Lung biopsy in children: when is it useful?

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ABSTRACT

Aim

To provide a further insight into the usefulness of lung biopsy in children.

Methods

Lung biopsies in children from January 2007 to December 2017 were reviewed (n=39). The histology results were categorised as: definitive diagnosis, normal lung parenchyma, inconclusive.

Results

Lung biopsy provided a definitive diagnosis in 25 (64%) cases. A suspected diagnosis was confirmed in 16 (41%) and a new diagnosis was found in 9 (23%) children. Histology was inconclusive in 11 (28%) cases and normal in 3 (8%). Fifteen (38%) of children had treatment altered due to the biopsy result.

Conclusion

Lung biopsy mostly confirmed the suspected diagnosis and was associated with a low procedure related morbidity (n=1) and mortality (n=0). Importantly, the biopsy result identified a pathology which altered treatment in over one third of patients. However, in a number of cases the histology was inconclusive, therefore careful patient selection is recommended to maximise diagnostic yield.

INTRODUCTION

Paediatric surgeons are commonly asked to carry out lung biopsies in children to obtain tissue for a definitive histological or microbiological diagnosis. A lung biopsy is an invasive diagnostic procedure however, often performed in children with significant comorbidities.[1] The decision of whether to perform a lung biopsy in this cohort of patients remains an important one, given the risks associated with the surgery. The reported diagnostic yield from lung biopsy is variable, and its utility in bringing a therapeutic change to patients remains largely uncertain.[1, 2] The European protocol for Interstitial Lung Disease in Children suggests performing a lung biopsy only if treatment will be changed as a result of the procedure.[3] Therefore, the selection of appropriate patients is important to maximise utility and avoid unnecessary surgical intervention in vulnerable children. This study aims to determine the diagnostic yield of paediatric lung biopsy in our centre and provide new data surrounding the usefulness of lung biopsy in children.

METHODS

All children who underwent diagnostic open or thoracoscopic lung biopsy in our centre between January 2007 to December 2017 were identified from clinical coding. All therapeutic lung resections and transbronchial lung biopsies were excluded for the purposes of this study.

In our centre, biopsy samples underwent histological processing by a number of different pathologists and a macroscopic and microscopic report was formulated. Each specimen was routinely processed followed by relevant staining including Gram, Grocott, dPAS and modified Ziehl-Neelsen to identify microorganisms within the sample. When clinical details suggested malignancy, samples underwent immunohistochemical staining for specific markers. In cases of significant uncertainty or rarity, specimens were sent externally for a secondary opinion.

Patient records, histology reports and operation notes were retrospectively reviewed for patient demographics, the indications for biopsy, preoperative investigations,

surgical technique, complications and the histological outcome. The results from lung biopsy were categorised into three distinct groups: definitive histological diagnosis, normal lung parenchyma, or inconclusive histology. Biopsy results were correlated against the preoperative provisional diagnosis. Medical records were reviewed to determine whether treatment was changed as a result of the histology results.

RESULTS

Thirty-nine patients were identified for inclusion in the study. Twenty-one were male (53.8%) and 18 were female (46.2%). Median age at biopsy was 3.5 years (7 days – 15 years). There were 33 open procedures and six thoracoscopic (15%). Median operative time for open biopsy was 61 mins (31-81), and for thoracoscopic biopsy was 83 mins (30-125). The median duration of a chest drain following surgery was 2 days (1-4). The complications associated with the procedure included one child who had a haemothorax. No persistent air leak or pneumothorax was reported in this cohort.

Four out of the 39 lung biopsy samples were sent for a second histological review at other specialist UK centres. In all four of these cases, the second opinion agreed with the original decision but provided further histological detail and supplementary information.

Lung biopsy provided a definitive histological diagnosis in 25 (64%) children, of which a suspected diagnosis was confirmed in 16 (41%) children, and a new diagnosis was found in 9 (23%). In the remaining children, 11 (28%) cases had a histology result which was inconclusive and 3 (8%) had normal histology (Table 1).

