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## Case Report

# Successful lymphatic embolization using N-butyl-2-cyanoacrylate for postoperative lymphorrhoea in a patient with renal pelvic cancer ☆,☆☆

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## ARTICLE INFO

## Article history:

Received 16 August 2020

Revised 24 August 2020

Accepted 24 August 2020

## Keywords:

Lymphatic embolization

N-butyl-2-cyanoacrylate

Node dissection

## ABSTRACT

We present a successful case of percutaneous lymphatic embolization using N-butyl-2-cyanoacrylate (NBCA) for postoperative lymphorrhoea in a patient with urothelial carcinoma of renal pelvis. A 75-year-old man with urothelial carcinoma of left renal pelvis with para-aortic lymph nodes metastases. The patient presented severe lymphorrhoea after neoadjuvant chemotherapy followed by laparoscopic total left nephroureterectomy and lymph nodes dissection. Since conservative treatments were ineffective, percutaneous lymphatic embolization using NBCA resulted in healing of the lymphorrhoea without recurrence. Percutaneous lymphatic embolization using NBCA followed by intranodal lymphography is a powerful treatment option for intractable postoperative lymphorrhoea after lymph nodes dissection.

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☆ **Keynote message:** Percutaneous lymphatic embolization using N-butyl-2-cyanoacrylate is a powerful treatment option for postoperative lymphorrhoea after node dissection.

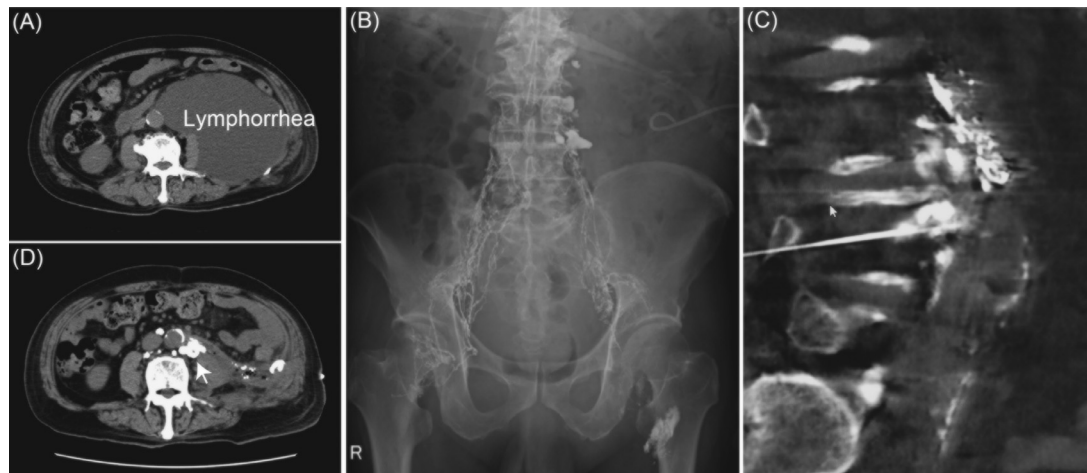
☆☆ **Competing interests:** Nothing to declare.

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<https://doi.org/10.1016/j.radcr.2020.08.051>

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**Fig. 1 – The representative image findings. (A) CT shows huge lymphorrhoea. (B) Lymphography findings in bilateral inguinal lymph nodes (arrow: leak point). (C) The representative image of a percutaneous direct puncture under fluoroscopy of the closest upstream lymph node to the lymphatic leak site, where lipiodol has accumulated by lymphangiography. (D) CT images after embolization (arrow; embolization sites with NBCA accumulation).**

## Introduction

Lymphorrhoea is a leak of serous or yellow-colored and iso-osmotic abdominal fluid from disrupted lymphatic system [1]. Lymphorrhoea is a rare adverse event after urological surgery, however it sometimes induces severe undernutrition and immune suppression. The first option of postoperative lymphorrhoea is cessation of oral intake. In addition, somatostatin analogues are used in cases that are resistant to cessation of oral intake [2]. Here, we report a case of successful intranodal lymphography and percutaneous lymphatic embolization using N-butyl-2-cyanoacrylate (NBCA) diluted to 33% with ethiodized oil (Lipiodol; Guerbet, Villepinte, France) for intractable lymphorrhoea after left total nephroureterectomy with para-aortic lymph nodes dissection.

