Infective thrombophlebitis after great saphenous vein cyanoacrylate embolization

Oliver Chen, BMed, MD,[a,b] Hamid Hajian, MD, PhD,[a] Ramon L. Varcoe, MBBS, MS (Vasc), PhD, MMed (ClinEpi),[a,b] *and* Shannon D. Thomas, BSc Med Hons, MBBS Hons,[a,b] *Randwick and Sydney, New South Wales, Australia*

ABSTRACT

The use of cyanoacrylate embolization has increased in interest as a safe, effective, and minimally invasive method to treat symptomatic saphenous reflux. The procedure is generally well tolerated by patients, and complications such as phlebitis are minor and usually self-limiting. Postprocedural infections have been described but occur infrequently and usually in the early postoperative course. In the present case report, we have described a late-onset infective thrombophlebitis of the great saphenous vein after cyanoacrylate embolization, requiring surgical excision of the treated vein. (J Vasc Surg Cases and Innovative Techniques 2021;7:577-80.)

Keywords: Complications; Cyanoacrylate; Infection; Phlebitis; Venous insufficiency

Endovenous therapies have become the recommended standard of care for the management of symptomatic great saphenous vein (GSV) reflux.[1,2] Cyanoacrylate embolization (CAE) has emerged as a minimally invasive method of treating GSV incompetence that has demonstrated satisfactory safety and efficacy profiles in multiple randomized trials.[3,4] Distinct from established thermal ablation therapies such as radiofrequency ablation and endovenous laser ablation, CAE does not require perivenous tumescent anesthesia or carry the risk of heat-associated complications to achieve similar rates of anatomic closure and symptom improvement.[4,5]

The reported adverse events after CAE have been infrequent, mild, and self-limiting. The most commonly reported complication has been phlebitis (range, 5%-20%).[6-8] Hyperpigmentation, access site infection, and hematoma are rare. Access site infection with underlying abscess formation has been reported early after treatment.[9] Recurrent infection and infection requiring surgical excision of the treated vein have not been previously reported. We have reported a case of infective thrombophlebitis occurring 13 months after CAE. Our patient provided written informed consent for the report of his case.

CASE REPORT

The patient had presented with a history of bilateral lower limb chronic venous insufficiency. The 45-year-old man had a medical history that included Klinefelter syndrome, diabetes mellitus, and previous pacemaker placement for bradyarrhythmia. His medications included aspirin and dabigatran for previous cardiac mural thrombus. His left leg was more severely affected in the setting of May-Thurner syndrome and post-thrombotic syndrome secondary to a deep vein thrombosis 9 years prior to presentation. The left common iliac and external iliac veins had been treated with stents in 2015. In 2018, he demonstrated clinical features of progressive venous insufficiency involving the left leg that was characterized by hemosiderosis, lipodermatosclerosis, and varicose veins (CEAP [clinical, etiologic, anatomic, pathophysiologic] clinical class 4). Left lower limb duplex ultrasound demonstrated GSV incompetence in the upper thigh and small saphenous vein incompetence in the lower calf. Examination of the deep system revealed femoral and popliteal vein incompetence and a partially occlusive thrombus extending from the profunda femoris vein to the common femoral vein that proximally involved the stent ostium. The stent was patent. Subsequent computed tomography angiography revealed that the thrombus had completely resolved, although its etiology remained unclear after hematology review and screening for thrombophilia.

The left GSV was subsequently ablated using the VenaSeal Closure System (Medtronic, Minneapolis, Minn). The entire GSV was treated in accordance with the manufacturer's instructions for use. Dabigatran was continued, and no postprocedural hematoma or other complications developed. Postprocedural duplex ultrasound confirmed successful ablation of the GSV and anterior accessory saphenous vein.

