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CASE REPORT

Direct EBUS-guided transtracheal lymphosclerosis for plastic bronchitis after Fontan

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Abstract

We report on a new puncture technique with direct transtracheal mediastinal lymphatic access to treat plastic bronchitis after Fontan repair. High resolution contrast-enhanced spiral CT identified enlarged lymph nodes in the paratracheal region. Inguinal intranodal Gadolinium Dynamic Contrast-enhanced Magnetic Resonance lymphangiography (DCMRL) confirmed the pathologic centrifugal lymph flow passing through these lymph nodes before leaking into the bronchial tree. The abnormal hypertrophic paratracheal, subcarinal, and hilar lymph nodes were punctured with a 22G needle through an endobronchial ultrasound bronchoscope. Occlusion of the lymph vessels was obtained by injecting a mixture of lipiodol/NBCA N-butyl cyanoacrylate (Histoacryl) 5/1 under fluoroscopic control. There was a total remission of PB with now 10 months of follow-up.

KEYWORDS

congenital heart disease, lymphangiography, lymphatic embolization, lymphatic leakage, n-butyl cyanoacrylate, plastic bronchitis

1 | INTRODUCTION

Plastic bronchitis (PB) after Fontan palliation is a rare but difficult clinical problem. Mostly it results from abnormal mediastinal lymphatics with centrifugal flow leaking into the bronchial tree.[1] Dori et al elegantly proved lymph leakage into the trachea by injecting a dye into the thoracic duct in patients with PB.[1] Moreover, they showed the possibility to embolize abnormal lymphatic vessels via cannulation of the thoracic duct with resolution of the bronchial casts.[1] However, this is a complex and demanding technique, especially when the thoracic duct is hypoplastic, stenotic, absent, or occluded in some segments.[2] We report on a new technique for direct mediastinal lymphatic access: transtracheal EndoBronchial UltraSound (EBUS)—guided puncture.

2 | CASE DESCRIPTION

A patient with Fontan circulation was referred for treatment of PB. He was born with hypoplastic right heart. After two modified Blalock-Taussig shunts, he had a bidirectional Glenn at 9 years and a Fontan intracardiac tunnel repair at 11 years. 1.5 years later he started to cough bronchial casts. He had very poor physical activity tolerance (NYHA III). The lymphosclerosis was performed at age 12.2 years under general anesthesia. Informed consent was obtained from the patient and his parents as well as approval by the UZ Leuven Medical Ethics Committee.

A high resolution contrast-enhanced spiral CT identified four enlarged lymph nodes (hilar parabronchial right; mediastinal subcarinal, paratracheal left, and paratracheal right, Figure 1). Subsequently, inguinal intranodal Gadolinium Dynamic Contrast-enhanced Magnetic Resonance lymphangiography (DCMRL) was used to confirm retrograde pulmonary lymphatic flow. It demonstrated obstruction or absent flow in the distal thoracic duct, with gadolinium being "pushed" into the mediastinum towards the four lymph nodes, distal lung, and neck (Figure 2). During the same anesthesia, lymphosclerosis was performed. White light bronchoscopy showed normal mucosae. During EBUS bronchoscopy the four lymph nodes were easily located. Nearby important vessel structures were identified making

