ORIGINAL ARTICLE

Open Lung Biopsy for Diffuse Parenchymal Lung Disease in Children

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Summary

An open lung biopsy was performed in 12 children with diffuse parenchymal lung disease. A definitive histopathological diagnosis was obtained from all procedures but determined treatment options in only 10 children (83%). Three (25%) children were ventilated for respiratory failure prior to the procedure. Four (44%) of the other 9 children required ventilatory support after the procedure. Three (25%) children developed post-op pneumothorax that resolved fully with chest tube drainage. There were no deaths as a direct result of the procedure. Open lung biopsy is useful in providing a definitive diagnosis in children with diffuse parenchymal lung disease and determining treatment in the majority of cases. The procedure was well-tolerated with minimal complications.

Key Words: Open lung biopsy, Diffuse parenchymal lung disease, Children

Introduction

Persistent respiratory symptoms in association with diffuse parenchymal lung disease in children represent a rather rare category of respiratory diseases that pose a diagnostic and therapeutic challenge for the clinician. The heterogenous nature of diffuse parenchymal lung disease makes determining the specific diagnosis immensely difficult without a histopathological diagnosis.

An open lung biopsy to obtain a diseased tissue sample for histopathological study remains the gold standard in the approach to this rare respiratory disorder in children [1]. Proceeding with an open lung biopsy in children with an already compromised respiratory status is obviously a difficult endeavor and is certainly associated with an elevated risk for procedure related morbidity and mortality.

We describe our experience with 12 children with persistent respiratory symptoms secondary to diffuse parenchymal lung disease who underwent an open lung biopsy for the determination of a definitive histopathological diagnosis. We also evaluated the procedure with regards to its determination of treatment, clinical outcome and procedure related morbidity and mortality.

Materials and Methods

We reviewed 12 children admitted between 1st January 1999 and 1st December 2002 who presented with persistent respiratory symptoms due to diffuse bilateral parenchymal lung disease evident on chest radiographs and high resolution computed tomography (HRCT) scan images. All children had extensive and comprehensive haematological, biochemical, microbiological, immunological and cytological

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investigations but they failed to provide a definitive diagnosis; therefore requiring a histopathological diagnosis from an open lung biopsy. A flexible fibre-optic bronchoscopy was also performed followed by a broncho-alveolar lavage (BAL) before the open lung biopsy procedure. Cytological and microbiological investigations were carried out on the BAL specimen obtained during the fibre-optic bronchoscopy.

The open lung biopsy was considered to determine treatment if the definitive treatment process initiated depended upon confirmation of the histopathological diagnosis.

Open lung biopsy

A suitable site for lung biopsy was determined by both the clinician and paediatric surgeon based upon the distribution of the disease on HRCT scan images. Areas of dense opacities were specifically avoided, as these areas were most likely to show extensive fibrosis and not contribute to a definitive histopathological diagnosis.

All procedures were performed under general anaesthesia. A short incision was made over the pre-determined site through the intercostal muscles. The lung site of interest was then mobilized upon gaining access into the pleural cavity. A clamp was applied on the lung site of interest and a lung biopsy measuring 2 to 4cm was then taken distal to the clamp. The lung was repaired with a continuous suture using polypropylene (Prolene). The surgical wound was then closed in layers and a chest drain was left in situ. The lung biopsy specimen was divided into 2 portions and sent for histopathogical and microbiological examination respectively.

Results

There were 6 boys and 6 girls with a median age of 6.7 years and age range between 2.5 and 11.5 years. There were 5 Chinese, 4 Malay and 2 Indian children. One child was Indonesian. The median duration of respiratory symptoms was 4.5 months with a range of between 1.0 and 36.0 months. Six (50%) children were oxygen dependent for between 2.0 and 4.0 weeks duration and 3 (25%) children developed respiratory failure and refractory hypoxaemia requiring ventilation prior to the procedure (Table I).

A definitive histopathological diagnosis was obtained from all procedures (Table II). However, the histopathological diagnosis determined definitive treatment in only 10 (83%) children. The 2 children for whom the procedure did not influence treatment had extensive fibrosis with histopathological changes consistent with bronchiolitis obliterans organizing pneumonia (BOOP) and cryptogenic organizing pneumonia (COP) respectively. Bronchoscopy with BAL sampling was performed in 11 (92%) children but did not yield significant cytological or microbiological findings that could assist in the diagnosis.

All but one child were admitted to the Paediatric Intensive Care Unit after the procedure. Four (44%) of the 9 children who were self-ventilating prior to the procedure required post-operative respiratory support (3 for less than 24 hours and 1 for 72 hours duration). Three (25%) children developed post-operative pneumothorax. Two of these resolved spontaneously and 1 tension pneumothorax resolved with adjustment of the chest tube. There were no deaths encountered as a direct result of the open lung biopsy.

Table I: Clinical parameters of 12 children with diffuse parenchymal lung disease

Case	Age (years)	Sex	Race	Predominant clinical features	Duration of symptoms (months)	Respiratory status
1	2.5	F	Ind	Breathless, wheeze	18.0	Stable
2	2.5	F	Chi	Cough, breathless, failure to thrive	3.0	Oxygen dependent
3	3.2	F	Mal	Fever, breathless, hypercalcaemia	2.0	Oxygen dependent
4	3.8	M	Indon	Breathless, wheeze, encephalopathy	5.0	Ventilated
5	4.5	M	Chi	Breathless	12.0	Ventilated
6	7.5	F	Chi	Fever, breathless	1.0	Oxygen dependent
7	7.8	M	Mal	Productive cough, clubbing	36.0	Stable
8	8.1	M	Mal	Breathless, wheeze	24.0	Oxygen dependent
9	9.3	F	Chi	Breathless, cyanosis	2.0	Oxygen dependent
10	9.5	F	Chi	Cough, breathless	3.0	Oxygen dependent
11	11.3	M	Ind	Fever, breathless	1.5	Ventilated
12	11.5	M	Mal	Productive cough	36.0	Stable

