Septicemia after cyanoacrylate glue closure of varicose veins

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ABSTRACT

Cyanoacrylate glue closure (CAC) is being increasingly used as a minimally invasive procedure for the treatment of symptomatic incompetent saphenous veins. The most common adverse event associated with CAC has been phlebitis, including hypersensitivity phlebitis, superficial thrombophlebitis, and granulomatous phlebitis. This complication can be serious and debilitating. In the present report, we have described a case of symptomatic septicemia after CAC that required surgical excision of the treated saphenous veins. (J Vasc Surg Cases Innov Tech 2022;8:653-6.)

Keywords: Bacteremia; Cyanoacrylate; Complications; Infection; Varicose veins

Cyanoacrylate glue closure (CAC) is a recently developed nonthermal, nontumescent technique for the treatment of incompetent saphenous veins. Several trials, some of which were sponsored by manufacturers, have reported CAC to be a safe procedure. However, serious complications, including hypersensitivity phlebitis and granuloma formation, have been described.

In the present report, we have described a case of septicemia that developed after CAC.

The present study was conducted in accordance with the 2013 revision of the Declaration of Helsinki. Our patient provided written informed consent for the report of her case details and imaging studies.

CASE REPORT

An 82-year-old woman had presented to another clinic with a 6-month history of dermatitis of the lower legs and had been treated by another vascular surgeon before referral to our hospital. She had a medical history of hypertension and dyslipidemia but no allergies or hypersensitivity reactions. She was diagnosed with CEAP (clinical, etiologic, anatomic, pathophysiologic) clinic class 4a stasis dermatitis on the distal dorsal side of the lower legs. No cellulitis was present on either leg. Duplex ultrasound revealed bilateral incompetent small saphenous veins (SSVs). Given her symptoms and SSV incompetence, the surgeon at the previous clinic had decided to perform endovascular CAC (VenaSeal Closure System; Medtronic, Minneapolis, MN). On the day of the procedure, the patient was afebrile. The skin was prepared using 0.05% chlorhexidine before sterile draping. A sterile CAC device package within the sterilization date was opened and used. With the patient under local anesthesia, the SSVs were cannulated at the dorsal distal part of the lower legs. A standard 7F sheath and a Sapheon outer catheter (Medtronic) were fed into the vein and placed distal to the saphenopopliteal junction. Glue injection was repeated nine times (21 cm; total of 0.9 mL) on the right side and eight times (19 cm; total of 0.8 mL) on the left side. After the procedure, the puncture sites were closed with Steri-Strips (3M, St Paul, MN) and covered with an adhesive waterproof dressing. The total operative time was 28 minutes. No anatomic abnormalities were observed, and no postoperative hematoma developed. Duplex ultrasound after the procedure confirmed successful occlusion of the SSVs and a patent deep venous system. No prophylactic antibiotics were administered during or after the operation. The patient did not receive postoperative compression therapy.

On the night of postoperative day (POD) 2, the patient reported pain and heat in her left calf. She subsequently developed a low-grade fever of 37°C. On POD 4, redness and swelling were observed in her left lower limb. The glue plug did not extrude. Ultrasound examination revealed no exudate. The patient was diagnosed with a foreign body reaction and treated with oral steroids (10 mg/d). On POD 7, her fever had increased to 38°C. An infection caused by the CAC was suspected.

On referral to our department from the previous clinic, the patient was immediately hospitalized. Computed tomography (CT) of both calves revealed no abscesses. Two bacterial cultures of blood samples confirmed the presence of methicillin-sensitive Staphylococcus aureus (MSSA). Antibiotics (cefazolin 3 g/d) were administered. Two days after admission, the patient underwent surgery under general anesthesia to excise the bilateral SSVs (Fig 1). Pus was found in the lumen of the left SSV, and the corresponding bacterial culture was positive for MSSA.
Histologic examination of the excised SSV specimens was subsequently performed. Inflammatory cell infiltration was observed from the intima to the adventitia of the vein wall. This mainly comprised mononuclear cells containing neutrophils. Inflammatory cell infiltration was also observed in the adipose tissue around the excised blood vessels. The intima was thickened, and necrotic exudate was present. However, gram staining revealed no bacteria cells (Fig 2).

