

# Pulmonary Glue Embolism

## An unusual complication following endoscopic sclerotherapy for gastric varices

\*Philips G. Michael,<sup>1</sup> Georgios Antoniadis,<sup>1</sup> Anca Staicu,<sup>2</sup> Shahid Seedat<sup>1</sup>

### السدة الصمغية الرئوية

مضاعفة غير عادية بعد العلاج التصليبي بالمنظار لدوالي المعدة

فيليبس جورج مايكل، جورجوس أنطونياديس، أنكا ستايكو، شاهد سيدات

**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.

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

**المخلص:** السدة الصمغية الرئوية هو مضاعفة غير عادي وقد تكون مميتة بعد علاج نزيف الدوالي، خاصة عند المرضى الذين يعانون من دوالي كبيرة تتطلب كميات كبيرة من المتصلب. وتشمل العوامل المساهمة الأخرى لحدوث السدة معدل الحقن ونسبة المكونات المكونة للمادة المتصلبة (أي-ن-بيوتيل-سيانوأكريليت والليبودولول). قد ترتبط هذه الحالة بحدوث قصور متأخر في التنفس ولذلك، فإن درجة عالية من اليقظة السريرية أمر ضروري للتشخيص المبكر وبخاصة في المرضى الذين يحدث لهم هبوط غير مبررة في وظائف الجهاز التنفسي و القلب أثناء أو بعد العلاج التصليبي بالمنظار. هذا تقرير حالة لرجل يبلغ من العمر 65 عامًا تم إدخاله إلى مستشفى هال الملكي، هال، المملكة المتحدة، في عام 2017 بسبب القيء واسوداد لون البراز. وفي وقت لاحق تطورت حالته مع حدوث متلازمة الضائقة التنفسية الحادة الثانوية نتيجة للسدة الرئوية بعد العلاج التصليبي الطارئ بالمنظار لأيقاف نزيف دوالي المعدة. كان المسببات المرضية المحتملة للانسداد هي مزيج من الحجم الكبير للدوالي المعدية والحجم الكبير من مادة السيانوأكريلات المستخدمة. بعد إجراء المنظار والعلاج، ظل المريض بدون أعراض خلال فترة متابعة لمدة ستة أشهر.

**الكلمات المفتاحية:** دوالي المعدة؛ السدة الرئوية؛ العلاج التصليبي؛ أي-ن-بيوتيل-سيانوأكريليت؛ الليبودولول؛ تقرير حالة؛ المملكة المتحدة.

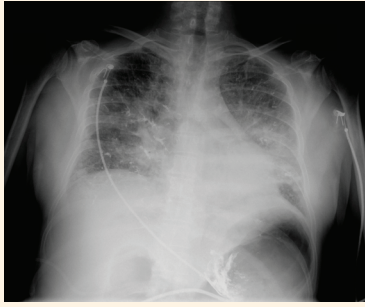
**A**LTHOUGH RARE, PULMONARY GLUE EMBOLI are potentially life-threatening complications which can arise following endoscopic sclerotherapy for the treatment of variceal bleeding.<sup>1</sup> Large volumes, the rate of injection and the ratio of components (i.e. the proportion of n-butyl-cyanoacrylate to lipiodol) of the sclerosant are thought to contribute to the condition.<sup>1,2</sup> Pulmonary glue emboli may be associated with delayed-onset respiratory compromise and may be overlooked in asymptomatic or mildly symptomatic patients.<sup>1,2</sup> 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.

## Case Report

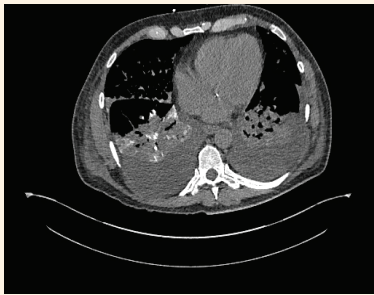
A 65-year-old man was admitted to the Accident & Emergency Department of the Hull Royal Infirmary, Hull, UK, in 2017 with a two-day history of coffee-coloured vomiting and *melaena*. He was known to have Child-Pugh class C liver cirrhosis secondary to alcoholic liver disease, type 2 diabetes mellitus and hypertension. Upon admission, the patient was hypotensive, tachycardic, icteric and encephalopathic. A physical examination revealed a distended abdomen due to *ascites* and moderate splenomegaly. A thoracic examination was unremarkable and no significant abnormalities were identified on a chest radiograph. Laboratory tests revealed haemoglobin levels of 6 g/L, white cell count of 14.9 x 10<sup>9</sup>/L, a prolonged pro-

<sup>1</sup>Department of Radiology, Hull Royal Infirmary, Hull, UK; <sup>2</sup>Department of Gastroenterology, Hull & East Yorkshire Hospitals National Health Service Trust, Hull, UK

\*Corresponding Author's e-mail: drphilipsgm@yahoo.com



**Figure 1:** Chest radiograph of a 65-year-old man following endoscopic sclerotherapy for the treatment of gastric varices showing diffuse infiltrates. Note the subtle radiopaque densities which were identified retrospectively to correlate with glue particles.