M = male, F = female, Mal = Malay, Chi = Chinese, Ind = Indian, Indon = Indonesian

Table II:Clinical parameters and histopathological diagnosis of 12 children with diffuse parenchymal lung disease

Case	Histopathological diagnosis	Post-op ventilation	Complication	Outcome	Biopsy determined treatment
1	Pulmonary fibrosis/ Bronchiolitis obliterans organizing pneumonia	No	No	Survivor	No
2	Diffuse Pulmonary Lymphangiomatosis	Yes	No	Survivor	Yes
3	Sarcoidosis Stage II/ Tuberculoisis	No	No	Survivor	Yes
4	Desquamating Interstitial Pneumonitis/ Hamman Rich Syndrome	*Yes	Yes	Died	Yes
5	Pulmonary Langerhans cell Histiocytosis	*Yes	Yes	Died	Yes
6	Inflammatory Pseudotumour	No	No	Survivor	Yes
7	Bronchiectasis/ Cryptogenic organizing pneumonia	No	No	Survivor	No
8	Desquamating Interstitial Pneumonitis	No	No	Survivor	Yes
9	Infiltrative Pulmonary Rhabdomysarcoma	Yes	No	Survivor	Yes
10	Bronchocentric Granulomatosis	Yes	No	Survivor	Yes
11	K_1 Pulmonary Non- Hodgkin Lymphoma	*Yes	No	Survivor	Yes
12	Pulmonary fibrosis/ Tuberculoisis	Yes	Yes	Survivor	Yes

*Ventilated prior to procedure

Discussion

Children who present with persistent respiratory symptoms and exhibit diffuse parenchymal lung changes on chest x-ray or computed tomography scan pose a diagnostic challenge. This clinical and radiological combination is due to a heterogenous category of respiratory disorders that includes interstitial lung disease, malignancy, lymphoproliferative disorders, chronic infections and vascular disorders[2,3,4]. However, the non-specific nature of the respiratory symptoms and diffuse radiological changes make a simple determination of the diagnosis difficult without extensive investigations. Unfortunately, a definitive diagnosis is still frequently not obtained despite extensive non-invasive investigations and is therefore increasingly dependent on a histopathological diagnosis [5].

Open lung biopsy under general anaesthesia remains the gold standard in obtaining a tissue specimen for histopathological study. The procedure allows for a direct visualization of the diseased lung and acquisition of adequate lung tissue for histopathological study. Our experience demonstrated that the yield of a definitive diagnosis from the open lung biopsy was high, and concurred with the experience described in the literature[6,7,8]. However, the safety of this procedure is often doubted as the potential risk for morbidity and mortality in this group of children is of major concern when administering a general anaesthesia. Our experience showed that the 4 children who required post-operative ventilation needed such support for a short duration only (median 24.0 hours) and the pneumothoraces that was encountered in 3 children resolved with minimal intervention. Even the 3 children who had extensive diffuse parenchyma lung disease requiring ventilatory support tolerated the procedure and general anesthesia. More importantly, no deaths occurred as a direct result of the procedure and it influenced treatment in a high proportion (83%) of these patients. It is therefore reasonable to proceed with an open lung biopsy in this group of children, as the procedure was generally well tolerated with manageable minimal complications.

The development of less invasive methods of obtaining diseased lung tissue namely bronchoscopic guided transbronchial biopsy (TBB), percutaneous lung biopsy and video-assisted thorascopic (VAT) guided lung biopsy offer attractive alternative avenues for diagnosis for this group of children[9, 10, 11]. The tissue samples obtained using a bronchoscopic guided TBB is very small and therefore has rather limited applicability except in pulmonary disorders that have very highly specific histopathological changes, for example alveolar microlisthiasis[12]. Its use in diffuse parenchymal lung disease like in our patients is less well established. A percutaneous lung biopsy guided by radio-imaging appears to be a rather appealing alternative in obtaining diseased lung tissue specimens The diagnostic yield of this procedure is reported to be between 58 - 100% with minimal complications[13, 14], which although appears good is not as consistent as the diagnostic yield of an open lung biopsy [15]. VAT guided lung biopsy has the advantages of direct visualization of the diseased lung without a thoracotomy, shorter operating time and less post-operative pain; but it still requires a general anaesthesia. The procedure has been shown to be comparable to an open lung biopsy in obtaining a histopathological diagnosis[16]. It is however technically more difficult and expensive requiring additional specialized equipment and trained staff dedicated to its operations and maintenance[17]. Moreover, it may not be suitable in younger children where the equipment size available cannot be applied effectively or appropriately.

The markedly heterogenous nature of the underlying aetiology of diffuse parenchymal disease in children is clearly demonstrated in the subjects reported here. All but 2 of the children reported here responded to treatment and were discharged well. Both children who succumbed from their illnesses were ventilated for respiratory failure and refractory hypoxaemia prior to the procedure and had very extensive diffuse parechymal and airway disease. Our experience with these 2 children suggests that if ventilatory support is already required prior to the open lung biopsy, the outcome is less likely to be favourable despite obtaining a histopathological diagnosis and initiating the appropriate treatment. Obtaining a histopathological diagnosis should therefore be considered a priority and performed as early as possible in this group of children.

In conclusion, diffuse parenchymal lung disease is a rare and heterogenous group of respiratory disorders in children. The histopathological diagnosis is fundamental in determining treatment for this group of children. An open lung biopsy under general anaesthesia is therefore important in this group of children as it has a high yield in obtaining a definitive diagnosis with minimal complications.

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