At 13 months after CAE, the patient developed a localized infection and abscess over the left calf at the puncture site. The infection

From the Department of Surgery, Prince of Wales Hospital, Randwick[a]; and the Faculty of Medicine, University of New South Wales, Sydney.[b]

Author conflict of interest: R.L.V. is a consultant for Abbott Vascular, Medtronic, Boston Scientific, Intact Medical, BD Bard, Surmodics, and Intervene. S.D.T. is a consultant for Abbott Vascular, Medtronic and Vexev. O.C. and H.H. have no conflicts of interest.

Correspondence: Oliver Chen, BMed, MD, Department of Surgery, Prince of Wales Hospital, Barker St, Randwick, New South Wales 2031 Australia (e-mail: oliver.chen01@gmail.com).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2468-4287

https://doi.org/10.1016/j.jvscit.2021.05.011

was managed with intravenous flucloxacillin, surgical incision, and drainage. An indurated sinus at the puncture site was excised and sent for microbial culture, which yielded no growth. He recovered well and was discharged with oral flucloxacillin.

The patient presented again 1 month later with a recurrent abscess proximal to the puncture site with associated cellulitis and phlebitis (Fig 1). On examination, tenderness was elicited along the palpable GSV cord from the calf to mid-thigh. No signs of systemic compromise were present. Intravenous flucloxacillin was recommended. Duplex ultrasound demonstrated a compressible GSV in the proximal thigh, which was noncompressible from the mid-thigh to the knee. In the calf, the abscess and surrounding GSV could not be imaged owing to the patient's discomfort.

The patient subsequently underwent ligation and excision of the GSV (Fig 2). Intraoperative examination of the abscess demonstrated fibrosed subcutaneous tissue that was adherent and a firm, enlarged segment of the GSV with purulent exudate. The CAE access site of the previous surgical incision demonstrated fibrotic inflammatory changes and was excised and left open to drain and heal via secondary intention. The GSV was sent in segments for histopathologic examination and bacterial, fungal, and mycobacterial culture. The bacterial culture yielded growth of *Citrobacter koseri* in the samples from the calf and proximal thigh. After consultation with the infectious diseases team, the patient was transitioned to oral cephalexin for a total of 2 weeks. No mycobacterial or fungal growth resulted from culture of the intraoperative specimen. Histopathologic examination of all segments of the excised vein demonstrated similar morphologic features, including widespread thrombophlebitis, segmental occlusion by foreign body embolic material with associated organizing thrombus, and a foreign body-type granulomatous reaction. The blood vessel wall demonstrated intimal and medial fibroplasia with a superimposed florid lymphocytic infiltrate, which extended into the adventitial fibroadipose tissue. The postoperative recovery was uncomplicated, and the surgical wound was well healed at the outpatient follow-up examination.

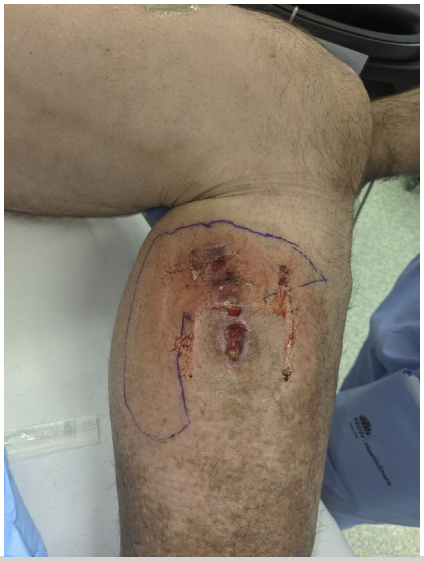

Fig 1. Photograph showing left calf recurrent abscess and cellulitis.

Fig 2. Great saphenous venectomy.

DISCUSSION

The safety of CAE has been established in multiple trials.[6,7,10,11] After the early postoperative period, infection related to CAE has not previously been reported in studies with 36 months of follow-up.[3-6,12-18] Phlebitis and erythema have been reported as late complications; however, these have not been specifically attributed to infection in the studies appraised.