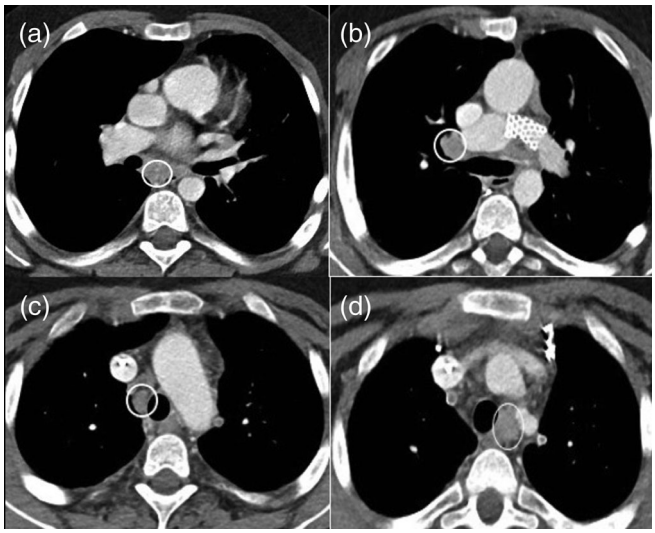

FIGURE 1 (a–d) Contrast-enhanced spiral CT to identify and localize enlarged mediastinal and hilar lymph nodes (white circles): (a) mediastinal subcarinal, (b) hilar parabronchial right, (c) paratracheal right, and (d) paratracheal left

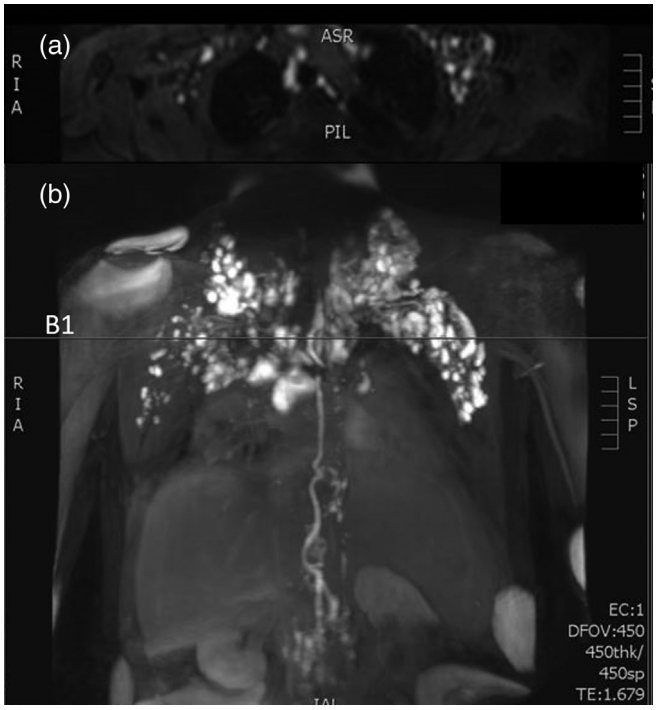

FIGURE 2 (a,b): Inguinal intranodal Gadolinium Dynamic Contrast-enhanced Magnetic Resonance lymphangiography DCMRL. (a) Axial image at level B1 shows relationship of lymph vessels around trachea; (b) Coronal image shows an obstruction at the cranial end of the thoracic duct TD. The gadolinium is "pumped" into the mediastinum by the TD with abnormal dilation of mediastinal and neck lymph vessels

inadvertent puncture unlikely. All abnormal enlarged lymph nodes were punctured with a 22G ViziShot EBUS needle (NA-201SX-4021; Olympus) through an endobronchial ultrasound bronchoscope

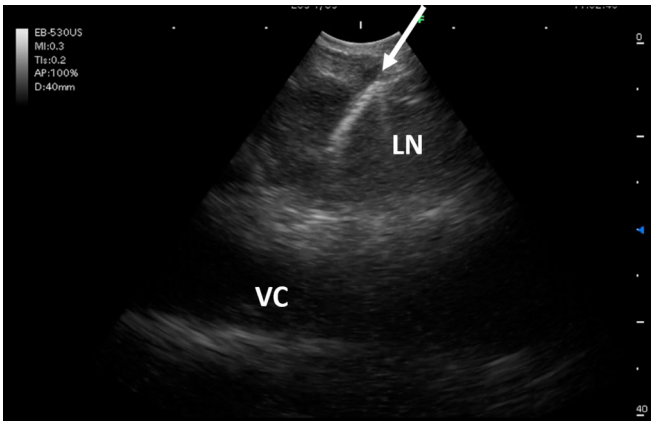

FIGURE 3 Endobronchial ultrasound image of guided needle puncture of the paratracheal lymph node corresponding to 1C. Arrow, needle; LN, lymph node; VC, vena cava [Color figure can be viewed at wileyonlinelibrary.com]

