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Non-thrombotic Pulmonary Embolism Following Cyanoacrylate Injection for Gastric Varices: A Case Series of Six Patients

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ABSTRACT

Background: Endoscopic injection of cyanoacrylate is a standard therapeutic approach for managing bleeding gastric varices in patients with portal hypertension. While generally effective, the procedure carries a risk of non-thrombotic pulmonary embolism (NTPE) resulting from the systemic migration of the biological glue. **Aim:** This study describes the clinical, radiological, and therapeutic characteristics of NTPE occurring after cyanoacrylate injection for gastric varices. **Methods:** A retrospective observational study was conducted at the Ibn Rochd University Hospital (Casablanca, Morocco) between January 2015 and December 2022. The study included patients who received biological glue injections for bleeding gastric varices and subsequently developed pulmonary embolism confirmed by chest radiography or computed tomography (CT) angiography. **Results:** Among 46 patients treated with a Glubran® 2 and Lipiodol® mixture during the study period, 6 patients (13%) developed NTPE. The mean patient age was 49 years. Clinical onset was primarily characterized by acute dyspnea and oxygen desaturation. Chest CT angiography confirmed the presence of hyperdense embolic material within the pulmonary arteries in all affected patients. Therapeutic management was predominantly supportive, relying heavily on oxygen therapy. Clinical outcomes were favorable with symptomatic treatment in three patients; however, one patient required transient mechanical ventilation, and one death occurred. **Conclusion:** NTPE is a rare but potentially severe complication of gastric variceal obturation. The risk highlights the need for meticulous injection techniques and close post-procedural respiratory monitoring, particularly in patients with large varices or those requiring higher injection volumes.

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KEYWORDS:

Gastric varices, cyanoacrylate, non-thrombotic pulmonary embolism, portal hypertension, biological glue, endoscopic hemostasi

INTRODUCTION

Upper gastrointestinal bleeding due to rupture of gastric varices is a serious complication of portal hypertension [1]. Endoscopic injection of biological glue into gastric varices is the most widely recommended therapeutic method for achieving hemostasis in cases of bleeding gastric varices [2–4].

Non-thrombotic pulmonary embolism (NTPE) is a rare but potentially life-threatening complication of cyanoacrylate injection for gastric varices, with a reported incidence ranging from 0.5% to 4.3% [5–7].

The aim of this study was to describe the clinical, radiological, therapeutic, and outcome characteristics of pulmonary embolism occurring after cyanoacrylate injection for gastric varices.

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MATERIALS AND METHODS

This was a retrospective observational descriptive study conducted in the Department of Hepato-Gastroenterology at Ibn Rochd University Hospital in Casablanca over an eight-year period, from January 2015 to December 2022.

The inclusion criteria comprised patients with gastric varices who underwent biological glue injection (cyanoacrylate injection) into these varices and subsequently developed pulmonary embolism after the procedure, confirmed by imaging. Diagnosis was established either by chest radiography demonstrating suggestive whitish reticulonodular opacities (Figure 1) or by chest computed tomography angiography revealing the presence of hyperdense material within the pulmonary vessels, consistent with migration of biological glue (Figure 2).

RESULTS

During the study period, 46 patients underwent biological glue injection for gastric varices. Six patients (13%) developed pulmonary embolism following the procedure.

The mean age of the patients was 49 years, ranging from 22 to 72 years. The sex distribution was balanced, with three men and three women.

The etiologies of portal hypertension were predominantly post-viral hepatitis C–related cirrhosis (2 cases), post-viral hepatitis B–related cirrhosis (1 case), cirrhosis of undetermined etiology (1 case), and portal hypertension of unspecified etiology (2 cases).

In all cases, the indication for glue injection was acute gastrointestinal bleeding. The glue used was **Glubran® 2** mixed with **Lipiodol®** in all patients. Five patients underwent a single injection session, whereas one patient required three sessions.

Clinically, five patients developed respiratory symptoms predominantly characterized by dyspnea (5 cases), dry cough (3 cases), and chest pain (2 cases). One patient remained asymptomatic. Five patients presented with oxygen desaturation below 90%, associated with respiratory instability, while hemodynamic status remained stable in all patients.

Chest radiography, performed in four patients, revealed bilateral reticulonodular opacities. Chest computed tomography angiography, performed in all patients, confirmed the presence of bilateral intravascular hyperdense material within the pulmonary arteries, consistent with glue embolism.

Management mainly consisted of oxygen therapy in five patients. One patient required transient tracheal intubation. Two patients received empirical antibiotic therapy, and one patient was transferred to the intensive care unit.