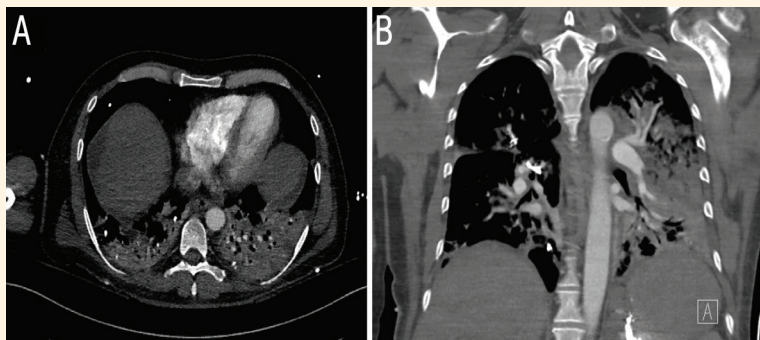
**Figure 2:** Axial computed tomography scan of a 65-year-old man following endoscopic sclerotherapy for the treatment of gastric varices demonstrating bilateral lower lobe consolidation and hyperdense linear structures within the *lumen* and branches of the pulmonary arteries.

thrombin time of 18 seconds, albumin levels of 19 g/L, bilirubin levels of 46  $\mu\text{mol/L}$ , alkaline phosphatase levels of 300  $\mu\text{L}$ , alanine transaminase levels of 194  $\mu\text{L}$ , urea levels of 6.4 mmol/L and creatinine levels of 55  $\mu\text{mol/L}$ .

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.

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.



**Figure 3:** Repeat computed tomography (CT) scans of a 65-year-old man in the (A) axial and (B) coronal views showing persistent hyperdense glue *emboli* following endoscopic sclerotherapy for the treatment of gastric varices.

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.<sup>2,3</sup> Alternative interventions—such as band ligation or transjugular intrahepatic portosystemic shunting—may be considered for the treatment of bleeding from gastro-oesophageal varices.<sup>1,2</sup> According to international recommendations, an injection of glue is the most cost-effective option for cases of uncontrolled gastric variceal bleeding.<sup>3–5</sup> 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.<sup>6,7</sup>

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 gastrosplenic shunt. Migrating glue particles often follow a complex pathway, travelling from the gastric varices through the gastrosplenic and splenorenal veins to the inferior vena cava, right side of the heart and into the pulmonary circulatory system.<sup>8–10</sup> Thus, in most cases, the lungs filter glue *emboli*; however, among patients with atrial septal defects, patent *foramina ovalia* 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.<sup>11</sup> 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.<sup>10–12</sup> The development of high-flow shunts such as the cardiobasilar vein can also carry clots or embolic material from injected varices to the pulmonary circulatory system.<sup>13,14</sup>

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.<sup>10</sup> 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.<sup>10</sup> 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.<sup>10</sup>

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%.<sup>15</sup> 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.<sup>16</sup> 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 gastrosplenic shunts have a higher risk of pulmonary embolism.<sup>11</sup> Similarly, Hwang *et al.* observed that injecting volumes of cyanoacrylate glue over 4.2 mL resulted in an increased risk of pulmonary embolism.<sup>12</sup> 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.<sup>9,10</sup> 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.<sup>17</sup> 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

asymptomatic patients to those with dyspnoea, pleuritic chest pain, coughing, tachycardia, hypoxia and cardiorespiratory arrest or sudden death.<sup>7,9–11,18</sup>

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.<sup>12,18</sup> A chest radiograph or non-contrast CT scan usually helps to establish the diagnosis.<sup>19–21</sup> 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.<sup>20,21</sup>

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.<sup>11–14</sup> 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.<sup>18</sup> 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.<sup>8</sup>

## 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

1. de Freitas Ribeiro BN, Sobral de Magalhães Oliveira AL, Marchiori E. Acute pulmonary embolism following endoscopic glue injection for sclerotherapy. *Arch Bronconeumol* 2016; 52:333. doi: 10.1016/j.arbr.2015.05.016.
2. Mahadeva S, Bellamy MC, Kessel D, Davies MH, Millson CE. Cost-effectiveness of N-butyl-2-cyanoacrylate (histoacryl) glue injections versus transjugular intrahepatic portosystemic shunt in the management of acute gastric variceal bleeding. *Am J Gastroenterol* 2003; 98:2688–93. doi: 10.1111/j.1572-0241.2003.08769.x.