## Case presentation

A 75-year-old man was referred to our department with macrohematuria. Urinary cytology indicated high grade urothelial carcinoma and abdominal CT revealed a left renal pelvis tumor with multiple swelling of para-aortic lymph nodes. Consistent with the abdominal CT, retrograde pyelography showed a defect in left renal pelvis. Then we diagnosed as invasive urothelial carcinoma of renal pelvis with lymph nodes metastases. The size of para-aortic lymph node significantly decreased by 3 cycles of gemcitabine and cisplatin chemotherapy. Then, he underwent laparoscopic left total nephroureterectomy and para-aortic lymph nodes dissection. The lymph nodes were removed from the level of left renal artery to the inferior mesenteric artery using a vessel sealing system (LigaSure, Medtronic, Tokyo, Japan). The surgery required 5 hours and 19 minutes. The patho-

logical diagnosis was high-grade invasive urothelial carcinoma.

After restarting oral intake on the second day after surgery, lymphorrhoea was observed. Since the volume of lymphorrhoea were not reduced by nil per os (NPO) for 7 days, somatostatin analogues were administrated 10 days after surgery. However, the volume of leakage was significantly increased over 1500ml / day and CT identified fluid collection with floating fat in the retroperitoneal cavity with 150 mm in diameter 16 days after surgery (Figs. 1A and 2). Then we performed intranodal lymphography from both inguinal lymph nodes using ethiodized oil (Lipiodol; Guerbet, Villepinte, France) 17 days after surgery which identified lymphorrhoea at 4th and 5th lumbar vertebra (Figs. 1B and 2).

As the volume of lymphorrhoea did not decrease following lymphography, we obtained written informed consent, then, a percutaneous lymphatic embolization using NBCA was performed on the 31st day after surgery. Since the accumulation of iodized oil in the upstream nodes closest to the lymphorrhoea was demonstrated on the CT scan, the direct puncture of these nodes was performed by using isocenter puncture technique under fluoroscopy (Fig. 1C). After we injected some ethiodized oil to visualize lymphorrhoea, the embolization was subsequently performed using NBCA diluted to 33% with iodized oil. Immediately after the embolization, lymphorrhoea successfully resolved (Fig. 1D). During this period, we performed drain flushing and replacement for the infection control. At present, the lymphorrhoea does not relapse without any adverse event for 9 months.

## Discussion

A cross reference of [N-butyl-2-cyanoacrylate] and [lymphatic] was used to select original articles of unduplicated cases focusing on lymphatic embolization in human clinical subject

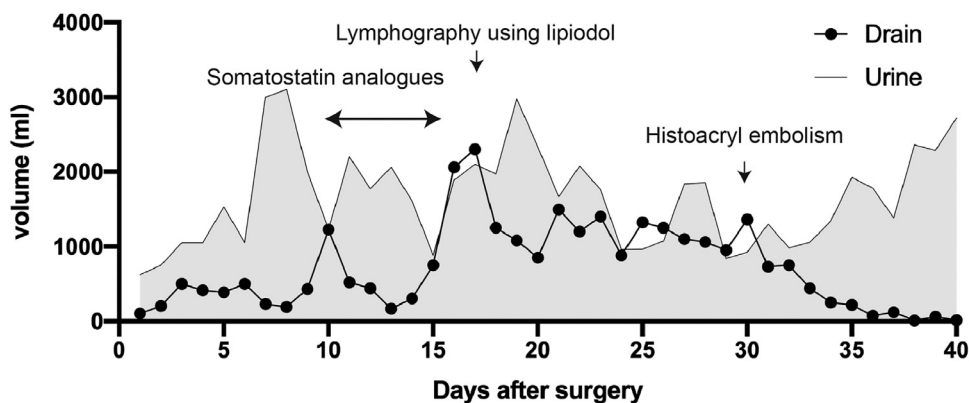


Fig. 2 – The changes in the volume of lymphorrhoea and the amount of urinary output. after the surgery.

