Spontaneous Haematomas in Anticoagulated Covid-19 Patients: Diagnosis and Treatment by Embolization

Lorena López-Martínez1 · Juan D. Molina-Nuevo1 · María J. Pedrosa-Jiménez1 · Enrique Juliá-Mollá1

Received: 21 June 2021 / Accepted: 17 December 2021 / Published online: 28 January 2022
© Springer Science+Business Media, LLC, part of Springer Nature and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) 2021

Abstract

Purpose To assess the safety and efficacy of embolization for spontaneous bleeding in anticoagulated patients with COVID-19.

Material and Methods Single center retrospective study in 9 patients with COVID-19 who experienced bleeding complications following anticoagulation. The study included 8 men and 1 woman aged from 48 to 80 years (mean 69.7 years), who had a total of 10 soft tissue haematomas: 1 in the thigh, 1 in the anterior abdominal wall, 6 retroperitoneal and 2 thoracic haematomas. All patients were referenced for vascular embolization, mostly with Onyx-18.

Results A total of 10 haematomas were embolized in 9 patients. Technical success was achieved in all patients. No complications or adverse events were noted. One patient required percutaneous drainage of an infected haematoma 88 days after embolization. The mean hemoglobin level before embolization was 8.64 mg/dL and increased to 9.08 mg/dL after embolization (p = 0.3). After embolization all patients recovered haemodynamic stability and blood pressure levels improved. Seven patients resumed anticoagulation therapy after embolization. There were no recurrences or new bleedings in all treated patients. No patients required any additional invasive therapies or surgery. Mean intensive unit care and hospital stay was 6.7 and 35.2 days, respectively. All patients were discharged and were well at follow-up clinic visits 2–7 months after embolization. Seven patients performed a control CT scan 1–6 months after embolization, showing complete resolution of the haematoma.

Conclusion Embolization is safe and effective to treat spontaneous haematomas in anticoagulated patients with COVID-19, allowing to resume anticoagulation therapy. Level of evidence IV Level 4, case-series.

Keywords Spontaneous haematoma · Active bleeding · COVID-19 · CT angiography · Embolization · Onyx · EVOH

Introduction

Bleeding complications in elderly patients on anticoagulant therapy are estimated at about 5%, [1] with an incidence of spontaneous haematomas of about 0.6%. [1] In large haematomas with hemodynamic instability, the prognosis is poor with multiple organ failure, [2] reaching a mortality of 30–50%. [3, 4] COVID-19 infection causes a disorder of haemostasis, [5] with a procoagulant state. This has led to the inclusion of thromboprophylactic (anticoagulant) therapy in most treatment protocols. [2–10] Recent studies refer to heparin-induced thrombocytopenia, [6, 10] and a percentage of patients develop renal failure in the coronavirus infection. This results in an increased half-life of heparin, which circulates in the plasma longer, [8] leading to “pseudo-overdosing”, increasing the risk of bleeding. In COVID-19 patients, the incidence of haematomas appears to be higher due to coagulation disorders caused by...
infection, coupled with thrombocytopenia due to heparin and overdose in patients with renal failure.

Computed tomography (CT) angiography is essential to the diagnosis of haematomas as it allows the size, location and artery responsible for the bleeding to be established, [11] identifying the location of the vascular origin of the bleeding in 95.2% of cases. [1]

The purpose of the study was assess the safety and efficacy of embolization for spontaneous bleeding in anticoagulated patients with COVID-19.

**Material and Methods**

Single center retrospective study in 9 patients with COVID-19 who experienced bleeding complications following anticoagulation.

The study included 9 patients, 8 men and 1 woman, aged from 48 to 80 years (mean 69.7 years), who had a total of 10 soft tissue haematomas: 1 in the thigh, 1 in the anterior abdominal wall, 6 retroperitoneal and 2 thoracic haematomas, with signs of active bleeding on CT angiography (Figs. 1 and 2). All patients included were receiving anticoagulant therapy. Other clinical variables were also collected and included in Table 1.

All patients were referenced for vascular embolization.

**Imaging Protocol**

Patients with clinically suspected active bleeding underwent CT angiography of the chest or abdomen, following a three-phase or two-phase protocol of the radiologist’s choice. All studies were performed on a General Electrics Revolution EVO (General Electrics Healthcare, Chicago, Illinois) or Philips Brillance (Philips Healthcare, Cleveland, Ohio) 64-row multidetector computed tomography (MDCT).