Clinical outcomes were favorable with symptomatic treatment in three patients. One patient showed improvement after transient mechanical ventilation. One death occurred during transfer to the intensive care unit. Another patient was discharged against medical advice.

DISCUSSION

Non-thrombotic pulmonary embolism (NTPE) represents a rare but potentially serious complication of biological glue injection used for the treatment of bleeding gastric varices. Most complications reported after variceal glue injection involve local events (ulcerations, pain), recurrent bleeding, or migration of the injected material into the porto-systemic circulation. However, NTPE represents a major systemic event that may compromise the immediate prognosis of patients who are already fragile due to advanced portal hypertension.

The literature reports variable incidences of this complication. Al-Bawardy et al. observed two cases of NTPE among 95 patients treated with cyanoacrylate [75], whereas Zhou et al. reported one case among 439 patients [5]. Cheng et al. identified one case among 753 injections [70], and Joo et al. reported two cases among 85 patients [69]. These data suggest a low incidence, generally below 3%, although some more recent series indicate a slightly higher frequency in specific clinical contexts. In our cohort, the incidence of NTPE was notably higher (6 cases among 46 glue injections), which may reflect technical particularities, larger injected volumes, or the presence of large porto-systemic shunts facilitating migration of the embolic material.

Comparison of the published series with our findings suggests that the risk of pulmonary embolism following gastric variceal glue injection does not depend solely on the type of glue used, whether **Histoacryl®** or **Glubran® 2**, nor exclusively on the injected volume. Even with moderate volumes and appropriate dilutions, embolic events may occur, highlighting the multifactorial nature of this complication, including injection technique, variceal blood flow, and the presence of porto-systemic shunts. These observations emphasize the importance of meticulous injection technique and constant vigilance to minimize the risk [82,94].

From a pathophysiological perspective, NTPE following glue injection results from systemic embolization of the cyanoacrylate–Lipiodol® mixture through porto-pulmonary or porto-systemic communications. This hypothesis is supported by several radiological studies demonstrating hyperdense deposits compatible with glue within the pulmonary arteries, suggesting a mechanical embolization rather than a classical thrombotic process.

Clinically, NTPE most frequently manifests as acute dyspnea occurring within minutes to a few hours after the glue injection procedure. The series by Rickman et al. [81] and De Freitas et al. [87] describe cases of sudden dyspnea immediately after injection, sometimes associated with tachypnea, oxygen desaturation, and chest pain. Asymptomatic presentations have also been reported in the

literature, occasionally diagnosed incidentally on imaging or during investigations of respiratory symptoms occurring after the procedure. In our series, five patients developed acute dyspnea, three of whom experienced symptoms immediately after glue injection.

Imaging plays a fundamental role in confirming the diagnosis. Contrast-enhanced chest computed tomography is considered the diagnostic modality of choice, demonstrating intravascular hyperdense emboli within the pulmonary arteries. Tangcheewinsirikul et al. [88] and Nawrot et al. [87] described characteristic findings of hyperdense material in pulmonary arterial branches corresponding to glue emboli, which can be distinguished from conventional thrombotic emboli by their higher density and their linear or segmental nodular morphology. Similar imaging findings were observed in our series.

The therapeutic management of NTPE remains essentially supportive. Oxygen therapy represents the cornerstone of initial treatment, with flow rates reported in the literature ranging between 4 and 10 L/min depending on the severity of hypoxemia. In our experience, oxygen therapy at 5 L/min resulted in clinical improvement in three patients. In severe cases, mechanical ventilatory support may be required, as reported by Chew et al. and observed in one of our patients. Some authors have suggested the use of corticosteroids (Parthiv Amin, 2022; Duarte M., 2023) or empirical antibiotic therapy; however, current evidence regarding their efficacy remains limited and heterogeneous. Consequently, no specific pharmacological treatment is currently recommended in guidelines for NTPE following glue injection.

Anticoagulation has no indication in this context because the embolism is not thrombotic in origin, and the use of anticoagulants could increase the risk of bleeding in these patients who are already predisposed to gastrointestinal hemorrhage.

The clinical outcome of NTPE varies across cases. Several series report complete recovery with simple oxygen therapy (Rickman et al., Alexander et al. [81,82]), which is consistent with our findings, where three patients showed favorable outcomes with symptomatic treatment alone. Nevertheless, unfavorable outcomes, including death, have been reported despite intensive management, notably in the series of Burke MP (2017), De Freitas (2016), and Marion Audibert et al. The death observed in our series highlights the potential severity of this complication in cases of severe respiratory involvement.

