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Krzysztof Dymek*, Estera Rodziewicz*, Paulina Szymańska, Konrad Kamiński, Irena Daniluk-Matraś, Przemysław Gałązka

THORACOSCOPIC LUNG BIOPSY IN DIAGNOSIS OF MALIGNANCY IN CHILDREN

TORAKOSKOPOWE BIOPSJE PŁUC W DIAGNOSTYCE CHORÓB NOWOTWOROWYCH U DZIECI

Oddział Kliniczny Chirurgii Ogólnej i Onkologicznej Dzieci i Młodzieży, Szpital Uniwersytecki nr 1,
Collegium Medicum, Bydgoszcz

(*) both authors contributed equally to the study

Summary

Introduction. Advances in technology and the increasing experience of surgeons have made the thoracoscopic approach possible in diagnostic process in pediatric oncology. The objective of this paper is the retrospective analysis of efficacy and safety of thoracoscopic lung biopsy in diagnosis of malignancy in children.

Material and methods. Between 2010-2012 thoracoscopy with lung biopsy was performed in 12 cases in 10 children, including 5 boys and 5 girls, aged 2-17 years.

Results. In 11 out of 12 cases the result was conclusive. In 5 cases the lung biopsy was done due to problems with initial diagnosis, and in 7 cases due to suspicion of relapse of malignant disease. In 3 cases the diagnosis of malignancy was confirmed as: Hodgkin lymphoma, non-Hodgkin lymphoma and soft tissue sarcoma. In the group of children diagnosed due to relapse suspicion, the lung biopsy was performed 3-33 months after initial diagnosis. Results were conclusive in all 7 cases. In 3 cases

malignancy was confirmed as Ewing sarcoma twice or neuroblastoma, and in 4 cases malignancy was not confirmed, including one case of diagnosis of invasive fungal infection. None of the children, who were excluded from malignant disease, experienced relapse during at least 2-year follow-up. The procedure of thoracoscopy with lung biopsy was safe. In the postoperative period only one patient required short-time Intensive Care Unit hospitalization because of respiratory insufficiency.

In 5 cases only minor problems occurred including 4 cases of small subcutaneous emphysema. Median time of pleural drainage was 2 days (0-5 days). There were no peri- and postoperative deaths.

Conclusions. Thoracoscopy with lung biopsy is a safe, effective approach for the evaluation and resection of pulmonary pathologic changes. The diagnostic yield of this method is very high in children.

Streszczenie

Wstęp Torakoskopowa biopsja płuc jest ważną metodą w diagnostyce i leczeniu dzieci ze zmianami chorobowymi miąższu płuc w celu uzyskania wyniku histopatologicznego. Celem pracy jest ocena przydatności torakoskopowej biopsji płuc w procesie diagnostycznym wykrywania chorób płuc u dzieci, wpływu na modyfikację procesu leczenia i występowanie ewentualnych powikłań.

Material i metody. Klinową resekcję płuc wykonano 12-krotnie (w tym u 2 dzieci dwukrotnie) u 10 dzieci (5 chłopców, 5 dziewczynek). W analizowanej grupie pacjentów mediana wieku wyniosła 9 lat (zakres 2-17 lat).

Wyniki. W 11 na 12 wykonanych biopsji udało się potwierdzić rozpoznanie i uzyskać wynik histopatologiczny, co miało wpływ na dalsze postępowanie terapeutyczne. W 5 przypadkach biopsja miała na celu pierwotne

rozpoznanie choroby (potwierdzono Hodgkin lymphoma, non-Hodgkin lymphoma oraz soft tissue sarcoma), a w 7 rozpoznaniu nawrotu choroby nowotworowej. W 3 przypadkach potwierdzono wznowę choroby nowotworowej (Ewing sarcoma lub neuroblastoma), a w 4 przypadkach wykluczono. U żadnego pacjenta u którego nie potwierdzono choroby nowotworowej, nie zdiagnozowano jej w okresie 2-letniej obserwacji. Po zabiegu operacyjnym tylko w jednym przypadku pacjent wymagał krótkotrwałej terapii w OIT z powodu niewydolności oddechowej, w 5 przypadkach

wystąpiły powikłania zaliczane do małych (w tym 4-krotnie do powstania niewielkiej odmy podskórnej). Mediana czasu utrzymania drenażu jamy opłucnej wyniosła 2 dni (zakres 0-5 dni). Nie odnotowano zgonów w okresie śród- i pooperacyjnym.