(Figures 3 and 4). After flushing with glucose 5% to prevent premature polymerization of N-butyl cyanoacrylate NBCA when contacting ions, occlusion was obtained by hand injection of a mixture of the non-ionic contrast agent Lipiodol (Guerbet, France) and NBCA (Histoacryl, B. Braun, Barcelona, Spain) in a ratio of 5/1. The injection was performed under ultrasound guidance in combination with fluoroscopic control with opacification of the lymph node and the dilated paratracheal, mediastinal, and hilar lymphatics. We aimed to fill the distal saccular vessels before polymerization occurred, and kept the injection going until no more progress or extravasation was observed distally and proximally. The needle was then removed and discarded. A new needle was used for every puncture site as the lumen is typically obstructed with glue. We punctured and infiltrated the four lymph nodes which were identified by CT; no additional lymph nodes were found useful to occlude. A total of 9.2 cc was injected. The radiation dose was DAP 15.2 Gy/cm^2.

Since the procedure, the patient has not coughed up any cast with follow-up of 10 months. There were no early nor late complications.

3 | DISCUSSION

Plastic bronchitis is a rare complication (1–5%) after Fontan type single-ventricle palliation, but with significant morbidity and mortality.[3] Adequate treatment should be based on understanding of the pathophysiology of the problem. A Fontan circuit clearly predisposes a patient for PB, but there is no clear relationship between the occurrence of PB and the detrimental essence of Fontan hemodynamics such as venous congestion and low circulatory output. This suggests local additional lymphatic problems such as flow hindrance (by thoracic duct hypoplasia or obstruction), abnormal centrifugal flow with leakage or other factors.[4] Knowledge on anatomy and function of the lymphatic system has recently greatly improved. Dori et al[1] showed that centrifugal pulmonary lymphatic flow from the central

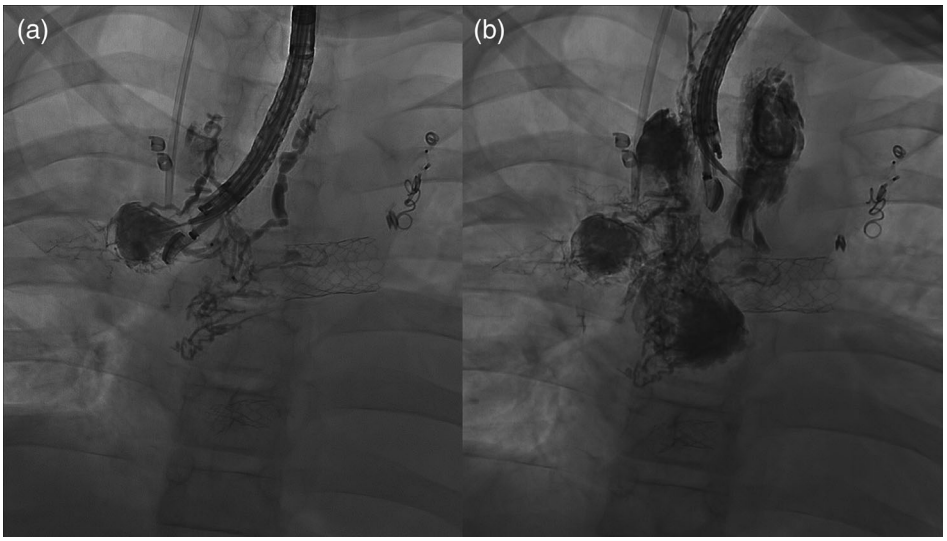

FIGURE 4 (a) Frontal view of an EBUS guided puncture of the enlarged hilar parabronchial right sided lymph node (corresponding to Figure 1b) with injection of NBCA/lipiodol mixture; dilated lymph vessels are filled with the glue. (b) Final view while obliterating the left sided paratracheal lymph node (corresponding to Figure 1d); the right hilar, subcarinal, and right sided paratracheal lymph node have already been infiltrated

lymphatic system was present in nearly all (17/18) Fontan patients with PB. Embolization or stent graft exclusion of these lymphatic networks, or even embolization of the TD proved effective in a large percentage of these patients.[1]

