AN EVALUATION OF THE EFFICACY OF THORACOSCOPIC LUNG BIOPSIES IN PEDIATRIC PATIENTS

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Abstract

Background: Thoracoscopic lung biopsy has been markedly more available in the pediatric population during the last decade than previously. The procedure has proven safer than open thoracic approaches and provides adequate tissue sample. The aim of this study is to assess whether thoracoscopic lung biopsies change therapy in the pediatric population and to assess the complications that arise from the procedure.

Methods: Thoracoscopic lung biopsies performed on patients at Phoenix Children's Hospital between January 2006 and May 2011 were retrospectively reviewed.

Results: Thirty patients (mean age 9 years ± 6 years, 33% female) underwent 32 thoracoscopic biopsies (78% immunocompromised, 72% diffuse disease, 28% focal disease). The only complication was persistent air leak (6%) with an incidence of 14% in immunocompetent patients versus 4% in immunocompromised patients and 9% in diffuse disease versus 0% in focal disease. Conversion to thoracotomy occurred in 19% of procedures with an incidence of with an incidence of 24% in immunocompromised patients versus 0% in immunocompromised patients and 33% in focal disease versus 13% in diffuse disease. The biopsies changed treatment in 97% of the cases (100% in focal disease, 96% in diffuse disease, 100% in immunocompetent patients, 96% in immunocompromised patients).

Conclusions: Thoracoscopic lung biopsies changed treatment with a low rate of complications. The procedure was beneficial in focal and diffuse disease as well as immunocompetent and immunocompromised patients. Persistent air leak was encountered in focal disease and not diffuse disease while conversion to thoracotomy occurred in immunocompromised patients and not immunocompetent patients.

Table of Contents

List of Tables

Background

Thoracoscopy was first used in children by Rogers and his colleagues in the 1970's.[3, 16] Since this first application, there have been advancements in optical equipment and anesthesia techniques. Thoracoscopic equipment has also been adapted for use in children. Promising research has shown that thoracoscopic surgery has significantly less morbidity with not only smaller scars and decreased pain, but also decreased rates of infection, dehiscence, and chest wall deformities, than open thoracic procedures.[8, 9, 10, 11, 12] These reasons have lead to an increased application of thoracoscopic lung biopsy in the pediatric population[3, 15] Currently, the procedure is utilized at the physician's discretion children for the diagnosis of various diseases including tumors, infection, and interstitial lung disease.[3,4]

With the increased availability of thoracoscopic lung biopsy, there has been significant research into the safety of the procedures. Several studies have shown that thoracoscopic lung biopsies pose a minimum risk.[5,6] There is also research showing that thoracoscopic lung biopsies are effective in providing adequate tissue sample for histological diagnosis.[1,7] Even small lesions deep in the lung parenchyma can be reached by using fluoroscopic-guided thoracoscopic surgical resection after computed tomography guided localization using microcoils.[14] There is less research evaluating the impact of thoracoscopic lung biopsies on the changes in treatment. Initial research by Rothenberg and colleagues, as well as research by Gluer and colleagues, suggest that thoracoscopic lung biopsies meaningfully impact the treatment protocol in pediatric patients.[1,2]

Methods

A retrospective study of the thoracoscopic lung biopsies performed in children at Phoenix Children's Hospital. After obtaining approval from the institutional review board, all patients who had undergone thoracoscopic surgery between January 2006 and May 2011 were reviewed. Patients who had undergone procedures other than thoracoscopic lung biopsies, such as mediastinal mass biopsies, blebectomies, and fistula repairs, were excluded. Demographic data (age, gender, and race) as well as clinical data (reason for biopsy, CT scan results, pathology from biopsy, complications from procedure, and follow up information) were collected and reviewed. Descriptive statistics was used for analysis of the data.

Results

During the study period, 32 video-assisted thoracoscopic lung biopsies were performed in 30 patients at Phoenix Children's Hospital from January 2006 to May 2011. The patients' ages ranged from 5 months to 19 years. Twenty were males and 10 were females. Fifteen were Hispanic, 10 were Caucasian, 4 were African American, and 1 was Native American. Seventy-eight percent of the procedures were performed in immunocompromised patients. Seventy-two percent were in diffuse disease while 28% were in focal disease.