Wnioski. Biopsja płuc odgrywa ważną rolę w diagnostyce chorób płuc u dzieci i jest metodą bezpieczną z niską ilością powikłań. W analizowanym materiale stwierdzono wysoki odsetek rozpoznań zgodnych ze stanem klinicznym.

Key words: thoracoscopy, lung biopsy, children, malignancy, complications

Słowa kluczowe: torakoskopia, biopsja płuc, dzieci, choroby nowotworowe, powikłania

INTRODUCTION

Advances in technology and the increasing experience of surgeons have made the thoracoscopic approach very popular in diagnostic process in oncology. With the evolution in technology, more advanced operations have been performed in pediatrics [1,2]. Children with cancer may develop lesions in the lung that may represent metastatic disease. Thoracotomy was considered the standard approach for resection of pulmonary nodules; however, recently thoracoscopic techniques have been applied in these situations [3]. With the improving resolution of computed tomography more lesions are identified; thus, it may present more diagnostic challenges. Since there are no consistent radiologic features to enable distinguishing benign from malignant lesions, clinicians often face sampling or removing these lesions for diagnostic purposes. Also, several pediatric malignancies are known to have pulmonary metastases including osteosarcoma, soft tissue sarcomas, hepatoblastoma, neuroblastoma, and endocrine tumors. In clinical practice lungs might be the only site of relapse and biopsy of pulmonary lesions is necessary for proper diagnosis and treatment.

The objective of this paper is the retrospective analysis of efficacy and safety of thoracoscopic lung biopsy in diagnosis of malignancy in children.

MATERIAL AND METHODS

Between 2010-2012 thoracoscopy with lung biopsy was performed in 12 cases in 10 children (in 2 children biopsy was performed twice), including 5 boys and 5 girls, aged 2-17 years (median 9 years). Patients were chosen for a minimally invasive procedure based on individual surgeon's decision as to whether this approach was appropriate.

RESULTS

Patients were selected if they had a focal lesion that was noted on computed tomography of the lung. In 5 cases the lung biopsy was done due to the problems with initial diagnosis, and in 7 cases due to suspicion of relapse of malignant disease (Table 1). In 11 out of 12 cases the result was conclusive.

In the group of children on initial diagnostic process, results were conclusive in 4 cases. Thus, in one case the biopsy was repeated. In 3 cases the diagnosis of malignancy was confirmed as: Hodgkin lymphoma, non-Hodgkin lymphoma and soft tissue sarcoma. In one case malignancy was not confirmed and the child was referred to reference center (Institute of Pulmonary Diseases, Rabka).

In the group of children diagnosed due to relapse suspicion, the lung biopsy was performed 3-33 months (median 19 months) after initial diagnosis or previous relapse in one case. Results were conclusive in all 7 cases, including a child with double biopsy. In 3 cases malignancy was confirmed (Ewing sarcoma twice, and neuroblastoma), and in 4 cases malignancy was not confirmed, including one case of diagnosis of invasive fungal infection. None of the children, who were excluded from malignant disease, experienced relapse during at least 2-year follow-up.

The procedure of thoracoscopy with lung biopsy was safe. In the postoperative period only one patient required short-time Intensive Care Unit hospitalization because of respiratory insufficiency. In 5 cases only minor problems occurred including 4 cases of small subcutaneous emphysema and mild case of pneumonia.

In all cases, small complications were resolved quickly within a few days. Pleural drainage was not necessary in 3 cases, while in remaining 9 cases it was necessary for 1-5 days (median 2 days). There were no peri- and postoperative deaths.

