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Case Report

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Type III coronary perforation during chronic total occlusion percutaneous coronary interventions treated with Cyanoacrylate glue embolization: case report and review of the technique

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Abstract

In recent times the outcome of chronic total occlusion (CTO) percutaneous coronary interventions (PCI) in dedicated centers has steadily gained high success rate (> 80%) and low rate of coronary complications. Nevertheless comparing with non-CTO PCI the complications rate is higher, due to the higher lesion and technical complexity. Among the complications Type III coronary perforations remain the most troublesome events of CTO PCI and still carry a significant risk of death for the patients. The management of Type III coronary perforations has been extensively described as a flow chart of interventions and techniques to obtain rapid cessation of the blood extravasation and sealing of the ruptured vessel. Several techniques have been described to obtain bleeding cessation also in small vessel (< 2 mm) perforations.In this paper we will describe two cases of CTO PCI with Type III small vessel coronary perforations treated with percutaneous Cyanoacrylate/(NBCA-MS)-based glue infusion through a conventional CTO microcatheter. This technique is fast and straightforward and can be applied to any conventional CTO microcatheter.

Keywords: Type III coronary perforations, coronary chronic total occlusion complication, cyanoacrylate/(NBCA-MS)-based glue

INTRODUCTION

Coronary chronic total occlusion (CTO) is characterized by heavy atherosclerotic plaque burden within the artery, resulting in complete occlusion of the vessel. Although the duration of the occlusion is difficult to determine, a coronary occlusion is defined as true CTO when the duration is at least 3 months or undetermined[1]. Patients with CTO usually develop collaterals, which can be visualized through coronary angiography, from ipsilateral or contralateral vessel. However, these collaterals often do not provide sufficient blood flow to prevent myocardial ischemia during exercise and therefore anginal symptoms may appear[2].

The incidence of CTO among patients who have a clinical indication for coronary angiography has been reported to be as high as 15% to 30%[3,4].

The first important step made in CTO revascularization was to recanalize the occluded vessel using coronary collaterals. The septal channel has historically been the first described solution.The progressive improvement in the the technology of guidewires and microcatheters expanded the ability to cross different collateral channels even in very complex cases. Nowadays, examples of collaterals which can be used in CTO procedures, also include epicardial collaterals, even ipsilateral, and occluded saphenous grafts. Experienced operators are able to successfully treat very difficult CTO lesions using a combination of different pathways and techniques.

The results of older data registry (early CTO era) showed low success rate and higher MACE compared with non-CTO PCI, whereas CTO revascularization performed in experienced centers has now proven success rate up to 80%-90%. On the other hand, due to the higher lesion and technical complexity, CTO complications rate has shown to be higher than non-CTO PCI (1.6% *vs.* 0.8%; $P < 0.0001$)[5].

Perforation is one of the most troublesome complications of CTO PCI. Despite the fact that coronary perforations are infrequent (0.33% of all cases) they are associated with poorer short- and long-term outcomes. In the British Cardiovascular Intervention Society Database CTO PCI was one of independent predictors of risk of perforation[6].

Coronary artery perforations (CAP) are categorized according to Ellis classification as: Type I, extraluminal crater without extravasation; Type II, epicardial fat or myocardial blush without contrast jet extravasation; Type IIIa, extravasation through frank (> 1 mm) perforation; Type IIIb "cavity spilling" (CS), which refers to perforations with contrast spilling directly into either the left ventricle, coronary sinus or other anatomic circulatory chamber [Table 1][7]. Grade I or II perforation are usually managed conservatively since they have a more benign clinical course. On the other hand, type III CAP was associated with a worse outcome. In earlier registers CAP Type III was associated with a very high in-hospital mortality rate (44%), with the majority of patients requiring emergency surgery (60%)[8], while more recent data shows lower mortality rate (15.2%) and lower rate of emergency surgery (16%)[9].

Among interventional collaterals suitable for CTO procedures, epicardial channels are considered the trickiest ones and appear more prone to perforation or rupture. This is caused by the relative high frequency of tortuosity and their small size (CC1 in Werner classification)[10]. Perforation of epicardial channels carries a higher risk of cardiac tamponade and death when the treatment is delayed. This is due to the spillage of blood directly into the pericardial space.