Table 1 – Result in Pubmed search by using [N-butyl-2-cyanoacrylate] cross reference with [lymphatic], then selecting original articles of nonduplicated cases focusing on lymphatic embolism of human clinical subject.

No.	Reference	N	Age	Sex	Cause	Location	Methods of injection	Complication	Recurrence
1	Muthusami JC, <i>Ann R Coll Surg Engl.</i> 2005; 87: 379.	1	45	F	Radical Neck Dissection	Thoracic duct at the neck	Direct injection	ND	ND
2	Blythe JN, <i>Br J Oral Maxillofac Surg.</i> 2011; 49: 486-7.	4	ND	ND	Radical Neck Dissection	Thoracic duct at the neck	Direct injection	None	None F/U period not described
3	Hwang PF, <i>JSL.S.</i> 2012; 16: 301-5.	1	37	M	Fundoplication	Thoracic duct at the T10	ULV	ND	None F/U period 8 months
4	Ching KC, <i>CardioVasc. Interv. Radiol.</i> 2014; 37: 1103-6.	1	68	M	Aorto-mesenteric bypass	Left para-aortic region at the L2–L3	CT-guided ULV	None	None F/U period 3 months
5	Weaver MV, <i>J Vasc Surg.</i> 2014; 59: 1109-11.	1	86	M	Endovascular abdominal aortic aneurysm repair	Left femoral region	ULV	ND	None F/U period 3 months
6	Dinc H, <i>Diagn Interv Radiol.</i> 2015; 21: 419-22.	1	58	M	Abdominal operations due to gastric cancer	Left para-aortic region at the L3	CT-guided LPA Direct percutaneous embolization through the ULV	ND	None F/U period 3 months
7	Baek Y, <i>CardioVasc. Interv. Radiol.</i> 2016; 39: 1728-35.	21	46 (37-49)	F 20 M 1	Mostly gynecologic surgeries	Mostly lumbar regions	ULV	None	None except 3 small lymphocle F/U period 11 months
8	Hur S, <i>J Vasc Interv Radiol.</i> 2016; 27: 1177-86 e1	8	ND	ND	Various surgeries including 4 urologic surgeries	Various region	LPA ULN ULV	mild transient leg edema	Success rate 85% F/U period not described
9	Quencer KB, <i>J Vasc Access.</i> 2017; 18: e45-e7.	1	ND	ND	Central vein catheter	Thoracic duct at the neck	Percutaneous injection	None	ND
10	Kayama E, <i>Clin Genitourin Cancer.</i> 2018; 16: e355-e71.	1	73	M	Nephrectomy	Left para-aortic region at the L3–L4	LPA ULV	None	ND
11	Smolock AR, <i>J Vasc Interv Radiol.</i> 2018; 29: 1462-5.	10	66	M 6 F 4	Surgery and vascular catheterization procedures	Groin region	ULN	mild transient leg edema	Success rate 80% F/U period not described
12	Yamamoto M, <i>CardioVasc. Interv. Radiol.</i> 2018; 41: 959-63.	2	72 (71-73)	M 1 F 1	Thoracic aorta replacement	Left para-aortic region at the T7-T8	ULV	ND	ND
13	Yildirim IO, <i>Transplantation.</i> 2018; 102: 1955-60.	13	56 (36-70)	M 9 F 4	Renal Transplantation	Intrapelvic region	ULV Percutaneous injection	None	Success rate 92% F/U period not described
14	Chu HH, <i>CardioVasc. Interv. Radiol.</i> 2019; 42: 873-9.	9	69 (62-78)	M 9	Radical prostatectomy	Intrapelvic region	LPA ULN	None	None F/U period 6 months
15	Guevara CJ, <i>J Vasc Interv Radiol.</i> 2019; 30: 772-4.	1	65	M	Radical prostatectomy	Intrapelvic region	ULN	None	None F/U period 3 months

ND; not described The methods of injection include LPA; Lymphopseudoaneurysm embolization ULN; Closest upstream lymphnode embolization ULV; Direct upstream lymphatic vessel embolization.