The indications for the thoracoscopic lung biopsies were pulmonary lesions in cancer patients, neutropenic fever in cancer patients, worsening respiratory status of unknown etiology, incidental pulmonary lesions, and pulmonary lesions in patients with other organ system dysfunction (table 1 and table 2). There was no significant blood loss or respiratory compromise resulting from the thoracoscopic biopsies. Chest tubes were placed after all of the thoracoscopies for an average of 3 days (ranging from1 day to 14 days). The only complication was persistent air leak (6%) with an incidence of 14% in immunocompetent patients versus 4% in immunocompromised patients and 9% in diffuse disease versus 0% in focal disease (table 3). However, 19% (or 6) of the thoracoscopies were converted to thoracotomies with an incidence of 24% in immunocompromised patients versus 0% in immunocompetent patients and 33% in focal disease versus 13% in diffuse disease (table 3). The reasons for the conversions were air leak and better visualization. Eighteen patients were sent to the intensive care unit after the thoracoscopic biopsies (5 of these were in the ICU before biopsies as well, 6 had conversion to thoracotomy, and 7 were sent due to hospital protocol). Two patients required repeat thoracoscopic biopsies (1 for new pulmonary lesions due to another disease process and 1 corroborated the previous biopsy's result).The thirty day mortality after the biopsies was 6%. The average time of follow up was 26 months ranging from 10 days to 70 months (table 1).

Diagnosis from the thoracoscopic biopsies included infection, malignancy, normal lymphoid tissue, cystic pulmonary airway malformation, bronchiolitis obliterans organizing pneumonia, sarcoidosis, juvenile xanthogranuloma, Churg-Strauss vasculitis, extralobar sequestration, and normal lung parenchyma (table 4). The biopsies changed treatment in 97% of the cases (100% in focal disease, 96% in diffuse disease, 100% in immunocompetent

patients, 96% in immunocompromised patients; table 5, table 6, and table 7). The biopsies lead to antimicrobial therapy selection, chemotherapy selection, initiation of steroids or immunosuppressants, and stop of therapy or transfer to hospice (table 5, table 6, and table 7).

Table 1: Description of the thoracoscopic lung biopsies cases

Age, Sex	Disease Extent	Clinical Background, CT Findings	Pathology	Management, Outcome	Follow-up, *Complications
5 mos M	Diffuse	Worsening respiratory status; patchy consolidation	Bronchiolitis obliterans organizing pneumonia	Antibiotics continued; died due to disease	8 mos
5 mos M	Focal	Cystic lesion on ultrasound and CT	Cystic pulmonary airway malformation type 1	Resection was treatment; well on follow up	42 mos
9 mos M	Diffuse	SCID; worsening respiratory failure; multiple lung nodules	Large B cell lymphoma	Chemotherapy started; died due to disease	2 mos *Converted to thoracotomy due to air leak
1 yr M	Focal	Incidental lung nodule	Extralobar sequestration	Resection was treatment; well on follow up	55 mos
2 yrs F	Focal	Hepatoblastoma; 2 lung nodules	Metastatic hepatoblastoma	Change in chemotherapy regiment; cancer remission	58 mos *Converted to thoracotomy for better visualization
2 yrs F	Diffuse	AML; patchy and nodular findings	Pneumonia; no organisms identified	Broad spectrum antibiotics continued; pneumonia resolved	59 months
2 yrs M	Diffuse	Stage IV neuroblastoma; fevers, and neutropenia; lung nodules	Metastatic neuroblastoma with unfavorable histology	Transferred to hospice; died due to disease	10 days
4 yrs M	Focal	AML on chemotherapy; fever and neutropenia; consolidation	Aspergillus infection with infarction	Micafungin and voriconazole started; amphotericin continued; pneumonia resolved	49 months *Converted to thoracotomy for better visualization
4 yrs F	Diffuse	Left renal mass on ultrasound; multiple lung and liver nodules	Metastatic Wilms' tumor	Metastasis and no anaplasia guided chemotherapy; cancer remission	31 mos