Table 1. *Indications, results and complications of thoracoscopic lung biopsy*

N	Sex	Age	Time [months]	Diagnosis	Clinical problem	Histologic result	Complications	Drainage [days]
1	F	15	20	Ewing sarcoma (ES)	relapse suspicion	ES relapse	Pneumonia	1
		17	29	Relapsed ES	relapse suspicion	ES relapse	No	0
2	M	13	8	Ewing sarcoma	relapse suspicion	Relapse excluded	Subcutaneous pneumatosis	1
3	F	3	3	Wilms tumor (WT)	relapse suspicion	Relapse excluded	Subcutaneous pneumatosis	5
4	M	7	33	Wilms tumor	relapse suspicion	Relapse excluded	Subcutaneous pneumatosis	3
5	M	9	18	Neuroblastoma (NBL)	relapse suspicion	NBL relapse	No	0
6	F	7	8	Acute lymphoblastic leukemia (ALL)	relapse suspicion	IFI diagnosis	Subcutaneous pneumatosis	1
7	F	17	0	Soft tissue sarcoma (STS)	diagnostic process	not conclusive	No	2
		17	3		diagnostic process	STS diagnosis	No	2
8	M	9	0	Non-Hodgkin Lymphoma (NHL)	diagnostic process	NHL diagnosis	Respiratory insufficiency	3
9	F	2	0	Mediastinal tumor	diagnostic process	malignancy excluded	No	2
10	M	15	0	Hodgkin lymphoma (HL)	diagnostic process	HL diagnosis	No	0

ES – Ewing sarcoma; NHL – Non-Hodgkin lymphoma; STS – soft Tissue sarcoma; HL – Hodgkin lymphoma; NBL – neuroblastoma; ALL – acute lymphoblastic leukemia; IFI – invasive fungal infection; M – male; F – female; N – number

DISCUSSION

Up to the last decade thoracotomy was considered the standard procedure to obtain tissue from the chest and mediastinum. Recently, thoracoscopy has gained acceptance because of important and practical benefits: less pain, shorter hospital stay, less scar formation, and less development of scoliosis [3]. Still, this method is not widely used in children, while it is widely accepted in adults [4].

In this paper we present our first experience with thoracoscopy followed by lung biopsy in children with suspected malignancy or relapse of previously diagnosed cancer. We were able to perform this procedure safely in all cases, and only one patient required short-term stay in intensive care unit. All other complications, mainly subcutaneous emphysema were resolved quickly. Our analysis confirmed high diagnostic efficacy, as in 11 out of 12 cases results were conclusive. Also, none of the children who were excluded from malignant disease, experienced relapse during at least 2-year follow-up. High efficacy of this method of lung biopsy in diagnostic process in children was also reported by other groups [1-3].

Thoracoscopy with lung biopsy can be regarded as an important future tool in diagnosis of primary and metastatic malignancy in children and adults. It is also used in therapy of metastases in sarcomatous lesions, such as osteosarcoma, soft tissue sarcoma and chondrosarcoma, as well as non- sarcomatous lesions

such as colorectal cancer, hepatocellular carcinoma, breast cancer, renal cell carcinoma, squamous cell gynaecological cancer, adenoid cystic cancer, biliary cancer and germ cell tumor [4,5]. Lung biopsy is a valuable diagnostic method in diagnosis of non-malignant diseases, including infectious [1,6-8] and non-infectious [9-12] complications after stem cell transplantation .

With improved optical visualization, more sophisticated instrumentation, and less postoperative discomfort, thoracoscopy is advantageous for diagnostic and other purposes [2]. The use of thoracoscopy will possibly result in increasing number of surgical procedures of diagnosis and therapy in infants and children [12].

CONCLUSIONS

Thoracoscopy with lung biopsy is a safe, effective approach for the evaluation and resection of pulmonary pathologic changes. The diagnostic yield of this method is very high in children.