Prevention of NTPE following glue injection relies on careful assessment of variceal blood flow, meticulous injection technique, and possibly the adoption of combined strategies such as the use of coils. Although cyanoacrylate injection remains highly effective for the treatment of gastric varices, vigilance is essential to minimize the risk of systemic migration and its pulmonary complications.

CONCLUSION

Pulmonary embolism following biological glue injection, although rare, may be severe and sometimes underdiagnosed. The risk appears to increase in patients with large gastric varices or in those requiring the injection of larger volumes of glue. Careful monitoring, even after the procedure, along with the adoption of appropriate technical strategies, is essential to prevent this complication and to optimize patient management.

Figure 1. Chest radiograph showing radiological features of pulmonary embolism following cyanoacrylate injection in our patients.

Figure 1a. Whitish reticulonodular opacities.

Figure 1b. Whitish reticulonodular opacities.

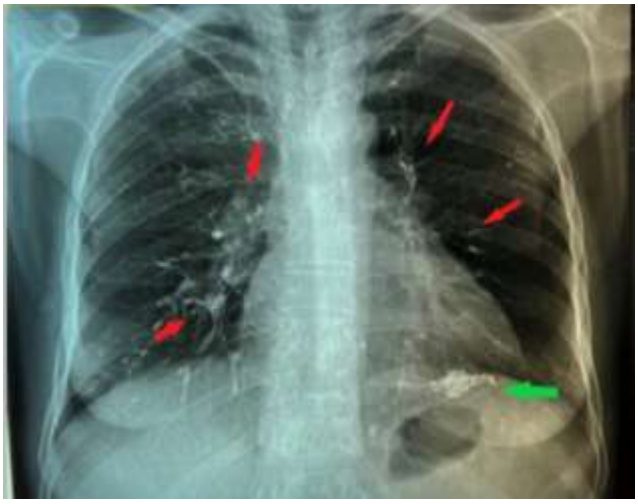
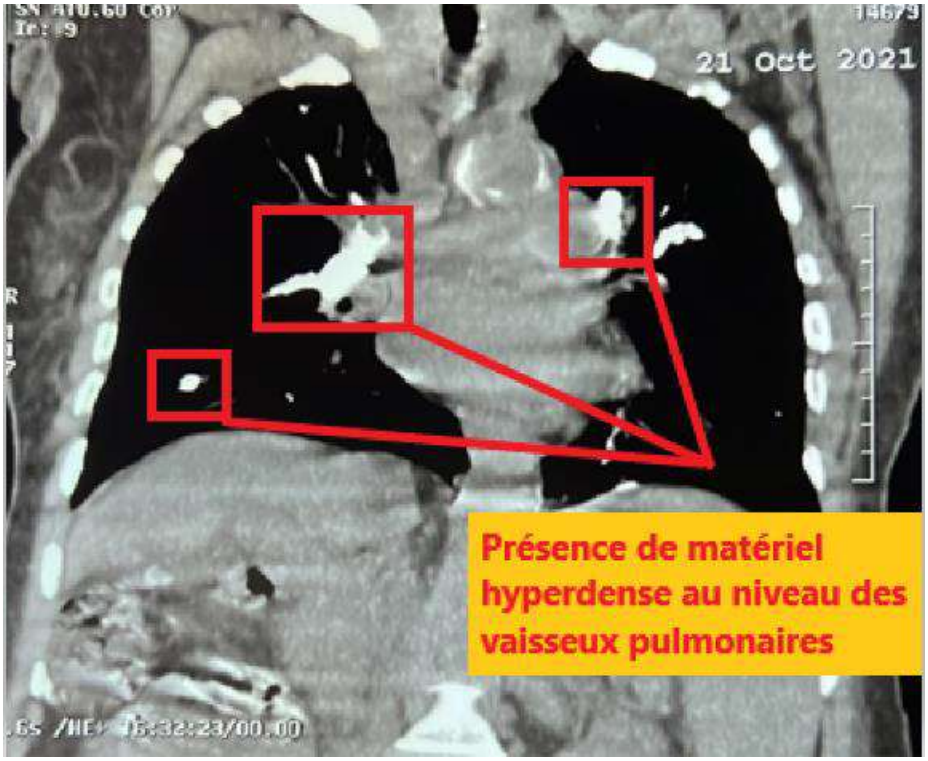


Figure 1c :

➔ **Whitish reticulonodular opacities.**

➔ **. Cyanoacrylate glue within the gastric varix.**

Figure 2. Chest CT angiography showing pulmonary embolism following cyanoacrylate injection in one of our patients.



Presence of hyperdense material within the pulmonary arteries.

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