The current endovascular treatment for perforated coronary arteries involves the use of prolonged balloon inflation and/or the use of covered stents (CS). The use of CS is feasible only when CAP is located in a large vessel due to the availability of CS starting just from a diameter of 2.25-2.5 mm[11]. Moreover, when collateral vessels emerge at a short distance from the CAP, the use of CS could lead to the occlusion of the collaterals and to the subsequent myocardial infarction. When CAP occurs in smaller vessels or collaterals (< 2 mm),

Table 1. Ellis classification of coronary artery perforations

ELLIS classification Types	Ellis 1	Ellis 2	Ellis 3a	Ellis 3b
Details	Extraluminal crater without extravasation	Epicardial fat or myocardial blush without contrast jet extravasation	Extravasation through frank (> 1 mm) perforation	Perforations with contrast spilling directly into either the left ventricle, coronary sinus or other anatomic circulatory chamber
Mortality	5.8%	5.2%	16.6%	0%

various materials, such as autologous clots or fat[12,13], gel foam[14], fibrin glue[15], microcoils[16] and polyvinyl alcohol form[17-23] can be embolized to the site in order to provide haemostasis and bleeding cessation.

When percutaneous treatment of CAP is not effective, surgical repair rapresent the bail out strategy. Efficacy of surgical repair however is not very high, as reported by a register from Al-Lamee *et al.*[9], where the rate of success was just 44.4%.

In this case report we used (NBCA-MS)-based glue embolization (GLUBRAN2, GEM s.r.l. ITALY) in order to seal the perforation of small vessels during retrograde and antegrade revascularization of two cases of CTO-PCI.

Sterile glue is available for medical use either as pure synthetic glue (Histoacryl), or as dual component fibrin glue (fibrin plus thrombin). Sterile glue has been described as an effective embolization material for neurointerventional indications[24,25], closure of oesophageal varices[26], femoral pseudoaneurysms[27], septal ablation in Hypertrophic Obstructive Cardiomyopathy[28] and as a surgical adjunctive tool to stick a patch over the myocardial wall after an acute myocardial infarction complicated with cardiac rupture[29,30]. The use of sterile glue has already been described for the embolization of the right coronary artery's distal portion[31].

The (NBCA-MS)-based glue can be injected pure or pre-mixed with Ethiodized oil (Lipiodol/Ethiodol). The mechanism of the (NBCA-MS)-based glue is related to his reaction to Na ions of tissue fluids. When (NBCA-MS)-based glue comes into contact with Na ions the glue solidifies in a variable amount of time which varies from a few seconds to one minute depending on the proportion of Ethiodized oil you pre-mix with [Table 2]. Ethiodized oil also works as a Contrast agent which produces radiopacity in the mixture and helps the physician to confirm the site of embolization. Na ions are also present in Heparin and in Contrast media therefore both sterile cup and the syringes used for mixing the components shouldn't have been in contact with blood and Heparin. Furthermore, the microcatheter should be carefully flushed with dextrose solution just before the injection of the (NBCA-MS)-based (pure or mixture) in order to clean the inner surface from blood or heparin residues. This flushing avoids the premature start of the glue polymerization process into the microcatheter, which could occlude it totally or partially and make the microcatheter useless for multiple injections.

The injection can be done in a "single shot" fashion or with multiple "sandwich" injections when the mixture is alternated with dextrose boluses.

Choosing the best proportion of ethiodized oil and the right amount of mixture is of paramount importance to achieve the best results. The proportion of (NBCA-MS)-based with ethiodized oil component in very small leakage of distal perforations can be 1:1 or 2:1 with a "single shot" 0.5-1 mL bolus. This strategy allows fast and effective sealing with the same microcatheter already in place. In case of a bigger leak when the perforation is more proximal or if there are other branches very close to the perforation site the multiple "sandwich" technique with (NBCA-MS)-based/ethiodized oil proportion of 1:2 to 1:4 with small boluses of 0.3-0.5 mL allows more precise embolization with smaller risk of back flow of the mixture which could cause side branch occlusion or thrombosis. After last embolization it is always advisable to perform a rapid

Table 2. Polymerization time based on the proportion of Lipidiol into the mixture (Ethiodized oil: Cyanoakrylate glue)

	Ethiodized oil 1:1	Ethiodized oil 2:1	Ethiodized oil 3:1	Ethiodized oil 4:1	Ethiodized oil 5:1	Ethiodized oil 6:1
Start polymerization	5 sec	10 sec	10 sec	18 sec	20 sec	25 sec
End polymerization	40 sec	60 sec	75 sec	85 sec	110 sec	120 sec

pull-back of the microcatheter ("hit and run") considering that the glue could solidify in the distal tip of the microcatheter or trap it into the coronary system.