Access site infection is uncommon after CAE. The VeClose (VenaSeal Sapheon Closure System vs Radiofrequency Ablation for Incompetent Great Saphenous Veins), WAVES (Lake Washington Vascular VenaSeal Post-Market Evaluation), and eSCOPE (European Sapheon Closure System Observational Prospective) trials were the first to evaluate the safety and efficacy of CAE for the management of symptomatic saphenous reflux. The most common adverse event in all three trials was phlebitis of the treatment zone (5%-20%). All cases were managed conservatively, and no procedure-related serious adverse events were reported in any of the studies (follow-up, 12-60 months).[5,7,8,11] In the eSCOPE study, localized infection at the access point was identified in 1.4% of patients, and this rate has been replicated consistently in reported studies.[10,18-20]

Some controversy surrounds the etiology of access site infections. They might be technique related. Yang et al[9] postulated that access site infections might be secondary to a retained adhesive clump that serves as an infective nidus in the subcutaneous tissue after removal of the delivery catheter. Our patient did develop an initial abscess at the puncture site. The etiology for this case is

not clear. However, the postulation by Yang et al[9] might explain our patient's presentation.

Cyanoacrylate is a commonly used tissue adhesive with broad medical applications, including closure of enteric fistulas, treatment of endoleaks, embolization of arteriovenous malformations, and surgical incision closure. Severe cutaneous hypersensitivity reactions have been reported[21]; however, infection has rarely been described. Machin et al[22] reported a review of the use of cyanoacrylate as an antimicrobial barrier to prevent postoperative wound infections, with no differences observed. The VenaSeal adhesive is an N-butyl-2-cyanoacrylate liquid. Within the vessel, it solidifies and induces a granulomatous foreign body reaction, leading to fibrotic occlusion of the lumen. These changes were consistent with the histopathologic findings of the excised vein in our patient. *C. koseri* is a gram-negative bacillus, and infection almost exclusively occurs among hospitalized and institutionalized patients.[23] It is possible that the chronic ulcer at the access site became infected and that during the subsequent hospital admission, the patient became colonized with *C. koseri*, which is resistant to the empirical antibiotic therapy used for skin organisms.

Intervention after CAE is generally performed to treat varicose tributaries, using adjunctive agents such as sclerotherapy or phlebectomy.[5,24] Although localized puncture site abscess requiring incision and drainage has been reported, our case differs because the onset of the infection was 13 months after intervention and recurred despite initial treatment with surgical incision and drainage. The use of CAE has increased in interest because it is minimally invasive and cost-effective. Although isolated, the findings from the present case have demonstrated the potential morbidity associated with this generally safe and well-tolerated procedure. Clinicians should be aware of these potential complications to facilitate the informed consent process when considering the management of symptomatic saphenous reflux.