using PubMed, resulting in 75 cases from 15 reports (Table 1). According to these reports, the median age of patients is 56 years old (range 37–86). The leak point was detected by ultrasound-guided intranodal lymphography in most cases, which included the lumbar region (85%), thoracic region (13%), and femoral region (2%). Although no report described adverse event, thoracic duct embolization were reported to include asymptomatic embolization of the pulmonary artery, leg edema [3], and chronic diarrhea as rare complications

[4]. Based on 3 reports with a median observation period of 4 months (3–11 months), the success rate of this procedure was 86% (range 80–92). These data indicate that the procedure is feasible and useful.

There is a few reports about postoperative lymphorrhoea in urological surgeries, including nephrectomy and para-aorta lymph node dissection treatment for testicular carcinoma [5,6]. Conservative therapies, such as oral intake cessation and the administration of somatostatin analogues are standard

therapies for lymphorrhea that improves in approximately 60%–70% [7].

Surgical interventions, that include the ligation of the disrupted lymph channel and splaying fibrin glue are performed for the cases resistant for conservative therapies. However it is difficult to identify the appropriate ligation points [8]. Furthermore, the patients with suppressed immune system are high risk for surgical intervention.

On the other hand, lymphography has been shed light on because of more effective and less invasive for the detection and treatment of lymphorrhea [9–11]. Lipiodol used in lymphography is feasible for detection the site of lymphorrhea as well as treating the leakage site by inflammatory reaction. However, the success rate of lipiodol lymphography for postoperative lymphorrhea is only 50% [12]. In the case of refractory lymphorrhea, it is essential to increase the resistance of the leaking space or to decrease the outflow from the lymphatic duct. Since oral or enteral nutrition may increase lymph flow, cessation of oral intake would be effective for lymph flow reduction [13]. The cyclic peptide hormone somatostatin widely exists and influences in central nerve system, pancreas, and gastrointestinal tract [14,15]. Although the mechanism of decreasing lymph flow by somatostatin is not fully elucidated, one hypothesis is that somatostatin may reduce triglyceride absorption from the intestine and inhibit lymphatic flow after traversing the liver in the presence of the vagus nerve [16,17]. The method of inducing inflammation by injecting ethanol into the leaking space (sclerotherapy) is an attempt to heal the lymphorrhea by increasing the resistance to the destination of the lymphatic outflow. Low-pressure lymphatic fluid leaks may benefit from the sclerotherapy. On the other hand, adjunctive percutaneous glue embolization techniques addition to lipiodol lymphangiography has recently become a minimally invasive interventions for the cases with the high-flow lymphatic leakage [12,18]. NBCA are instantaneous adhesives used since the 1950s. After encountering blood plasma, NBCA starts to polymerize. Since NBCA does not depend on biogenic coagulants, it is effective for patients with coagulopathy [19]. NBCA is indicated for various conditions regardless of the location of the target lesion [20,21]. Since high-flow lymphatic leakage was suspected in this case, we chose direct puncture and NBCA injection therapy instead of sclerotherapy. The dilution rate of the NBCA was determined according to previous studies in which a 33%–50% dilution was used for direct puncture of lymphatic leaking sites [12]. A total amount of 1.5ml of NBCA and Lipiodol mixture was injected to the punctured lymph nodes and draining lymphatic ducts.

In conclusion, intranodal lymphography and percutaneous lymphatic embolization using NBCA is a powerful treatment option for intractable postoperative lymphorrhea after node dissection.

### Patient Consent Statement

We obtained written informed consent, then, a percutaneous lymphatic embolization using NBCA was performed on the 31st day after surgery. And we also carefully explained and

obtained the consent from him about the publication for the case report.