Age, Sex	Disease Extent	Clinical Background, CT Findings	Pathology	Management, Outcome	Follow-up, *Complications
4 yrs F	Diffuse	Asthma; recurrent pneumonia; worsening respiratory status; ground glass opacities	Sarcoidosis	Prednisone started; well on follow up	45 mos
5 yrs M	Focal	ALL on chemotherapy; neutropenia; lung nodule	Aspergillus infection with necrotizing granulomas	Voriconazole and caspofungin started; pneumonia resolved	70 mos
7 yrs M	Diffuse	Recurrent AML on chemotherapy; neutropenia and worsening respiratory status; areas of consolidation	Recurrent metastatic AML	Therapy stopped; died due to disease	12 days
7 yrs F	Diffuse	Acute renal failure and chronic cough; consolidation and ground glass opacities	Viral pneumonia; no evidence of vasculitis	Prednisone started for p-ANCA vasculitis of kidney; well on follow up	59 mos
7 yrs F	Diffuse	Recurrent severe pneumonia; multiple cysts	Cystic pulmonary airway malformation type 1	Resection was treatment; well on follow up	5 mos
9 yrs M	Focal	Wilms' tumor s/p resection, radiation, and chemotherapy (in remission); lung nodule	Coccidioidomycosis infection with necrotizing granulomas	Fluconazole started; pneumonia resolved	45 mos
10 yrs M	Diffuse	Non-Hodgkin's lymphoma; lung nodules	Juvenile xanthogranuloma	Chemotherapy continued; transferred to hospice due to lymphoma	18 mos
10 yrs M	Diffuse	Osteosarcoma; fevers and neutropenia; multiple lung nodules	Candida infection with necrosis	Voriconazole started; amphotericin continued; required another lung biopsy	13 mos

Age, Sex	Disease Extent	Clinical Background, CT Findings	Pathology	Management, Outcome	Follow-up, *Complications
10 yrs M	Diffuse	Osteosarcoma; neutropenia; persistent and new lung nodules despite therapy	Candida infection with infarction	Amphotericin started; Voriconazole continued; pneumonia resolved	9 mos *Converted to thoracotomy for better visualization
10 yrs M	Focal	Laryngeal synovial sarcoma s/p resection; 2 lung nodules	Intrapulmonic lymphoid tissue; negative for malignant tumor	Local radiation; no systemic chemotherapy; cancer remission	45 mos
11 yrs M	Diffuse	Ewing sarcoma; fever and neutropenia; multiple lung nodules	Metastatic Ewing sarcoma	Antibiotics stopped; chemotherapy continued; died due to disease	2 mos
13 yrs F	Diffuse	AML on chemotherapy; neutropenia, fevers, chest pain, and cough; multiple lung nodules	Proteinosis and multinucleated giant cells suggestive of viral disease	Ganciclovir started; chemotherapy continued (metastasis to breasts); required another biopsy	4 mos *Persistent air leak requiring chest tube
13 yrs F	Diffuse	AML on chemotherapy; neutropenia, fevers, and cough; multiple lung nodules	Aspergillus infection with focal necrosis	Voriconazole started; chemotherapy held; transferred to hospice in 2 mos	2 mos
13 yrs M	Focal	Ewing sarcoma; lung nodule	Coccidioidomycosis infection with multiple granulomas	Fluconazole started; pneumonia resolved	28 mos *Converted to thoracotomy for better visualization
14 yrs F	Diffuse	Pericarditis and hypereosinophilia; ground glass opacities	Churg-Strauss Vasculitis	Prednisone and cyclophosphamide started; well on follow up	26 mos *Persistent air leak requiring chest tube placement
15 yrs M	Diffuse	Osteosarcoma on chemotherapy; multiple lung nodules	Metastatic high grade osteosarcoma	Chemotherapy regiment changed; transferred to hospice	29 mos

