Pulmonary Glue Embolism

**Case Report**

A 65-year-old man was admitted to the Accident & Emergency Department of the Hull Royal Infirmary, Hull, UK, in 2017 with a two-day history of coffee-coloured vomiting and melaena. He was known to have Child-Pugh class C liver cirrhosis secondary to alcoholic liver disease, type 2 diabetes mellitus and hypertension. Upon admission, the patient was hypotensive, tachycardic, icteric and encephalopathic. A physical examination revealed a distended abdomen and moderate splenomegaly. Laboratory tests revealed haemoglobin levels of 6 g/L, white cell count of 14.9 x 10^9/L, a prolonged prothrombin time and moderate coagulopathy. Renal function tests showed impaired function with a creatinine of 223 μmol/L. Initial investigations showed positive hepatitis B and C serology and a high viral load. Laboratory tests confirmed a diagnosis of hepatitis B and C infection. The patient underwent transjugular intrahepatic portosystemic shunting twice to control the bleeding, after which he recovered satisfactorily.

**Keywords:** Gastric Varices; Pulmonary Embolism; Sclerotherapy; N-butyl-cyanoacrylate; Lipiodol; Case Report; United Kingdom.

**Abstract:** A pulmonary glue embolism is an unusual but potentially life-threatening complication following the treatment of variceal bleeding, especially in patients with large varices requiring large volumes of sclerosant. Other contributory factors include the rate of injection and ratio of the constituent components of the sclerosant (i.e. n-butyl-cyanoacrylate and lipiodol). This condition may be associated with a delayed onset of respiratory compromise. Therefore, a high degree of clinical suspicion is essential in patients with unexplained cardiorespiratory decline during or following endoscopic sclerotherapy. We report a 65-year-old man who was admitted to the Hull Royal Infirmary, Hull, UK, in 2017 with haematemesis and melaena. He subsequently developed acute respiratory distress syndrome secondary to a glue embolism following emergency sclerotherapy for bleeding gastric varices. The aetiology of the embolism was likely a combination of the large size of the gastric varices and the large volume of cyanoacrylate needed. After an endoscopy, the patient underwent transjugular intrahepatic portosystemic shunting twice to control the bleeding, after which he recovered satisfactorily.

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Although rare, pulmonary glue emboli are potentially life-threatening complications which can arise following endoscopic sclerotherapy for the treatment of variceal bleeding.1 Large volumes, the rate of injection and the ratio of components (i.e. the proportion of n-butyl-cyanoacrylate to lipiodol) of the sclerosant are thought to contribute to the condition.12 Pulmonary glue emboli may be associated with delayed-onset respiratory compromise and may be overlooked in asymptomatic or mildly symptomatic patients.12 This case report describes a patient who developed acute respiratory distress syndrome due to a pulmonary glue embolism following endoscopic sclerotherapy. This article highlights the variable clinical spectrum, complex pathophysiology and risk factors of this condition.

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An emergency upper gastrointestinal endoscopy revealed a large fundal gastric varix with active bleeding and the stomach was filled with blood. Endoscopic sclerotherapy of the varix was carried out using a solution of 4 mL of n-butyl-cyanoacrylate and 8 mL of lipiodol. Immediately after the procedure, the patient was haemodynamically stable with an oxygen saturation of 98%. However, on the following day, the patient developed tachycardia and became febrile with a temperature of 39°C. His oxygen saturation proportion had dropped to 90% and his fraction of inspired oxygen requirements increased from 0.4 to 0.8. Fine crepitations were audible throughout the chest area. Another chest radiograph revealed diffuse infiltrates in both lungs, thought to be due to aspiration pneumonia [Figure 1].

A computed tomography (CT) scan revealed diffuse ground glass opacities in both lungs along with consolidation throughout both lower lobes. Hyperdense linear structures were observed within the lumen and branches of the pulmonary arteries, along with similar tubular larger volume hyperdense structures within the gastric fundal varices [Figure 2]. These findings were consistent with multiple pulmonary glue emboli from the injected sclerosant, with parenchymal changes suggesting acute respiratory distress syndrome. Retrospectively, a review of the initial chest radiograph indicated the presence of subtle radiopaque densities, corresponding with glue particles. The patient was subsequently intubated, ventilated and treated conservatively with intravenous diuretics. Broad-spectrum antibiotics were also prescribed empirically to prevent spontaneous bacterial peritonitis and to treat the aspiration pneumonia. Five days after the initial CT scan, repeat scans of the chest, abdomen and pelvis were performed due to further variceal bleeding; these showed that the glue emboli had persisted [Figure 3]. The patient subsequently required a transjugular intrahepatic portosystemic shunt to control the haemorrhage.

After being transfused with six units of packed red blood cells along with fresh frozen plasma and cryoprecipitate, the patient was transferred to the Intensive Care Unit and prescribed terlipressin, antibiotics and standard treatment for variceal bleeding.
Over the next two days, the patient’s oxygen requirements gradually decreased. A repeat chest radiograph indicated the resolution of the pulmonary parenchymal changes. The patient was subsequently weaned off ventilation and extubated. A repeat endoscopy immediately before discharge revealed ulceration from the sclerotherapy procedure, but no further active bleeding. The patient required two further transjugular intrahepatic portosystemic shunt procedures to control the haemorrhage, after which he had an uneventful recovery and remained asymptomatic over the following six months.

