was 11 children (12.1%), prolonged intubation (6), oxygen dependency (2), hematoma (1), bronchopleural fistula (1) and septic shock in one, but procedure-related morbidity 3/91 (3.2%). Mortality was six (6.5%) (within 1 month), with only one (1.1%) procedure-related.
surface, with less morbidity than the mini-thoracotomy. Also with the availability of finer instruments, VATS is now feasible even in the smaller group of children. We find that it is safe despite reports of high morbidity and mortality in other studies.

The main issue when considering a lung biopsy is whether or not there is a practical benefit from the invasive procedure with its associated morbidity and mortality. This is especially true in sicker children with immunosuppression from chemotherapy/postBMT where the benefits should be weighed with the risks developed. We found that it is a good tool to reach a specific diagnosis and this is similar to other reports from other groups, but it is not as high when it comes to having a positive tissue culture. For that reason, specific change in therapy was not high as well. Floreani et al. have collected 14 reports of 625 patients where the total yield in immunocompromised patients was found to be ranging between 45-83%, however, when it comes to change in therapy, only 32% which conclude that lung biopsy can only benefit as high as 30% in immunocompromised children.[10] However, Kramer et al. reported 46% change in therapy but mortality was as high as 39% for immunocompromised children.[2] Hayes-Jordan et al. has reported 63% survival.[4] But, these obviously are not procedure-related mortality. However, when we compared it to our overall morbidity was 12.1% and overall mortality was 6.5%, but procedure related morbidity and mortality was 3.2% and 1.1% respectively. The yield was partly poor especially in the group who had postchemotherapy and postBMT for about 20.6%. This may be partly due to the fact that these children with persistent and severe neutropenia are empirically started with broad-spectrum antibiotics and antifungal drugs and the lung biopsies performed often later in the course of the illness. Also despite negative result from the lung biopsy, many continued on the above therapy on the presumption of the infection in the clinical ground. Nevertheless, the lung biopsy was helpful in making specific diagnosis and giving more comfort to continue in treating the infection, particularly when it comes to fungal infection especially Aspergillosis, which carry high morbidity and mortality if not treated properly.[14,15] It was also noted in our patient group that the higher morbidity and mortality of patient with those immunocompromised patients.

We think from our results, it may be helpful if the lung biopsy was done early in the course of disease before embarking on starting empiric therapy, which we think that it has contributed to low tissue culture result. As we usually tend to be keen in doing our lung biopsy earlier in the course of disease before serious deterioration of clinical condition contributed to a lower morbidity and mortality compared to other series. We still continue to use lung biopsy as a tool for the purpose of diagnosing pulmonary infiltrate as it benefits around 30% of the patients in regard to change of therapy, however, it benefit the rest of the group in continuing using the same management and has given comfort to the treating physician to continue the same line of management.

CONCLUSION

We wish to reiterate that lung biopsy is a sensitive diagnostic tool to reach specific histological diagnosis (95%). However, it is only helpful in (32%) to make change in therapy. Change in therapy is less likely in those postchemotherapy and BMT, as yield in tissue culture, is lower compare to the rest of the group. Our morbidity and mortality are low and considered to be safe in our institution as procedure-related morbidity (3.2%) and mortality (1.1%). OLB still considered diagnostic and therapeutic in suspected lung metastasis. Earlier lung biopsy in the course of the disease may be considered before starting an empiric treatment (antibiotic) to get higher tissue culture positive results.

REFERENCES

10. Floreani AA, Sisson JH, Gurney J, Romberger DJ, Anderson LC,

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