



Case Report *Vascular and Interventional Radiology*

Interruption during drug-eluting beads transarterial chemoembolization procedure by presumed allergic shock requires careful follow-up on the development of vascular lake phenomenon

Akihiro Ogawa¹, Yuki Wada¹, Katsunori Iijima², Naoko Mori¹

¹Department of Radiology, Akita University Graduate School of Medicine, ²Division of Gastroenterology, Hepato-biliary-pancreatology and Neurology, Akita University Graduate School of Medicine, Akita, Japan.



***Corresponding author:**

Naoko Mori,
Department of Radiology, Akita
University Graduate School of
Medicine, Akita, Japan.

naokomori7127@gmail.com

Received: 26 April 2024

Accepted: 21 June 2024

Published: 31 July 2024

DOI

10.25259/JCIS_47_2024

Quick Response Code:



ABSTRACT

We present a case involving a 60-year-old male with multifocal hepatocellular carcinoma (HCC), emphasizing the critical need for vigilant post-procedural monitoring following the interruption of drug-eluting beads transarterial chemoembolization (DEB-TACE) due to an allergic reaction. The patient, who had a history of various treatments for HCC, underwent DEB-TACE. During the procedure, he experienced an anaphylactic shock, presumably due to an allergy to the treatment components (iodinated contrast agent), resulting in the procedure's discontinuation. Initially stable, the patient was later found to have intra-abdominal bleeding, a complication associated with the vascular lake phenomenon (VLP), detected on post-procedural imaging. Re-embolization using gelatin particles was performed to address the VLP. It remains unclear whether the shock experienced during the DEB-TACE procedure was due to the allergic reaction or the rupture of the VLP. This case underscores the complexities in managing DEB-TACE, the necessity of careful monitoring for VLP, and the challenges in diagnosing and managing allergic reactions during such procedures. In conclusion, it is crucial to consider that VLP can occur at any time during or after DEB-TACE. Assessing the presence of VLP using digital subtraction angiography before the termination of the procedure is essential. However, when an allergy to the iodinated contrast agent is suspected, as in this case, careful follow-up with abdominal ultrasound and computed tomography might be necessary to assess the presence of intra-abdominal hemorrhage associated with VLP.

Keywords: Vascular lake phenomenon, Drug-eluting beads transarterial chemoembolization, Hepatocellular carcinoma, Shock

INTRODUCTION

The vascular lake phenomenon (VLP) is one of the adverse events observed during drug-eluting beads transarterial chemoembolization (DEB-TACE) for hepatocellular carcinoma (HCC). VLP may result from the rupture of fragile vessels within the tumor and can occur at any point during the DEB-TACE procedure or even up to 1 month afterward. The reported frequency of VLP varies in the literature, ranging from approximately 12–32%.^[1-4] Several studies have indicated better treatment outcomes for HCC in patients experiencing VLP compared to those who do not.^[1-3] We present a case in which a DEB-TACE procedure was interrupted due to a presumed allergic shock. Subsequent imaging in the next day revealed intra-abdominal bleeding,

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2024 Published by Scientific Scholar on behalf of Journal of Clinical Imaging Science

which was considered to be caused by VLP and required re-embolization.

CASE REPORT

A male patient in his 60s, who tested positive for hepatitis C virus antibodies, was admitted to our hospital for treatment of HCCs. He has previously undergone 13 treatments for HCCs: 10 times conventional transarterial chemoembolization (c-TACE), once DEB-TACE, and twice transhepatic arterial infusion chemotherapy. On admission, his hematological examination results were as follows: Hemoglobin (HG) 13.1 g/dL, blood urea nitrogen 14.9 mg/dL, creatinine 0.78 mg/dL, total bilirubin 3.6 mg/dL, albumin 2.7 g/dL, prothrombin time 10.3 s, and prothrombin time international normalized ratio 0.95. Encephalopathy was negative, ascites was positive, and the patient's Child-Pugh Score was assessed as C. Dynamic contrast-enhanced computed tomography (DCE-CT) showed multifocal tumors in the right and left lobes of the liver with contrast enhancement in the arterial phase and wash-out in the portal venous phase, indicating multifocal HCCs [Figure 1]. Notably, a tumor (suspicious of HCC) protruded prominently outside the liver in segment 8 (S8).

Based on these imaging findings and the patient's hepatic function, we decided to perform DEB-TACE only on the right hepatic artery. DEB-TACE was performed under sterile conditions and under local anesthesia, through the right femoral artery using a 4-Fr sheath (Medikit, Tokyo, Japan) and in a retrograde fashion. A 4F catheter was selectively inserted into the superior mesenteric and celiac trunks to outline the anatomy of the hepatic artery, identify the tumor's feeding artery, and assess portal vein patency with iodinated contrast agent (Iohexol (Fuji Pharma Co., Ltd., Tokyo, Japan)). The celiac arterial angiography revealed multifocal tumor stains in right and left lobes of the liver [Figure 2].