CASE REPORT

The first patient is a 78-year old male with stable angina Canadian Class Society[3]. He was admitted 1 month earlier for stable angina and the coronary angiography showed a severe coronary artery disease with critical stenosis of left anterior descending artery (LAD) and left circumflex artery (LCX) and a CTO of the right coronary artery (RCA) [Figure 1A]. The case was discussed in Heart Team and surgical revascularization was excluded by patient's preference.

After revascularization of the LAD and LCX, revascularization of the CTO of RCA was staged after 1 month.

JCTO score of the RCA CTO was 3 and the most appealing interventional collateral from LAD to RCA was a septal branch and a very tortuous epicardial vessel from distal LAD [Figure 1B]. After several unsuccessful attempts to advance the guidewire on the septal, we managed to cross the epicardial vessel with regular SION guidewire (Asahi Intecc). The guidewire successfully crossed the most tortuous section of the channel but it was unable to progress further for lack of support from the microcatheter which was stocked at the entry point of the epicardial channel. We tried to rotate and push the Corsair microcatheter (Asahi Intecc) in order to advance closer to the guidewire`s tip [Figure 1-C], but during the manipulation the catheter suddenly stepped forward out of the vessel and a type 3 perforation occurred [Figure 1D]. After confirming the site of the coronary rupture, we placed the microcatheter 10-20 mm proximal to the perforation. Promptly a Ethiodized oil and Glubran mixture (1:1 ratio) was prepared. After flushing the microcatheter with a dextrose solution, the mixture was injected into the distal LAD [Figure 1E]. After 10-15 seconds cessation of the bleeding extravasation was observed [Figure 1F]. The patient remained stable and asymptomatic. No significant pericardial effusion was observed after several echocardiographic exams. The patient was discharged after 7 days. A new attempt of the recanalization is planned in the next few months.

The second patient is a 82-year old female affected by arterial hypertension, dyslipidaemia and mild carotid atherosclerosis. The patient had no cardiovascular history; she complained of effort dyspnoea and legs oedema. At the Echocardiography we observed a dilatation of the left ventricle with diffuse hypokinesia and moderate impairment of the ejection fraction (EF 40%) and moderate functional mitral regurgitation. Because of the new onset of heart failure, we planned a coronary angiography. The angiography showed a severe, calcific tri-vessel coronary disease, involving the left main and proximal LAD, and a total occlusion of the mid LAD and RCA [Figure 2A]. During the Heart Team discussion, the patient was refused from the cardiac surgeon because of advanced age and frailty and a complete percutaneous revascularization was planned.The CTO of the RCA was short and a visible microchannel seemed to give a good chance to cross with sliding technique. Thus, we decided to perform recanalization of RCA first, with antegrade approach avoiding double access due to absence of coronary collaterals from left coronary system and severe left main disease. We readly crossed the lesion with a soft polymeric guidewire Fielder XT-R (Asahi intecc), [Figure 2B]. After reaching the distal vessel and confirming the position of the wire with multiple projections we performed several dilatations with small compliant balloons. After dilatation, we observed a severe perforation of the posterior-lateral branch, probably due to the guidewire positioned distally in a smaller branch [Figure 2C]. We planned to implant a covered stent crossing and covering the small branch