Iodinated contrast medium Omnipaque 300 (General Electrics Healthcare, Chicago, Illinois) was used, with 60 ml for thoracic studies and 80–100 ml for abdominal studies. In patients with kidney failure, Visipaque 320 (General Electrics Healthcare, Chicago, Illinois) was used.

CT angiography confirmed haematoma with active bleeding in 9 patients, one of them with 2 concomitant haematomas. The location, size of the haematoma and the artery responsible for the bleeding are detailed in Table 2.

**Endovascular Treatment**

The embolization procedure was performed with a General Electrics Innova 4100 angiographic system (General Electrics Healthcare, Chicago, Illinois). A right or left femoral vascular access was preferentially performed. In

![Fig. 1 (case 5) a (MDCT) and b (VR reconstruction) Right pectoral haematoma with active bleeding (short arrow). c Arteriography of the lateral thoracic branch with contrast extravasation (circle). d Control after embolization of lateral thoracic and thoracoacromial branches, with no contrast extravasation, with Onyx-18 cast (long arrow)](image)
all cases a 5F introducer sheath (Terumo, Shibuya-Ku, Tokyo) was used. The catheters used were: Multi-purpose 4F (Cordis, Miami, FL), Cobra 2 4F (Cordis, Miami, FL) or Simmons 1 4F (Cordis, Miami, FL). The microcatheters used were Progreat 2.7 (Terumo, Shibuya-Ku, Tokyo) or Rebar 18 (Covidien Medtronic, Irvine, CA).

The choice of embolising agent was based at the operator’s preferences. The embolization material was Ethylene–Vinyl Alcohol (EVOH) Copolymer Onyx-18 (Covidien Medtronic, Irvine, CA) in 7 cases (Fig. 1 and Fig. 2), one of them in combination with Gelita-Spon Powder (Absorbable Gelatin Powder Hemostat) (Gelita Medical, Eberbach, Germany). Pushable microcoils (Interlock 2D (Boston Scientific, Malborough, MA) and Hilal embolization microcoils (COOK Medical’s, Bloomington, IN)) were used in one case. Glubran2 (N-butyl-2-cyanoacrylate (NBCA)) (GEM, Viareggio, Italy) was used in one case. Gelita-Spon Powder (Gelita Medical, Eberbach, Germany) was used in one case. The treatments and materials used are detailed in Table 2.

Results

In the study, CT angiography detected active bleeding in all cases, assessed haematoma volume and severity of clinical status.

The study, in line with current literature, shows a predominance of spontaneous haematomas, with a total of 10 soft tissue haematomas, which were embolised in 9 patients. In the context of coagulation disorders, it was decided in most cases to treat with a liquid embolic agents, predominantly Onyx-18.

Technical success was achieved in all cases, without complications during or after the embolization procedure.

The mean hemoglobin level before embolization was 8.64 mg/dL and increased to 9.08 mg/dL after embolization with standard deviation of 1.3 ($p = 0.3$).

There were no recurrences or new bleedings in all treated patients. None of them required surgery. Seven patients resumed anticoagulation therapy after embolization (Table 1).

Mean intensive unit care (ICU) and hospital stay was 6.7 and 35.2 days, respectively. All patients experienced a progressive improvement until they were discharged.

Seven patients performed a control CT one month and 6 months after embolization, showing resolution of all treated haematomas. One patient required percutaneous drainage of an infected haematoma 88 days after embolization (Fig. 2).

Eight patients were reviewed in consultation at 2 and 7 months and were asymptomatic.
Table 1  Demographic and laboratory