Discussion

Sclerotherapy of gastric fundal varices is the treatment of choice for patients with portal hypertension associated with hepatic cirrhosis who present with acute uncontrolled gastric variceal bleeding.1,2 Alternative interventions—such as band ligation or transjugular intrahepatic portosystemic shunting—may be considered for the treatment of bleeding from gastro-oesophageal varices.3,4 According to international recommendations, an injection of glue is the most cost-effective option for cases of uncontrolled gastric variceal bleeding.3-5 The glue consists of a mixture of n-butyl-cyanoacrylate, which is an aqueous solution, and lipiodol, which is an oil-based agent. N-butyl-cyanoacrylate causes almost instant haemostasis by undergoing rapid polymerisation when it comes into contact with blood, while the role of lipiodol is to delay the polymerisation process, thus reducing the likelihood of glue particles adhering to the endoscope or needle. Nevertheless, there is a risk of distal embolisation and potentially devastating complications.6,7

The blood supply of gastric varices is usually derived from the short gastric and gastroepiploic veins that drain into the left renal vein via a large gastrorenal shunt. Migrating glue particles often follow a complex pathway, travelling from the gastric varices through the gastrorenal and splenoportal veins to the inferior vena cava, right side of the heart and into the pulmonary circulatory system.8-10 Thus, in most cases, the lungs filter glue emboli; however, among patients with atrial septal defects, patent foramina ovale or arteriovenous pulmonary shunts, the embolisation of glue particles into systemic circulation may occur, with the glue particles potentially becoming lodged within the cerebral, splenic or coronary arteries with catastrophic consequences.11 Alternatively, glue emboli can migrate via the superior vena cava and the azygos vein; however, this more commonly occurs in cases of oesophageal rather than cardiac or gastric varices.10-12 The development of high-flow shunts such as the cardiotuberositarian vein can also carry clots or embolic material from injected varices to the pulmonary circulatory system.13,14

In a previous study, Marion-Audibert et al. injected a mixture of 3 mL of lipiodol and cyanoacrylate into the right cardiac cavity of a pig via a Swan-Ganz catheter in the intrapulmonary artery; subsequently, the authors noted an immediate dramatic rise in pulmonary artery pressure, along with an associated drop in cardiac output.15 Simultaneously, transoesophageal echocardiography demonstrated a sudden dilation of the right cavities of the heart, followed by right-sided heart failure that quickly progressed to global heart failure, ventricular fibrillation and cardiac arrest, at which point the animal died.15 In this case, death occurred as a result of the pulmonary glue embolism and was not secondary to chemical acute respiratory distress syndrome. A histological analysis also confirmed that the pulmonary embolism was due to the mechanical occlusion of the pulmonary arteries and not the secondary activation of coagulation.10

The precise incidence of glue migration following variceal embolisation is not known, since chest imaging is not routinely performed for patients with mild post-procedural hypoxaemia. In a review article, Saraswat et al. concluded that the risk of embolisation is between 0.5–4.3%.15 Another review of 753 cases by Cheng et al. identified distant embolisation in five patients (0.7%), of which one embolism was pulmonary, one was cerebral and three were splenic.16 According to Alexander et al., the volume of glue used, rate of injection and size of the gastric varices being treated contribute to the risk of embolisation; in particular, large-sized varices with high blood flow rates frequently associated with gastrorenal shunts have a higher risk of pulmonary embolism.11 Similarly, Hwang et al. observed that injecting volumes of cyanoacrylate glue over 4.2 mL resulted in an increased risk of pulmonary embolism.12 Altering the composition of the glue by varying the ratio of lipiodol to cyanoacrylate has been explored as a useful strategy to decrease the risk of embolisation.8,10 Irisawa et al. found that diluting the cyanoacrylate solution to less than 40% increased the likelihood of such migration; the researchers suggested that a concentration of at least 62.5% be used in treating gastric fundal varices larger than 12 mm in diameter.17 However, it remains difficult to prevent some migration of the glue beyond the bleeding varix.

Pulmonary glue emboli can cause an extremely wide spectrum of clinical presentations, ranging from
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An unusual complication following endoscopic sclerotherapy for gastric varices

... asymptomatic patients to those with dyspnoea, pleuritic chest pain, coughing, tachycardia, hypoxia and cardiorespiratory arrest or sudden death. In symptomatic patients, it is important to note that the timing of the onset of respiratory symptoms is highly variable, ranging from a few minutes to hours after the cyanoacrylate injection. A chest radiograph or non-contrast CT scan usually helps to establish the diagnosis. However, the presence of hyperdense cyanoacrylate glue emboli may be masked by the intravenous contrast medium in CT pulmonary angiography, potentially resulting in a misdiagnosis. It has been observed that imaging findings do not correlate well with the clinical condition of patients and that the radiographic features of glue emboli can persist despite evidence of clinical improvement.

The management of patients with pulmonary glue emboli is mainly supportive and there is usually no need for thrombolysis or anticoagulative measures. For most symptomatic patients who survive, the embolic consequences and clinical symptoms of the condition seem to resolve with time, although the precise mechanism by which this occurs is not yet fully understood. Apart from pulmonary emboli, other adverse effects of a glue injection include splenic infarctions, thrombosis of the portal and splenic veins and persistent sepsis due to the embolism. More commonly, complications associated with cyanoacrylate injections include transient pain, fever, incomplete obliteration of the varix and tissue necrosis around the injection site leading to deep ulceration, early rebleeding and occasional perforation.

Conclusion
A pulmonary glue embolism should be suspected among patients who develop acute respiratory distress syndrome following endoscopic sclerotherapy. In the current case, the cause of the pulmonary glue embolism was likely a combination of the large size of the gastric varices and the large volume of cyanoacrylate needed to treat them.

References