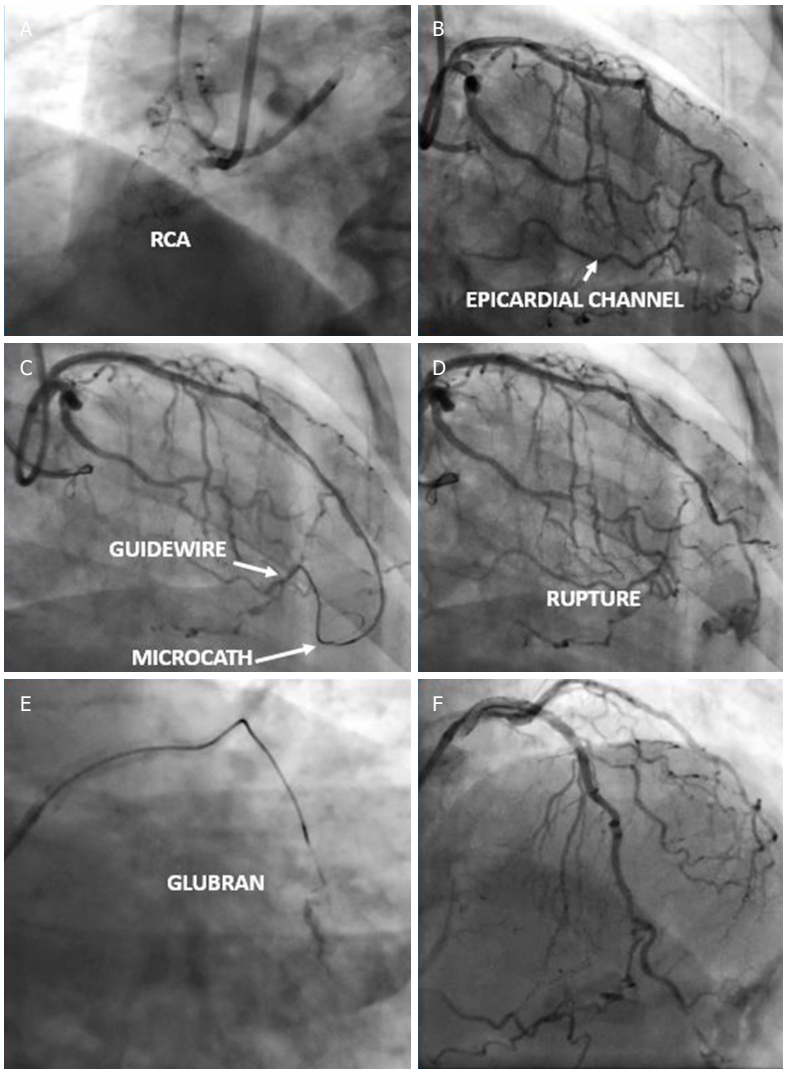

Figure 1. First case presented. A: lesion at RCA; occluded at proximal portion; B: epicardial channels from LAD to RCA; C: Guidewire into the epicardial channel; D: Evidence of extra vasal bleeding from distal LAD; E: (NBCA-MS)-based glue injection; F: Final result

involved in the coronary rupture. Because the patient was stable and the vessel was diffusely calcified and narrowed, we decided to perform PTCA and stenting of the RCA proximally to the rupture in order to facilitate the CS progression. After 2 long DES implantation (3 mm × 28 mm and 3 mm × 40 mm), a low-profile CS (Aneugraft) it was not able to advance in the posterior descending artery (PDA) more than just at the origin of the vessel and we decided to deploy it there. Nevertheless the postero-lateral (PL) branch was still patent and at the angiography the bleeding extravasation was still present [Figure 2D]. We eventually decided to wire the small branch, advance a microcatheter and perform an embolization with (NBCA-MS)-based glue [Figure 2E]. After mixing Lipidiol and (NBCA-MS)-based glue (3:1), the mixture was injected through a microcatheter Finecross (Terumo, Japan) using the "sandwich" technique for 3 overall "shots". In the last angiographic control, the rupture appeared closed and the bleeding stopped [Figure 2F]. The RCA and posterior descending showed a final TIMI 3 flow. We concluded the procedure with a PCI and 2 drug eluting stent (DES) implantation on left main artery to LAD-LCX (LM-LAD-LCX) bifurcation with a double kissing (DK) crush technique and CTO-PCI of LAD and LCX was planned as a staged procedure.