Table 1: Histological results from lung biopsy

Single suspected preoperative diagnosis			
CONFIRMATIVE OF SUSPECTED PREOPERATIVE DIAGNOSIS			
Preoperative diagnosis	Histology	N	N=10
PTLD ^a	PTLD	3	
Pulmonary Hypertension	Pulmonary Hypertension	2	
Lymphangiectasis	Lymphangiectasis	2	
Metastasis	Wilms Tumour metastasis	1	
Lung dysplasia	Alveolar capillary dysplasia	1	
IPEX ^e associated pneumonia	Features of immunodeficiency	1	
NEW HISTOLOGICAL DIAGNOSIS			
Preoperative diagnosis	Histology	N	N=5
Fungal infection	Chronic granulomatous disease	2	
Alveolar capillary dysplasia	Chronic diffuse pneumonitis	1	
Metastatic disease	Acute haemorrhagic infarction	1	
Pseudomonas infection	Miliary tuberculosis	1	
NORMAL LUNG PARENCHYMA			
Preoperative diagnosis	Histology	N	N=2
Parenchymal lung disease	Normal	1	
CPAM ^c	Normal	1	
INCONCLUSIVE HISTOLOGY			
Preoperative diagnosis	Histology	N	N=5
Infection NOS	Non-specific changes	3	
Fungal infection	Non-specific interstitial pneumonitis	1	
EBV ^d lymphoproliferation	Non-specific changes	1	
Multiple preoperative differential diagnoses			
CONFIRMATIVE OF A SUSPECTED PREOPERATIVE DIAGNOSIS			
Preoperative diagnoses	Histology	N	N=6
PTLD/infection NOS	PTLD	1	
Fungal infection/Residual Lymphoma	Diffuse Large B-Cell Lymphoma	1	
Chemotherapy reactive lesions/Fungal infection	Chemotherapy-related interstitial pneumonitis	1	
Fungal infection/mycobacterial infection	Aspergillus infection	1	
Lymphoma/Fungal infection/Mycobacterial	Non-tuberculous mycobacterial infection	1	
Lymphoma/infection NOS	Classical Hodgkin's Lymphoma	1	
NEW HISTOLOGICAL DIAGNOSIS			
Preoperative diagnoses	Histology	N	N=1
Pulmonary Hypertension/Surfactant protein B deficiency	Pulmonary interstitial glycogenesis	1	
NORMAL LUNG PARENCHYMA			
Preoperative diagnoses	Histology	N	N=1
Lymphoproliferation/Bronchiolitis obliterans	Normal	1	
INCONCLUSIVE HISTOLOGY			
Preoperative diagnoses	Histology	N	N=2
Fungal infection/PTLD	Non-specific thrombi related disease	1	
GvHD ^f /Fungal infection/CMV ^g /TB ^g	Non-specific pneumonitis	1	
No specific preoperative diagnosis			
NEW HISTOLOGICAL DIAGNOSIS			
Indication for biopsy	Histology	N	N=3
Interstitial infiltrate on CXR ^h	Interstitial pneumonitis	1	
Respiratory condition of new-born of unknown aetiology	Pulmonary interstitial glycogenesis	1	
Persistent pulmonary infiltrates on CXR	Necrotising pneumonia	1	
INCONCLUSIVE HISTOLOGY			
Indication for biopsy	Histology	N	N=4
Respiratory distress of unknown aetiology	Mild non-specific changes	1	
Unknown cause of chronic lung disease	Minimal interstitial non-specific fibrosis	1	
Query cause of pneumonia	No specific evidence of cause	1	
Abnormal CT chest opacification	Non-specific changes	1	

^aPost-transplant lymphoproliferative disorder, ^bimmunodysregulation polyendocrinopathy enteropathy X-linked syndrome, ^ccongenital pulmonary airway malformation, ^dEpstein-Barr virus, ^egraft versus host disease, ^fcytomegalovirus, ^gtuberculosis, ^hChest x-ray, ⁱcomputerised tomography

In the cases where the histology was inconclusive, 64% had a preoperative indication querying an infective cause. In seven children, no specific preoperative diagnosis was stated, and in this group, 57% of histology reports were inconclusive. When the indication for biopsy was a suspected neoplasm, a definitive diagnosis was achieved in 90% of cases, making it the indication with the highest diagnostic yield.

Fifteen (38%) children had their treatment altered due to the biopsy results. In these cases, the biopsy result identified a new diagnosis or confirmed one of the several suspected diagnoses that were queried pre-operatively, and therefore guided management.