Lymphatic vessels in mammals are known to connect to systemic veins; this can occur at any level, but the standard option is first to merge and then connect as a large vessel to the subclavian vein.[5] The TD is such a large vessel connecting the abdominal cysterna chyli to the left subclavian vein. However, the TD is not a simple pathway as suggested by its name, but rather a multivalved contractile vessel functioning like a pump, allowing to propel fluid at a differential pressure as high as 40–70 mmHg [6,7]. The junction of the TD with the subclavian vein is guarded by a valve, but in chronic venous congestion blood may enter the dilated TD and coagulate within the lymphatic vessel. If the normal passage to the subclavian vein is obstructed or ill-directed, this powerful pump may then "blow" its content into the mediastinum and neck region. The overdistended submucosal lymphatics can then leak and allow lymph to flow into the bronchial space, causing the typical casts of PB.

These new insights explain the success or failure of older techniques to treat PB after Fontan repair and open new clinical options. The different treatment strategies and the practical handles are enumerated in Table 1. The medical management of the failing Fontan circulation typically aims to decrease venous congestion and lymph production by diuretics, fenestration, pulmonary vasodilators, streamline and desobstruct Fontan pathways, a veno-pulmonary pump, Fontan take-down, or heart transplant.[4] Run-off from the TD to the subclavian vein can be enhanced when obstructed [8-11]. Dori et al[1] reported on obstructing major lymphatic side vessels from the TD to the leaks: in 17 patients this involved cannulation of the TD (17/17) and exclusion of the side vessels with a covered stent (2/17) or embolization of these large side vessels with coils or NBCA glue (12/17). Alternatively, the pump function of the TD can be destroyed by ligation or embolization (4/17).[1,12] If the TD cannot be cannulated, lymph access to the TD can be reduced by destruction of the cisterna chyli by needle maceration.[2] Finally, the distal leaks can be sealed either by sclerosing effect of lipiodol from inguinal node or after direct cannulation of the TD[13]; more efficient is direct puncture of intrathoracic lymph vessels/nodes with glue injection, either percutaneous[14] or transtracheal as reported in this manuscript.

TABLE 1 Strategies to treat PB after Fontan and practical applications

Decrease venous congestion and lymph production	• Diuretics, diet • Fenestration • Pulmonary vasodilators • Streamline—desobstruct Fontan pathways • Veno-pulmonary pump • Fontan take-down • Heart transplant
Enhance or desobstruct run-off to the subclavian vein	• Open or stent lympho-venous connection • Relocate drainage site to low pressure
Obstruct major lymphatic side vessels from the TD to the leaks	• Covered stent in TD • Embolization (coils, NBCA glue)
Destroy the pump function of the TD	• Ligate or embolise the TD
Limit lymph access to the TD	• Needle destruction of the cisterna chyli
Seal the distal leaks	• Lipiodol from inguinal node or after direct cannulation of the TD • Direct puncture of mediastinal lymph vessels/nodes with NBCA glue (percutaneous or transtracheal)

Abbreviations: NBCA, N-butyl cyanoacrylate; PB, plastic bronchitis; TD, thoracic duct.