Postoperatively, the patient had a persistently high fever of 39°C to 40°C, and her inflammatory marker levels remained elevated (white blood cell count, 12,900/μL; C-reactive protein, 21.45 mg/dL). She also reported lower back pain. On POD 6 after the second surgery, contrast-enhanced CT revealed abscess formation in the right greater psoas and erector spinae muscles (Fig 3) and bilateral patent deep venous systems with no thrombi. Contrast-enhanced CT on PODs 20, 34, and 50 also revealed no thrombi in the bilateral deep venous system. Antibiotic therapy was continued, and the patient fully recovered. Her surgical wound healed well. She was discharged on POD 42. At 21 months of follow-up, the patient had not experienced any recurrence of an allergic reaction or infection.

**DISCUSSION**

A common complication of CAC is a distinctive erythematous dermal reaction within the first few weeks, possibly due to a delayed type IV hypersensitivity reaction. This reaction can persist and even require glue cast removal. Sumarli et al found that <0.3% of patients will experience an intense form of this reaction complicated by secondary infection. However, when it occurs, surgical debridement of the exit skin site is required, together with portions of the ablated saphenous vein and extravasated glue cast for source control. The patient in the present case was diagnosed with a foreign body reaction, with 10 mg/d of oral steroids
administered; however, this was insufficient for successful treatment.

Infection is another complication associated with the presence of a foreign body. A previous study found that localized infection at the access point occurred in 1.4% of patients treated with CAC. A study reported a 2.0% incidence of superficial infection from glue clumps after CAC that had required excision and drainage. Chen et al. reported a case of late-onset infective thrombophlebitis of the great saphenous vein after CAC that required surgical excision of the treated vein.

The precise mechanism by which the glue used in CAC becomes infected and causes symptomatic bacteremia is unclear. MSSA is a part of the normal bacterial flora of the skin. We hypothesized that, in the present case, the source of the infection was the catheter insertion site.

We excised the bilateral SSVs to prevent bacteremia in the right leg due to glue infection. Although no significant symptoms were observed in the right leg at surgery, we could not confirm whether the right leg glue had already become infected. The patient could also have had an allergic reaction to the glue.

Our patient developed abscesses in the right greater psoas muscle and erector spinae muscles. Although the precise mechanism was unclear, we presumed that the bacteria had been hematogenously implanted in the muscles owing to the bacteremia. We could not determine whether the patient’s fever and inflammatory response were caused by the muscle abscesses or the CAC itself. In either case, it appeared to be an iatrogenic event caused by the CAC procedure, followed by puncture site infection. However, the rapid onset of the septicemic manifestations suggested that the infection might have begun preoperatively, despite the absence of overt manifestations or cellulitis on the day of surgery.

Clinicians should be aware of the risk of the rare, but potentially fatal, complication of septicemia after CAC. Patients should be duly informed of the risk before treatment with this generally safe and well-tolerated procedure for symptomatic incompetent saphenous veins.

CONCLUSIONS

We have reported a case of symptomatic septicemia after CAC for incompetent SSVs. Clinicians should factor the risk of this rare, but serious, complication into their decision-making, and patients should be informed of the risk before undergoing CAC.

REFERENCES

1. 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.
2. 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.
3. 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;8:397-89.
4. 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;61:918-9.
5. Watts TJ, Thursfield D, Haque R. Allergic contact dermatitis caused by VenaSeal tissue adhesive. Contact Dermatitisis 2019;80:393-5.
6. Parsi K, Kang M, Yang A, Kossard S. Granuloma formation following cyanoacrylate glue injection in peripheral veins and arteriovenous malformation. Phlebology 2020;35:115-23.
7. Park I, Jeong MH, Park CJ, Park WI, Park DW, Joh JH. Clinical features and management of ‘phlebitis-like abnormal reaction’ after cyanoacrylate closure for the treatment of incompetent saphenous veins. Ann Vasc Surg 2019;55:239-45.

8. Pillutla A, Hendrix MP, Ha J. Endovenous glue-induced thrombosis in nonthermal glue closure therapy for greater saphenous vein insufficiency: a single-center experience. J Vasc Interv Radiol 2019;30:1075-80.

9. Jones AD, Boyle EM, Woltjer R, Jundt JP, Williams AN. Persistent type IV hypersensitivity after cyanoacrylate closure of the great saphenous vein. J Vasc Surg Cases Innov Tech 2019;5:372-4.

10. Sumarli SA, Lee QWS, Yap HY, Tay HTL, Chong TT, Tang TY. Exit site complications following cyanoacrylate glue endovenous ablation of incompetent truncal veins for chronic venous insufficiency. J Vasc Surg Cases Innov Tech 2020;6:500-4.

11. 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.

12. Chen O, Hajian H, Varcoe RL, Thomas SD. Infective thrombophlebitis after great saphenous vein cyanoacrylate embolization. J Vasc Surg Cases Innov Tech 2021;7:577-80.

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