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REFERENCES

1. Qualter E, Satwani P, Ricci A, Jin Z, Geyer MB, Alobeid B, Radhakrishnan K, Bye M, Middlesworth

- W, Della-Letta P, Behr G, Muniz M, van de Ven C, Harrison L, Morris E, Cairo MS: A comparison of bronchoalveolar lavage versus lung biopsy in pediatric recipients after stem cell transplantation. *Biol Blood Marrow Transplant* 2014;20:1229-1237.
2. Guye E, Lardy H, Piolat C, Bawab F, Becmeur F, Dyon JF, Marteau M, Lavrand F, Lefebvre F, Podevin G, Reinberg O, Varlet F: Thoracoscopy and solid tumors in children: A multicenter study. *J Laparoendosc Adv Surg Tech A* 2007;17:825-829.
 3. Gow KW, Saad DF, Koontz C, Wulkan ML: Minimally invasive thoroscopic ultrasound for localization of pulmonary nodules in children. *J Pediatr Surg* 2008;43:2315-2322.
 4. Han KN, Kang CH, Park IK, Kim YT: Thoracoscopic approach to bilateral pulmonary metastasis: Is it justified? *Interact Cardiovasc Thorac Surg* 2014;18:615-620.
 5. Fernandez-Pineda I, Daw NC, McCarville B, Emanus LJ, Rao BN, Davidoff AM, Shochat SJ: Patients with osteosarcoma with a single pulmonary nodule on computed tomography: A single-institution experience. *J Pediatr Surg* 2012;47:1250-1254.
 6. Arva NC, Schafernak KT: Rare presentations of Epstein Barr virus-associated smooth muscle tumor in children. *Pediatr Dev Pathol* 2015
 7. Naiditch JA, Barsness KA, Rothstein DH: The utility of surgical lung biopsy in immunocompromised children. *J Pediatr* 2013;162:133-136 e131.
 8. Candoni A, Caira M, Cesaro S, Busca A, Giacchino M, Fanci R, Delia M, Nosari A, Bonini A, Cattaneo C, Melillo L, Caramatti C, Milone G, Scime R, Picardi M, Fanin R, Pagano L: Multicentre surveillance study on feasibility, safety and efficacy of antifungal combination therapy for proven or probable invasive fungal diseases in haematological patients: The SEIFEM real-life combo study. *Mycoses* 2014;57: 342-350.
 9. Yanik GA, Grupp SA, Pulsipher MA, Levine JE, Schultz KR, Wall DA, Langholz B, Dvorak CC, Alangaden K, Goyal RK, White ES, Collura JM, Skeens MA, Eid S, Pierce EM, Cooke KR: Tnf-receptor inhibitor therapy for the treatment of children with idiopathic pneumonia syndrome. A Joint Pediatric Blood and Marrow Transplant Consortium and Children's Oncology Group study (ASCT0521). *Biol Blood Marrow Transplant* 2015;21:67-73.
 10. Seo S, Renaud C, Kuypers JM, Chiu CY, Huang ML, Samayoa E, Xie H, Yu G, Fisher CE, Gooley TA, Miller S, Hackman RC, Myerson D, Sedlak RH, Kim YJ, Fukuda T, Fredricks DN, Madtes DK, Jerome KR, Boeckh M: Idiopathic pneumonia syndrome after hematopoietic cell transplantation: Evidence of occult infectious etiologies. *Blood* 2015;125:3789-3797.
 11. Goldstein G, Keller N, Bilik R, Bielora B, Toren A: Do immunocompromised children benefit from having surgical lung biopsy performed? *Acta Haematol* 2015;133:205-209.
 12. Chellapandian D, Lehrnbecher T, Phillips B, Fisher BT, Zaoutis TE, Steinbach WJ, Beyene J, Sung L: Bronchoalveolar lavage and lung biopsy in patients with cancer and hematopoietic stem-cell transplantation recipients: A systematic review and meta-analysis. *J Clin Oncol* 2015;33:501-509.

Address for correspondence:

dr n. med. Irena Daniluk-Matraś
Oddział Kliniczny Chirurgii Ogólnej i Onkologicznej
Dzieci i Młodzieży,
Szpital Uniwersytecki nr 1,
Collegium Medicum,
ul. Curie-Skłodowskiej 9
85-094 Bydgoszcz
e-mail: idmatras@cm.umk.pl

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