Age, Sex	Disease Extent	Clinical Background, CT Findings	Pathology	Management, Outcome	Follow-up, *Complications
15 yrs M	Focal	Ewing sarcoma in remission; lung nodule	Coccidioidomycosis infection with necrotic granuloma	Resection of granuloma; antifungals continued; pneumonia resolved	76 mos
15 yrs F	Diffuse	Persistent pulmonary nodules despite chemotherapy for metastatic osteosarcoma	Metastatic osteosarcoma	Chemotherapy discontinued; well on follow up	1 week *Converted to thoracotomy for better visualization
16 yrs M	Diffuse	ALL in remission; ill-defined nodular opacities	Chronic pneumonitis and granuloma; no organisms; no malignant tumor	Fluconazole and ampicillin continued; pneumonia resolved	7 mos
16 yrs M	Diffuse	Sarcoma on chemotherapy; multiple lung nodules	Intrapulmonic lymphoid tissue; negative for malignant tumor	Chemotherapy continued; well on follow up	24 mos
17 yrs F	Diffuse	Pre B cell ALL; neutropenia and persistent fevers despite antibiotics; consolidation and patchy infiltrate	Necrotizing pneumonia; no organism identified	Continued same antibiotic regiment; chemotherapy held; died due to disease	39 days
17 yrs M	Diffuse	Ewing sarcoma; multiple lung nodules	Metastatic Ewing sarcoma	Guided chemotherapy; transferred to hospice	26 mos
19 yrs M	Diffuse	Osteosarcoma; fevers and neutropenia; nodules and ground glass opacities	Well developed normal lung tissue	Continued on voriconazole; nodules continued to increase in size; placed on hospice and then died due to disease	5 mos

Key: AML = Acute myelogenous leukemia; ALL= Acute lymphoblastic leukemia; SCID = Severe combined immunodeficiency; s/p = status post; p-ANCA = perinuclear anti-neutrophil cytoplasmic antibodies; mos = months; yrs = years

Table 2: Indications for thoracoscopic lung biopsies		
Pulmonary lesion in cancer patients	47%	15
Neutropenic fever in cancer patients	25%	8
Worsening respiratory status	13%	4
Incidental pulmonary lesion	9%	3
Pulmonary lesion with other organ system dysfunction	6%	2

Table 3: Incidence of complications and conversions in thoracoscopic lung biopsies		
Persistent air leak	6%	2
Diffuse disease	9%	2
Focal disease	0%	0
Immunocompetent patients	14%	1
Immunocompromised patients	4%	1
Conversion to thoracotomy	19%	6
Focal pulmonary disease	33%	3
Diffuse pulmonary disease	13%	3
Immunocompromised patients	24%	6
Immunocompetent patients	0%	0

Table 4: Diagnosis from thoracoscopic lung biopsies		
Infection	41%	13
Fungal		8
Viral		2
No organism identified		3
Malignancy	28%	9
Ewing		2
Osteosarcoma		2
Lymphoma		1
Hepatoblastoma		1
Neuroblastoma		1
Wilms' tumor		1
AML		1
Lymphoid tissue (no malignancy	6%	2
Cystic pulmonary airway malformation type 1	6%	2
Bronchiolitis obliterans organizing pneumonia	3%	1
Sarcoidosis	3%	1
Juvenile xanthogranuloma	3%	1
Churg-Strauss vasculitis	3%	1
Extralobar sequestration	3%	1
Normal lung parenchyma	3%	1

Table 5: Outcomes of thoracoscopic lung biopsies		
Change in treatment	97%	31
Guided antimicrobial therapy		13
Guided chemotherapy or radiation		10
Steroids or immunosuppressants started		3
Therapeutic resection		3
Therapy stopped or transferred to hospice		2
Died		2
No change in treatment	3%	1

Table 6: Outcomes of thoracoscopic lung biopsies in diffuse disease versus focal disease				
	Diffuse disease (23)		Focal disease (9)	
Change in treatment	96%	22	100%	9
Guided antimicrobial therapy		8		5
Guided chemotherapy or radiation		8		2
Steroids or immunosuppressants started		3		0
Therapeutic resection		1		2
Therapy stopped or transferred to hospice		2		0
Died		2		0
No change in treatment	4%	1	0%	0