### REFERENCES

- [1] Lemaitre J, Segers B, Lebrun E. The use of lanreotide in the management of lymphorrhea after an aortic valve replacement. *Interact Cardiovasc Thorac Surg* 2012;15:762–3.
- [2] Carcoforo P, Soliani G, Maestroni U, et al. Octreotide in the treatment of lymphorrhea after axillary node dissection: a prospective randomized controlled trial. *J Am Coll Surg* 2003;196:365–9.
- [3] Itkin M, Kucharczuk JC, Kwak A, Trerotola SO, Kaiser LR. Nonoperative thoracic duct embolization for traumatic thoracic duct leak: experience in 109 patients. *J Thorac Cardiovasc Surg* 2010;139:584–9 discussion 9–90.
- [4] Laslett D, Trerotola SO, Itkin M. Delayed complications following technically successful thoracic duct embolization. *J Vasc Interv Radiol* 2012;23:76–9.
- [5] Guglielmo N, Melandro F, Nudo F, et al. Chylous leakage after a laparoscopic live-donor nephrectomy: case report and literature review. *Exp Clin Transplant* 2016;14:338–40.
- [6] Kim BS, Yoo ES, Kim TH, Kwon TG. Chylous ascites as a complication of laparoscopic nephrectomy. *J Urol* 2010;184:570–4.
- [7] Lv S, Wang Q, Zhao W, et al. A review of the postoperative lymphatic leakage. *Oncotarget* 2017;8:69062–75.
- [8] Geary B, Wade B, Wollmann W, El-Galley R. Laparoscopic repair of chylous ascites. *J Urol* 2004;171:1231–2.
- [9] Matsumoto T, Yamagami T, Kato T, et al. The effectiveness of lymphangiography as a treatment method for various chyle leakages. *Br J Radiol* 2009;82:286–90.
- [10] Kawasaki R, Sugimoto K, Fujii M, et al. Therapeutic effectiveness of diagnostic lymphangiography for refractory postoperative chylothorax and chylous ascites: correlation with radiologic findings and preceding medical treatment. *AJR Am J Roentgenol* 2013;201:659–66.
- [11] Gruber-Rouh T, Naguib NNN, Lehnert T, et al. Direct lymphangiography as treatment option of lymphatic leakage: indications, outcomes and role in patient's management. *Eur J Radiol* 2014;83:2167–71.
- [12] Hur S, Shin JH, Lee JJ, et al. Early Experience in the management of postoperative lymphatic leakage using lipiodol lymphangiography and adjunctive glue embolization. *J Vasc Interv Radiol* 2016;27 1177–86 e1.
- [13] Mallick A, Bodenham AR. Disorders of the lymph circulation: their relevance to anaesthesia and intensive care. *Br J Anaesth* 2003;91:265–72.
- [14] Stueven AK, Kayser A, Wetz C, et al. Somatostatin analogues in the treatment of neuroendocrine tumors: past, present and future. *Int J Mol Sci* 2019;20.
- [15] Pradayrol L, Jornvall H, Mutt V, Ribet A. N-terminally extended somatostatin: the primary structure of somatostatin-28. *FEBS Lett* 1980;109:55–8.
- [16] Nakabayashi H, Sagara H, Usukura N, et al. Effect of somatostatin on the flow rate and triglyceride levels of thoracic duct lymph in normal and vagotomized dogs. *Diabetes* 1981;30:440–5.
- [17] Karaca S, Gemayel G, Kalangos A. Somatostatin treatment of a persistent chyloperitoneum following abdominal aortic surgery. *J Vasc Surg* 2012;56:1409–12.
- [18] Inoue M, Nakatsuka S, Yashiro H, et al. Lymphatic intervention for various types of lymphorrhea: access and treatment. *Radiographics* 2016;36:2199–211.
- [19] Frodsham A, Berkmen T, Ananian C, Fung A. Initial experience using N-butyl cyanoacrylate for embolization of

- 
- lower gastrointestinal hemorrhage. *J Vasc Interv Radiol* 2009;20:1312–19.
- [20] n BCATI. N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations: results of a prospective, randomized, multi-center trial. *AJNR Am J Neuroradiol* 2002;23:748–55.
- [21] Cantasdemir M, Adaletli I, Cebi D, Kantarci F, Selcuk ND, Numan F. Emergency endovascular embolization of traumatic intrarenal arterial pseudoaneurysms with N-butyl cyanoacrylate. *Clin Radiol* 2003;58:560–5.