REFERENCES

1. Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg 2011;53(Suppl):2S-48S.
2. Wittens C, Davies AH, Baekgaard N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's choice — management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2015;49:678-737.
3. Gibson K, Morrison N, Kolluri R, Vasquez M, Weiss R, Cher D, et al. Twenty-four month results from a randomized trial of cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord 2018;6:606-13.
4. Eroglu E, Yasim A. A randomised clinical trial comparing N-butyl cyanoacrylate, radiofrequency ablation and endovenous laser ablation for the treatment of superficial venous incompetence: two year follow up results. Eur J Vasc Endovasc Surg 2018;56:553-60.
5. Morrison N, Kolluri R, Vasquez M, Madsen M, Jones A, Gibson K. Comparison of cyanoacrylate closure and radiofrequency ablation for the treatment of incompetent great saphenous veins: 36-month outcomes of the VeClose randomized controlled trial. Phlebology 2019;34:380-90.
6. Proebstle TM, Alm J, Dimitri S, Rasmussen L, Whiteley M, Lawson J, et al. The European multicenter cohort study on cyanoacrylate embolization of refluxing great saphenous veins. J Vasc Surg Venous Lymphat Disord 2015;3:2-7.
7. Morrison N, Gibson K, Vasquez M, Weiss R, Jones A. Five-year extension study of patients from a randomized clinical trial (VeClose) comparing cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord 2020;8:978-89.
8. Gibson K. Cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of post-procedure compression: a post-market evaluation of the VenaSeal system (WAVES trial): twelve month data. Phlebology 2017;32(Suppl 1):14.
9. Yang GK, Parapini M, Gagnon J, Chen JC. Comparison of cyanoacrylate embolization and radiofrequency ablation for the treatment of varicose veins. Phlebology 2019;34:278-83.
10. Morrison N, Gibson K, McEnroe S, Goldman M, King T, Weiss R, et al. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). J Vasc Surg 2015;61:985-94.
11. Gibson K, Ferris B. Cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of post-procedure compression: initial outcomes of a post-market evaluation of the VenaSeal System (the WAVES Study). Vascular 2017;25:149-56.
12. Bellam Premnath KP, Joy B, Raghavendra VA, Toms A, Sleeba T. Cyanoacrylate adhesive embolization and sclerotherapy for primary varicose veins. Phlebology 2018;33:547-57.
13. Tang TY, Rathnaweera HP, Kam JW, Chong TT, Choke EC, Tan YK. Endovenous cyanoacrylate glue to treat varicose veins and chronic venous insufficiency—experience gained from our first 100+ truncal venous ablations in a multi-ethnic Asian population using the Medtronic VenaSeal closure system. Phlebology 2019;34:543-51.
14. Hwang JH, Park SW, Kim KH, Yang WY, Hwang JJ, Lee SA, et al. Regression of varicose veins after cyanoacrylate closure of incompetent great saphenous veins without a localized concomitant procedure. J Vasc Surg Venous Lymphat Disord 2019;7:375-81.
15. Morrison N, Gibson K, Vasquez M, Weiss R, Cher D, Madsen M, et al. VeClose trial 12-month outcomes of cyanoacrylate closure versus radiofrequency ablation for incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord 2017;5:321-30.
16. Bozkurt AK, Yilmaz MF. A prospective comparison of a new cyanoacrylate glue and laser ablation for the treatment of venous insufficiency. Phlebology 2016;31(Suppl):106-13.
17. Almeida JI, Javier JJ, Mackay EG, Bautista C, Cher DJ, Proebstle TM. Thirty-sixth-month follow-up of first-in-human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. J Vasc Surg Venous Lymphat Disord 2017;5:658-66.
18. Almeida JI, Javier JJ, Mackay E, Bautista C, Proebstle TM. First human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. J Vasc Surg Venous Lymphat Disord 2013;1:174-80.
19. Chan YC, Law Y, Cheung GC, Ting AC, Cheng SW. Cyanoacrylate glue used to treat great saphenous reflux: measures of outcome. Phlebology 2017;32:99-106.
20. Vos CG, Unlu C, Bosma J, van Vlijmen CJ, de Nie AJ, Schreve MA. A systematic review and meta-analysis of two novel techniques of nonthermal endovenous ablation of the great saphenous vein. J Vasc Surg Venous Lymphat Disord 2017;5:880-96.
21. Davis MD, Stuart MJ. Severe allergic contact dermatitis to Dermabond Prineo, a topical skin adhesive of 2-octyl cyanoacrylate increasingly used in surgeries to close wounds. Dermatitis 2016;27:75-6.

22. Machin M, Liu C, Coupland A, Davies AH, Thapar A. Systematic review of the use of cyanoacrylate glue in addition to standard wound closure in the prevention of surgical site infection. Int Wound J 2019;16:387-93.
23. Russo TA, Johnson JR. Diseases caused by gram-negative enteric bacilli. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 20 ed. New York, NY: McGraw-Hill Education; 2018.
24. Gibson K, Minjarez R, Gunderson K, Ferris B. Need for adjunctive procedures following cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of postprocedure compression: three-month data from a postmarket evaluation of the VenaSeal System (the WAVES Study). Phlebology 2019;34:231-7.

Submitted Feb 22, 2021; accepted May 18, 2021.