| Case | Sex | Age | Cr | DD | Fibrinogen | Inflammatory markers | Platelets | Coagulation | Hb | Hb reduction | Hb after embolization | Anticoagulant therapy | Resumption of anticoagulant therapy | Days to resume | Days of ICU/hospital admission | Discharge date | Control CT |
|------|-----|-----|----|----|------------|----------------------|-----------|-------------|----|--------------|----------------------|----------------------|----------------------------------|---------------|-------------------------------|---------------|------------|
| 1    | M   | 48  | 1.4| 4607| 316        |                      | F 1754    | PA 64%      | 7.9| 3.9          | 9.5                  | Enoxaparin           | 80 mg/12 h           | No                | –             | 7/36             | 17/4/2020   | –           |
| 2    | M   | 69  | 2.7| 682 | 318        |                      | F 1723    | PA 69%      | 5.7| 6.8          | 8                    | Enoxaparin           | 60 mg/12 h           | Enoxaparin         | 25            | 15/30          | 25/4/2020   | 19/10/2020 |
| 3    | M   | 60  | 1.79| 6349| 316        |                      | F 1505    | PA 78%      | 6.9| 6.4          | 7.2                  | Enoxaparin           | 80 mg/12 h           | Enoxaparin         | 11            | 20/29          | 11/5/2020   | 23/11/2020 |
| 4    | M   | 66  | 0.5| 929 | 351        |                      | F 723     | PA 55%      | 9   | 2            | 9                    | Enoxaparin           | 60 mg/12 h           | Enoxaparin         | 2             | 3/46           | 12/5/2020   | 5/11/2020  |
| 5    | M   | 80  | 1.2| 2280| 877        |                      | F 410     | PA 65%      | 9   | 1.6          | 9.9                  | Enoxaparin           | 80 mg/24 h           | Enoxaparin         | 8             | 2/27           | 5/8/2020    | 7/9/2020   |
| 6    | M   | 71  | 1.9| 1350| 183        |                      | F 11.666  | PA 58%      | 9.8| 1.9          | 9.5                  | Enoxaparin           | 80 mg/24 h           | Enoxaparin         | 8             | 2/37           | 15/10/2021  | 23/4/2021 |
| 7    | F   | 79  | 1.06| 742 | 421        |                      | F 1340    | PA 44%      | 9.5| 2.5          | 9                    | Enoxaparin           | 80 mg/12 h           | Enoxaparin         | 8             | 2/39           | 20/2/2021   | 13/8/2021 |
| 8    | M   | 77  | 1.4| 901 | 196        |                      | F 496     | PA 74%      | 11.7| 1.3         | 9.6                  | Enoxaparin           | 60 mg/24 h           | Enoxaparin         | 9             | 4/40           | 22/2/2021   | 9/8/2021   |
| 9    | M   | 78  | 0.48| 2024| 308        |                      | F 3839    | PA 72%      | 8.3| 1.2          | 9.7                  | Enoxaparin           | 60 mg/12 h           | Enoxaparin         | 15            | 3/33           | 27/2/2021   | 7/6/2021   |

Sex (M: male, F: female), age: years, Cr (creatinine): mg/dL, DD (D-dimer): mcg/L, fibrinogen: mg/dL, F (ferritin): ng/dL, CRP (C reactive protein): mg/dL, platelets: 10^9/mcl, PA (prothrombin activity): %, INR (international normalised ratio), Hb (haemoglobin): g/dL (at the time of bleeding), Hb reduction (haemoglobin reduction): points of haemoglobin reduction from the previous laboratory tests, Hb after embolization (24 h): g/dL, Anticoagulant therapy (at the time of bleeding), Resumption of anticoagulant therapy: treatment and doses, Days to resume: days to resume the anticoagulant therapy after embolization, Days of ICU (Intensive Care Unit)/hospital admission, Discharge date: clinical discharge date, Control CT: date of follow-up CT scan showing resolution of haematoma.
Discussion

Endovascular treatment with embolization of the arterial contributions of the haematoma is a minimally invasive, safe and effective technique, less invasive and more selective than surgery, [2, 3] with a technical success of 90%. [1] It is currently the technique of choice for the treatment of active arterial bleeding, as it does not carry the disadvantages associated with surgery. Patients have an early recovery, with a shortened hospital and ICU stay. [10] Recurrence after embolization is rare and usually occurs in patients with severe consumptive coagulopathy. [1]

There are different materials and devices to perform embolization, and the selection of one over another depends on multiple factors, such as characteristics of bleeding (morphology and caliber of the responsible artery), the ability to access the bleeding site (“local” or “distant” embolization), the operator’s experience with the different materials and others inherent to patient’s condition (existence of coagulopathy, etc.). There are now retrospective studies suggesting the advantages of liquid embolic agents as they provide rapid complete occlusion compared to others such as coils. [12]

In the study, most of the embolization were performed with Onyx-18 (Table 2). The selection of this material was mainly based on two factors, on the one hand the morphology of the responsible artery, in all cases small calibre arteries, and on the other hand the presence of a coagulation disorder. Onyx-18 is a non-adhesive permanent liquid emboliser that allows complete, rapid and safe vascular occlusion of the vascular lumen by polymerization, especially in patients with coagulation disorders (unlike other materials that require coagulation activation to achieve effective vascular closure). It allows complete control, with no microcatheter adherence or migration of embolization material. No special preparation is required for COVID-19 patients.