Thirteen (33%) of the patients died in a median of 85 days (1-666 days) post biopsy. These deaths were not directly attributable to the surgical procedure, and rather reflect the severe nature and complexity of such conditions which warrant a lung biopsy. A large number of our patients had complex and rare conditions which made them extremely sick and vulnerable. Two (5%) of our patients died within 30 days of surgery. The first child was a 6-week old baby who died the day after the biopsy due to legionella pneumonia with lung necrosis. The second child was a 2-week old baby with alveolar capillary dysplasia, who died on the second postoperative day.

DISCUSSION

In our centre, lung biopsy is performed thoracoscopically for older children where intercostal space allows 10mm trocar for the staplers. For smaller children, the thoracotomy approach is used. CT-guided percutaneous lung biopsy has been successful in children,[4] however, there is a significant radiation risk which must be considered. Therefore, open or thoracoscopic lung biopsy remain the standard procedure in our centre.

Although all specimens obtained from biopsy were suitable for histological analysis, a definite diagnosis was reached in only 64% of cases. This is lower than some studies, which report close to an 80% diagnosis rate.[5] This may be because a

significant proportion of our patients are immunocompromised with diffuse lung lesions, greatly complicating their pathologies and treatments. Although morbidity and mortality from paediatric lung biopsies are reported to be high,[2, 5] in our study only one haemothorax was noted as a procedure-related morbidity with zero procedure related mortality, supporting the relative safety of lung biopsy as a diagnostic investigation.

In four cases the biopsy sample was sent externally for a second opinion. Paediatric lung disorders form a heterogeneous group, with each individual possessing complex and rare pathologies. In our study, although all second opinions agreed with the original pathologists' conclusion, they provided supplementary knowledge and further histological detail. A nationwide approach to paediatric lung histology may provide a higher diagnostic yield through the process of learning across specialist centres, given the rarity of such conditions.

In our series, lung biopsy provided a definitive histological diagnosis in 64% of cases. In 41% of cases, a preoperative suspected diagnosis was confirmed. Therefore, if the preoperative workup is strongly suggestive of a diagnosis, an additional lung biopsy may not be necessary. However, in 23% of children, lung biopsy provided a new diagnosis which was not suspected preoperatively. Of this group, 6 (67%) had a suspected pre-operative diagnosis that was proven incorrect on biopsy, and 3 (33%) had no definitive preoperative diagnosis. In 28% of cases, the results from lung biopsy were inconclusive which did not aid management, and further clinical and radiological investigations were recommended. Therefore, surgeons and paediatricians must carefully select patients for lung biopsy, especially in groups which were shown to have a lower diagnostic yield.

CONCLUSION

In our cohort, lung biopsy mostly confirmed a suspected preoperative diagnosis and was associated with a low procedure related morbidity (n=1) and mortality (n=0). Importantly, the biopsy result identified a pathology which altered treatment in over one third of patients. However, in a number of cases the histology was inconclusive. A higher incidence of inconclusive histology was identified when the indication for biopsy queried an infective cause or when no specific preoperative diagnosis was stated. Therefore, careful patient selection is recommended to maximise diagnostic yield.

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Competing Interests:

Non-declared.

Contributorship Statement:

1. Corey David Chan was the lead author of this paper and undertook the vast majority of the data collection, data processing and data analysis.
2. Anindya Nyogi assisted with data collection and data processing and contributed significantly to the writing of the paper.
3. Bruce Jaffray offered guidance and significant input into the writing of the discussion of this paper.
4. Malcolm Brodlie contributed to the writing of this paper and provided a significant input of clinical knowledge.
5. Hany Gabra was the overall supervisor of the project and assisted in facilitating the data collection and contributed to the writing of the paper.

What is already known on this topic:

Lung biopsy in children is used as a diagnostic tool and is associated with significant morbidity and mortality.

Lung biopsy is performed in children who have very serious and complicated conditions.

The diagnostic yield of lung biopsy in children is variable and limited guidelines exist on when to carry out this procedure.

What this study adds:

Lung biopsy results altered treatment in 38% of children.

Paediatric lung biopsy was associated with a low procedure related morbidity (n=1) and mortality (n=0).

A higher rate of inconclusive histology was identified when looking for an infective cause or when no specific preoperative diagnosis was stated.

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