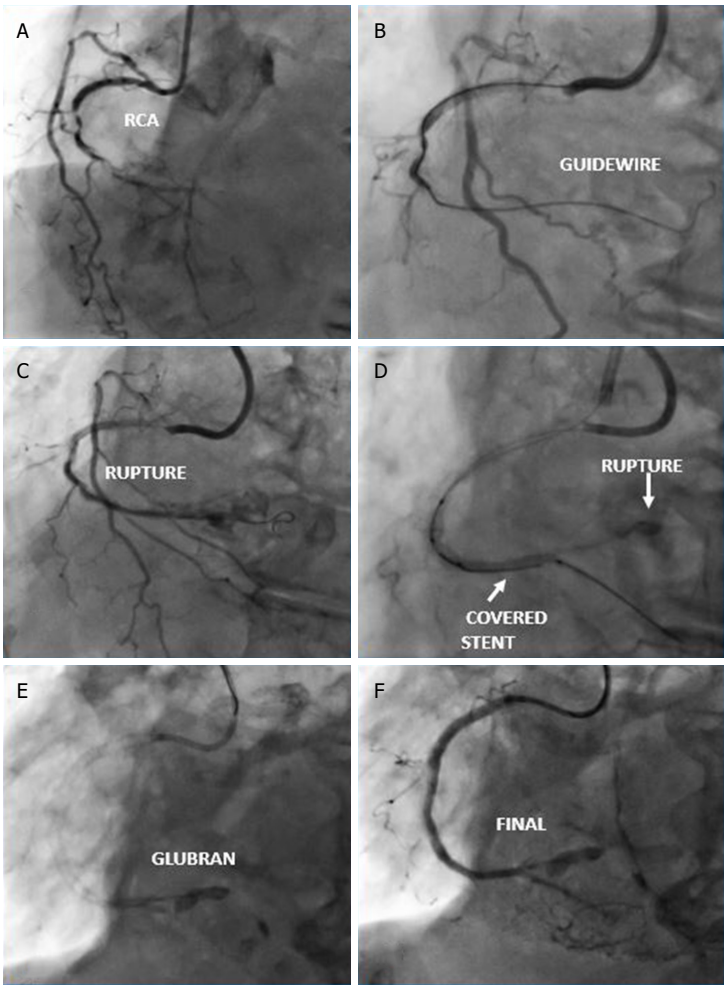

Figure 2. Second case presented. A: CTO of the RCA (Antegrade injection); B: Guidewire in the PL branch after crossing the CTO lesion; C: Evidence of extravasal bleeding at the level of the PL branch; D: persistence of extravasal bleeding at the distal edge of the covered stent; E: (NBCA-MS)-based glue injection; F: Final result. CTO: chronic total occlusion

DISCUSSION

Coil embolization for the treatment of small vessel Ellis type III perforations is considered the gold standard for emergent sealing. CTO operators always keep a set of different coils ready in the catheterization laboratory and should know the compatibility of the coils with different microcatheters used for CTO PCI[32]. Ideally, coils should be delivered in every CTO microcatheter but this is not always true. Moreover, sealing perforations with coils can be time-consuming and significantly costly when multiple coils are needed. On the other hand, auxiliary embolization material such as subcutaneous fat tissue or clots or trombin, are troublesome and inconvenient to prepare and are not adequately precise and reliable to deliver. For these reasons we believe that (NBCA-MS)-based glue should be an effective and inexpensive tool to keep in every catheterization laboratory as an alternative to the embolization coils.

On the other hand, the use of (NBCA-MS)-based glue compared with coils requires some experience to be delivered in a precise and safe manner. The adverse events described after glue embolization are basically divided in three main categories: inadvertent vascular embolization, suboptimal agent polymerization time, and catheter retention[33]. Both the suboptimal agent polymerization time and the catheter retention are related to the operator's inexperience. Correct proportion of the mixture (NBCA-MS)-based glue/ethiodized oil and use of small boluses or sandwich technique make the procedure safer and keep such complications infrequent.

On the other hand when the bleeding site is very close to major branches, coiling is always preferable because risk of inadvertent vascular embolization is not negligible, though coiling is definitely more onerous and time-consuming[34,35].

Another point in favor of (NBCA-MS)-based glue is his ability to create a sort of wide patch of polymeric material around the rupture that can cover different size of coronary perforations. This could be of adjunctive help in epicardial perforations when coiling from one side of the collateral could be not enough to stop the bleeding, and coiling from the other side could be troublesome if the CTO is not recanalized. The mechanism of the sealing in this setting could be explained with formation of aggregates of chain growth polymers in the tissue around the spillage, along with the obstruction of the afferent vessel.

Interestingly no tissue adverse reactions was described after embolization despite the wide spectrum of medical use of (NBCA-MS)-based glue.

DECLARATIONS

Authors' contributions

All authors contributed to the manuscript.

Availability of data and materials

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Conflicts of interest

All authors declared that there are no conflicts of interests.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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