Conclusion

Bleeding complications in COVID-19 patients are a major cause of increased morbidity and mortality in these patients. Utmost care should be taken in COVID-19 patients treated with heparin at therapeutic doses, avoiding the risk of overdosing.

In cases of suspected active bleeding, early diagnosis and treatment are essential to ensure patient survival. CT angiography is the diagnostic tool of choice.

Embolization is safe and effective to treat spontaneous haematomas in anticoagulated patients with COVID-19,
allowing to resume anticoagulation therapy and should be considered as first choice treatment. Onyx-18 is a rapid and safe vascular occluder, particularly in patients with coagulation disorders.

**Funding** This study was not supported by any funding.

**Declarations**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Consent for Publication** For this type of study consent for publication is not required.

**Ethical Approval** For this type of study formal consent is not required.

**Informed Consent** For this type of study informed consent is not required.

**References**

1. Doham A, Darnige L, Sapoval M, Pellerin O. Spontaneous soft tissue hematomas. Diagn Interv Imaging. 2015;96:789–96.
2. Bargellini I. Spontaneous bleedings in COVID-19 patients: an emerging complication. Cardiovasc Intervent Radiol. 2020. https://doi.org/10.1007/s00270-020-02507-4.
3. Palumbo D, Guazzarotti G, De Cobelli F. Spontaneous major haemorrhage in covid-19 patients: another brick in the wall of SARS-Cov-2- associated coagulation disorders? JVIR sep. 2020;31(9):148–50. https://doi.org/10.1016/j.jvir.2020.06.010.
4. Vergori A, Pianura E, Lorenzini P, D’Abramo A, et al. Spontaneous ilio-psoas haematomas (IPHs): a warning for COVID-19 inpatients. Annals of Medicine. 2021;53(1):295–301.
5. Erdine B, Raina JS. Spontaneous retroperitoneal bleed coincided with massive acute deep vein thrombosis as initial presentation of Covid-19. Cureus. 2020;12(8):e9772. https://doi.org/10.7759/cureus.9772.
6. Dorgalaleh A. Bleeding and bleeding risk in COVID-19. Seminars in Trombosis and Hemostasis n7/2020. 2020;46:815–8. https://doi.org/10.1055/s-0040-1713434.
7. Rogani S, et al. Spontaneous muscle hematoma in older patients with COVID-19: two case report and literature review. BMC Geriatr. 2020;20:539. https://doi.org/10.1186/s12877-020-01963-4.
8. Mattioli M, Benfaremo D, Fustini E, Gennarini S. Atypical spontaneous haematomas in a patient with severe coronavirus disease 2019 (COVID-19). Semin Thromb Hemost. 2020;46:856–8. https://doi.org/10.1055/s-0040-1715092.
9. Zidane MT, Schram MT, Planken EW, Molenkrijgh WH, Roosdald FR, van der Meer FJ, et al. Frequency of major hemorrhage in patients treated with unfractionated intravenous heparin for deep venous thrombosis or pulmonary embolism: a study in routine clinical practice. Arc Intern Med. 2000;160(15):2369–73.
10. Lucatelli P, De Rubeis G, Citone M, Lucarelli NM, Pasqualini V, Sturiale M, Giuliani S, Rosati M, Ceccherini C, Corona M, Mosconi C, Ustil A, Arigi R. Heparin-related major bleeding in Covid-19-positive patients: perspective from the outbreak. Cardiovasc Intervent Radiol. 2020;43:1216–7. https://doi.org/10.1007/s00270-020-02532-3.
11. Nakamura H, Ouchi G, Miyagi K, Higure Y, Otsuki M, Nishiyama N, Kinjo T, Nakamatsu M, Tateyama M, Kuikita I, Fujita J. Case Report: iliopsoas hematoma during the clinical course of severe COVID-19 in two male patients. Am J Trop Med Hyg. 2021;104(3):1018–21.
12. Klausenitz C, Kuehn J-P, Noeckler K, Radosa CG, Hoffmann R-T, Teichgraeber U, Mensel B. Efficacy of transarterial embolisation in patients with life-threatening spontaneous retroperitoneal haematoma. Clinincal Radiol. 2021;76(2):157.e11-157.e18. https://doi.org/10.1016/j.crad.2020.10.003.

**Publisher’s Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.