3. Scottish Intercollegiate Guidelines Network. Management of acute upper and lower gastrointestinal bleeding: A national clinical guideline. From: [www.sign.ac.uk/assets/sign105.pdf](http://www.sign.ac.uk/assets/sign105.pdf) Accessed: Jan 2018.
4. de Franchis R; Baveno V Faculty. Revising consensus in portal hypertension: Report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 2010; 53:762–8. doi: 10.1016/j.jhep.2010.06.004.
5. National Institute for Health and Clinical Excellence. Acute upper gastrointestinal bleeding: Management. From: [www.spq.pt/wp-content/uploads/2015/11/2012-NICE-UGIB.pdf](http://www.spq.pt/wp-content/uploads/2015/11/2012-NICE-UGIB.pdf) Accessed: Jan 2018.
6. Singer AD, Fananapazir G, Maufa F, Narra S, Ascher S. Pulmonary embolism following 2-octyl-cyanoacrylate/lipiodol injection for obliteration of gastric varices: An imaging perspective. *J Radiol Case Rep* 2012; 6:17–22. doi: 10.3941/jrcr.v6i2.845.
7. Kazi S, Spanger M, Lubel J. Education and imaging: Gastrointestinal - Pulmonary embolism of cyanoacrylate glue following endoscopic injection of gastric varices. *J Gastroenterol Hepatol* 2012; 27:1874. doi: 10.1111/jgh.12002.
8. Hamad N, Stephens J, Maskell GF, Hussaini SH, Dalton HR. Case report: Thromboembolic and septic complications of migrated cyanoacrylate injected for bleeding gastric varices. *Br J Radiol* 2008; 81:e263–5. doi: 10.1259/bjr/30231294.
9. Ashraf P, Haqqi SA, Shaikh H, Wakani AJ. Glue embolism: A rare cause of pulmonary embolism. *J Coll Physicians Surg Pak* 2011; 21:574–6. doi: 09.2011/JCPSP:574576.
10. Marion-Audibert AM, Schoeffler M, Wallet F, Duperret S, Mabrut JY, Bancel B, et al. Acute fatal pulmonary embolism during cyanoacrylate injection in gastric varices. *Gastroenterol Clin Biol* 2008; 32:926–30. doi: 10.1016/j.gcb.2008.07.009.
11. Alexander S, Korman MG, Sievert W. Cyanoacrylate in the treatment of gastric varices complicated by multiple pulmonary emboli. *Intern Med J* 2006; 36:462–5. doi: 10.1111/j.1445-5994.2006.01086.x.
12. Hwang SS, Kim HH, Park SH, Kim SE, Jung JI, Ahn BY, et al. N-butyl-2-cyanoacrylate pulmonary embolism after endoscopic injection sclerotherapy for gastric variceal bleeding. *J Comput Assist Tomogr* 2001; 25:16–22.
13. Wind P, Alves A, Chevallier JM, Gillot C, Sales JP, Sauvanet A, et al. Anatomy of spontaneous splenorenal and gastrosplenic venous anastomoses: Review of the literature. *Surg Radiol Anat* 1998; 20:129–34. doi: 10.1007/s00276-998-0129-8.
14. Kull E, Hernandez M, Richer JP, Borderie C, Silvain C, Beauchant M. [Severe pulmonary embolism after obturation of gastric varices with a butyl-cyanoacrylate and lipiodol combination]. *Gastroenterol Clin Biol* 1999; 23:1095–6.
15. Saraswat VA, Verma A. Gluing gastric varices in 2012: Lessons learnt over 25 years. *J Clin Exp Hepatol* 2012; 2:55–69. doi: 10.1016/S0973-6883(12)60088-7.
16. Cheng LF, Wang ZQ, Li CZ, Lin W, Yeo AE, Jin B. Low incidence of complications from endoscopic gastric variceal obturation with butyl cyanoacrylate. *Clin Gastroenterol Hepatol* 2010; 8:760–6. doi: 10.1016/j.cgh.2010.05.019.
17. Irisawa A, Obara K, Sato Y, Saito A, Orikasa H, Ohira H, et al. Adherence of cyanoacrylate which leaked from gastric varices to the left renal vein during endoscopic injection sclerotherapy: A histopathologic study. *Endoscopy* 2000; 32:804–6. doi: 10.1055/s-2000-7702.
18. Chew JR, Balan A, Griffiths W, Herre J. Delayed onset pulmonary glue emboli in a ventilated patient: A rare complication following endoscopic cyanoacrylate injection for gastric variceal haemorrhage. *BMJ Case Rep* 2014; 2014:bcr2014206461. doi: 10.1136/bcr-2014-206461.
19. Al-Hillawi L, Wong T, Tritto G, Berry PA. Pitfalls in histoacryl glue injection therapy for oesophageal, gastric and ectopic varices: A review. *World J Gastrointest Surg* 2016; 8:729–34. doi: 10.4240/wjgs.v8.i11.729.

20. Prytuła A, Veereman-Wauters G, Duval EL. Pulmonary embolism due to injection of histoacryl and lipiodol during endoscopic sclerotherapy of fundic varices. *Acta Gastroenterol Belg* 2008; 71:387–9.
21. De Luca D, Piastra M, Pietrini D, Rollo M, Conti G. “Glue lung”: Pulmonary micro-embolism caused by the glue used during interventional radiology. *Arch Dis Child* 2008; 93:263. doi: 10.1136/adc.2007.134445.