We recently reported our results of treatment of protein losing enteropathy PLE after Fontan type repair with elective percutaneous direct transhepatic embolization of periportal lymph vessels.[14] Analogous to this technique we decided for PB to target directly the dilated paratracheal lymph vessels by direct puncture. We reported in one patient percutaneous direct transthoracic cone-beam guided puncture of the paratracheal lymph vessels and subsequent injection of NBCA.[14] In that patient, there was a total remission of PB, now with 23 months of follow-up. Interventional radiologists used this direct puncture technique for diagnosis of intrathoracic cancers[15,16]; adequate guidance is essential to leave important structures such as the ascending aorta, the superior caval vein and the pulmonary arteries untouched. Many regions such as the distal parabronchial, subcarinal, and some peritracheal zones cannot safely be reached.

In contrast, a flexible EndoBronchial UltraSound EBUS bronchoscope can easily reach the entire paratracheal and peribronchal region. Interventional bronchoscopists now use this direct puncture technique for diagnosis and staging of intrathoracic cancers. The ultrasound component not only allows to identify and avoid important vascular structures, but moreover allows to identify the enlarged lymph nodes, which then can be safely punctured with a dedicated EBUS needle and used as a "distributor" for the NBCA glue. This technique proved to be highly effective in our current patient with a good lasting clinical result.

When comparing CT-guided paratracheal percutaneous puncture of lymph vessels and EBUS guided transtracheal puncture technique of lymph nodes, we find the transtracheal puncture more elegant, easier, safer, and more complete with less radiation than the percutaneous puncture.

NBCA is used since years for occlusion of veins[17] and arteries,[18] and more recently also for lymphatic vessels[19]; it polymerizes when in contact with ions. It is mixed with the non-ionic ethiodized oil to allow visualization with fluoroscopy, and to delay the polymerization process during the injection. The distance of occlusion will determine success: ideally all leaks and afferent vessels need to be sealed, but possibly also determines the incidence and type of complication. The distance of occlusion is determined by the flush with glucose (no ions), the washout of that glucose by the lymph, the resistance of the needle lumen, the injection pressure, the viscosity of the mixture, and the polymerization of the NBCA when finally contacting ions. The ideal concentration NBCA/lipiodol still needs to be determined; in this case, we used a mixture of 5/1.

Mediastinal lymphatic anatomy and function was investigated preferably by inguinal intranodal gadolinium DCMRL. This visualization is not required for this direct puncture technique, but is essential to understand why lymphatics fail in a specific patient and what the treatment options are for that patient.

Our patient most likely could have been treated with superselective lymph vessel or TD embolization as described by Dori et al.[1] This technique is more complex and demanding. It also involves direct abdominal TD cannulation which requires inguinal lipiodol lymphography, which can cause cerebral emboli (1/18 in Dori's report[1,20]). In some series, the cysterna chyli could not be punctured, or the TD could not be cannulated because of stenosis, absence or exclusion.[2] A possible drawback for the direct transtracheal puncture technique is that the TD still functions, generating increased lymphatic pressures in the upper mediastinum which predisposes these patients more for PB recurrence. Time will tell if destruction of the TD will yield better long-term results. These techniques are not mutually exclusive but should be considered as complementary.

4 | CONCLUSION

Direct lymph occlusion is effective in PB and obviates the need for transabdominal ductal access. A transtracheal EBUS guided puncture is an elegant, easy and apparently safe approach to treat PB after Fontan palliation. Further experience is required to assess early and late results.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