Table 7: Outcomes of thoracoscopic lung biopsies in immunocompromised versus immunocompetent patients				
	Immunocompromised (25)		Immunocompetent (7)	
Change in treatment	96%	24	100%	7
Guided antimicrobial therapy		12		1
Guided chemotherapy or radiation		10		0
Steroids or immunosuppressants started		0		3
Therapeutic resection		0		3
Therapy stopped or transferred to hospice		2		0
Died		2		0
No change in treatment	4%	1	0%	0

Discussion

Thoracoscopic lung biopsy has been markedly more available in the pediatric population during the last decade than previously. The procedure has been shown to be very safe in children. Initial research by Rothenberg and colleagues as well as Gluer and colleagues, suggests that thoracoscopic lung biopsies alter treatment in pediatric patients.[1,2] This study reviewed 32 video-assisted thoracoscopic lung biopsies that were performed in pediatric patients at Phoenix Children's Hospital from January 2006 to May 2011. Ninety-seven percent of the biopsies provided diagnosis while 3% showed normal lung tissue confirming that thoracoscopic lung biopsies provide adequate samples for tissue diagnosis (table 1 and table 4). All of the biopsies that provided a diagnosis lead to a change in treatment. Furthermore, thoracoscopic biopsies altered treatment in all groups (100% in focal disease, 96% in diffuse disease, 100% in immunocompetent patients, and 96% in immunocompromised patients as seen in table 5, table 6, and table 7). Thus, thoracoscopic lung biopsies alter treatment in pediatric patients and this change is seen regardless of extent of pulmonary disease or immune system status.

Furthermore, thoracoscopic lung biopsy has a low risk of complications. The only complication encountered was persistent air leak with an incidence of 6%. There was an increased incidence of persistent air leak in diffuse disease (9% versus 0% in focal disease) and in immunocompetent patients (14% versus 4% in immunocompromised patients) as seen in table 3. The increased risk of persistent air leak in diffuse disease is likely related to the widespread damage of lung parenchyma making the lung more vulnerable and creates a slightly higher threshold for referral for thoracoscopic lung biopsy in patients with diffuse disease. However, thoracoscopic lung biopsies pose a minimum risk surgery as no other complications occurred and the persistent air leaks resolved with chest tube placement.

In addition to complications, a portion of the thoracoscopic lung biopsies were converted to thoracotomies. Nineteen percent of thoracoscopic lung biopsies were converted to thoracotomies with an increased incidence in focal disease (33% versus 13% in diffuse disease) and in immunocompromised patients (24% versus 0% in immunocompetent patients) as seen in table 3. This increased risk of conversion to thoracotomy in immunocompromised

patients creates an increased threshold for referral for thoracoscopic lung biopsy since these patients are often very ill. For these patients undergoing an invasive procedure, such as a thoracotomy, is a significant risk.

In conclusion, thoracoscopic lung biopsies alter treatment in the pediatric population with a low risk of complications. The only complication with the procedure was persistent air leak. The increased risk of persistent leak seen in diffuse disease was resolved with chest tube placement. However, an increased threshold for referral can be used in immunocompromised patients as they had an increased risk of conversion to thoracotomy. However, since thoracoscopic lug biopsy impacts treatment in pediatric patients with minimum risk, the procedure has a vital role in pediatric diagnostics.

Future Directions

A larger scale study or meta-analysis is needed to develop strict prediction rules to understand which pediatric patient populations (focal versus diffuse disease or immunocompromised versus immunocompetent) benefit the most from video-assisted thoracoscopic lung biopsies. This will guide physicians on which pediatric patients to refer for the procedure.

Conclusions

Thoracoscopic lung biopsies changed treatment with a low rate of complications. The procedure was beneficial in both focal and diffuse disease as well as immunocompetent and immunocompromised patients. Persistent air leak was encountered in focal disease and not diffuse disease while conversion to thoracotomy occurred in immunocompromised patients and not immunocompetent patients.

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