The authors have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Dori Y, Keller MS, Rome JJ, et al. Percutaneous lymphatic embolization of abnormal pulmonary lymphatic flow as treatment of plastic bronchitis in patients with congenital heart disease. Circulation. 2016; 133:1160-1170.
2. DePopas EM, Veress LA, Ahmed F, Rausch CM, Annam A, Gupta R. Percutaneous thoracic duct intervention to treat plastic bronchitis related to Fontan palliation. Pediatr Pulmonol. 2017;52:E97-E101.
3. Wilson TG, Shi WY, Iyengar AJ, et al. Twenty-five year outcomes of the lateral tunnel Fontan procedure. Semin Thorac Cardiovasc Surg. 2017;29(3):347-353. https://doi.org/10.1053/j.semtcvs.2017.06.002.
4. Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. Circulation. 2019;1: CIR0000000000000696.
5. Semo J, Nicenboim J, Yaniv K. Development of the lymphatic system: new questions and paradigms. Development. 2016;143(6):924-935.
6. Aboul-Enein A. Pumping failure of the lymph versus thoracic duct outlet obstruction and their significance in ascites. Med Chir Dig. 1974;3:109-112.
7. Mohanakumar S, Telinius N, Kelly B, et al. Morphology and function of the lymphatic vasculature in patients with a Fontan circulation. Circ Cardiovasc Imaging. 2019;12(4):e008074. https://doi.org/10.1161/CIRCIMAGING.118.008074.

8. Hraska V. Decompression of thoracic duct: new approach for the treatment of failing Fontan. Ann Thoracic Surg. 2013;96:709-711.
9. Kreutzer C, Kreutzer G. The lymphatic system: the achilles heel of the Fontan-Kreutzer circulation. World J Pediatr Congenit Heart Surg. 2017;8(5):613-623. https://doi.org/10.1177/2150135117720685.
10. Antonio M, Gordo A, Pereira C, Pinto F, Fragata I, Fragata J. Thoracic duct decompression for protein-losing enteropathy in failing Fontan circulation. Ann Thoracic Surg. 2016;101:2730-2733.
11. Smith CL, Hoffman TM, Dori Y, Rome JJ. Decompression of the thoracic duct: a novel transcatheter approach. Catheter Cardiovasc Interv. 2020;95(2):E56-E61. https://doi.org/10.1002/ccd.28446.
12. Parikh K, Witte MH, Samson R, et al. Successful treatment of plastic bronchitis with low fat diet and subsequent thoracic duct ligation in child with Fontan physiology. Lymphology. 2012;45(2):47-52.
13. Kos S, Haueisen H, Lachmund U, Roeren T. Lymphangiography: forgotten tool or rising star in the diagnosis and therapy of postoperative lymphatic vessel leakage. Cardiovasc Intervent Radiol. 2007;30(5):968-973.
14. Maleux G, Storme E, Cools B, et al. Percutaneous embolization of lymphatic fistulae as treatment for protein-losing enteropathy and plastic bronchitis in patients with failing Fontan circulation. Catheter Cardiovasc Interv. 2019;94(7):996-1002.
15. Zwischenberger JB, Savage C, Alpard SK, et al. Mediastinal transthoracic needle and core lymph node biopsy. Chest. 2003;41(4):1165-1170. https://doi.org/10.1378/chest.121.4.1165.
16. Demetrian A, Dobrinescu A, Bălă S, Demetrian C, Gheonea IA, Albulescu DM. Transthoracic needle biopsy (TNB) under different guiding methods: the experience of the thoracic surgery clinic of craiova after the first 235 cases tumor location. 2015;41(3):239-245. https://doi.org/10.12865/CHSJ.41.03.08.
17. Maleux G, Stockx L, Wilms G, Marchal G. Ovarian vein embolization for the treatment of pelvic congestion syndrome: long-term technical and clinical results. J Vasc Interv Radiol. 2000;11(7):859-864.
18. Berenstein AB, Krall R, Choi IS. Embolization with N-butyl-cyanoacrylate in the manage-ment of CNS lesions. Am J Neuroradiol. 1989;10:883.
19. Guez D, Nadolski GJ, Pukenas BA, Itkin M. Transhepatic lymphatic embolization of intractable hepatic lymphorrhea. J Vasc Interv Radiol. 2014;15:149-150.
20. Kirschen MP, Dori Y, Itkin M, Licht DJ, Ichord R, Vossough A. Cerebral lipiodol embolism after lymphatic embolization for plastic bronchitis. J Pediatr. 2016;176:200-203. https://doi.org/10.1016/j.jpeds.2016.05.036.

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