A microcatheter was inserted into the tumor's feeding artery using a super-selective catheterization technique. A solution

impregnated with HepaSphere Bead (50–100 μm) (Merit Medical, Tokyo, Japan) 25 mg and cisplatin powder (IACALL[®] [Nippon Kayaku, Tokyo, Japan]) 25 mg was administered through the tumor's feeding artery from the right hepatic artery to perform DEB-TACE. However, during infusion, the patient experienced abdominal pain and sneezed repeatedly at the time of infusion of 17.5 mg of IACALL. The patient's blood pressure dropped to the 60-mmHg, indicating shock and fluid boluses rehydration was administered. The patient's blood oxygen saturation dropped to 91%, and oxygen was administered through a nasal cannula at 2 L/min. Despite these treatments, the patient's condition did not improve, and he began to complain of pharyngeal discomfort. It was determined that the patient was experiencing an allergic reaction, and he was administered a glycyrrhizin-glycine-cysteine solid combination 20 mg, etilefrine 10 mg, and hydrocortisone 200 mg each. After this treatment, the patient's blood pressure recovered to the 80–90 mmHg range. Further, DEB-TACE treatment was ruled out, and the procedure was terminated. The patient's vital signs in the ward that evening were stable. The next day, a hematological examination revealed anemia with HG 10.7 g/dL compared to the pre-procedural HG 13.1 g/dL. An abdominal ultrasound revealed increased ascites fluid with high echogenicity, which seemed to be hemogenous. Pre-contrast images of DCE-CT showed a high-density area on the dorsal part of the previously identified S8 protruding HCC, presumed to be a hematoma [Figure 3a]. In addition, a speckled enhancement that seemed to be VLP was observed within the hematoma in the arterial phase of DCE-CT [Figure 3b]. Based on these imaging findings, we considered that this intra-abdominal hemorrhage was related to VLP and its rupture into the abdominal cavity. The patient, then, underwent re-embolization by transcatheter angiography using Iopamidol (Hikari Pharmaceutical Co., Ltd., Tokyo, Japan) as the contrast agent. Since it could not be completely ruled out that the shock during DEB-TACE was caused by the iodinated contrast agent (Iohexol),

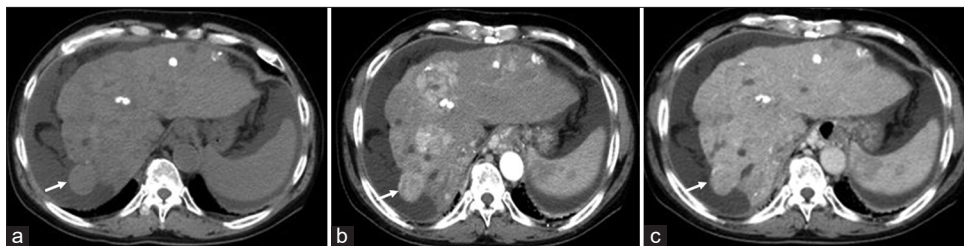


Figure 1: A 60s male patient with multifocal hepatocellular carcinoma (HCC) who was admitted to our hospital for treatment of HCCs. Abdominal dynamic contrast-enhanced computed tomography was performed before the drug-eluting beads transarterial chemoembolization (DEB-TACE). (a) The pre-contrast image shows multifocal low-density tumors suggestive of HCCs in the right and left lobes of the liver (white arrows). (b) The arterial phase shows contrast enhancement of the tumors, one of which protruded prominently outside the liver in segment 8 (white arrows). (c) The portal venous phase shows washout compared to the arterial phase (white arrows).

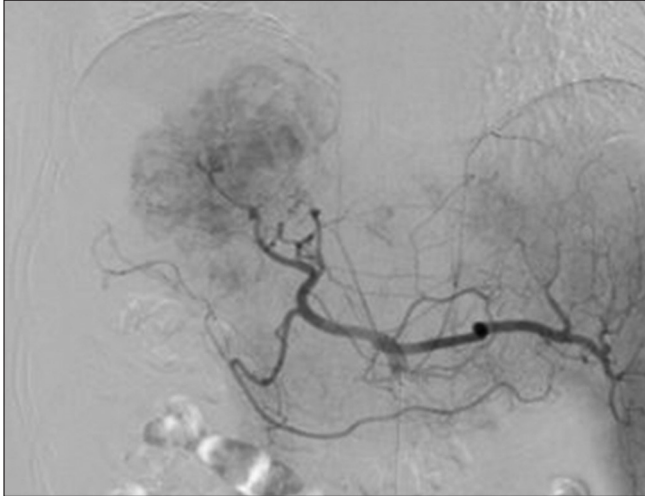


Figure 2: Digital subtraction angiography from the celiac arterial angiography during the drug-eluting beads transarterial chemoembolization. Multiple tumor stains in the right and left lobes of the liver are found.

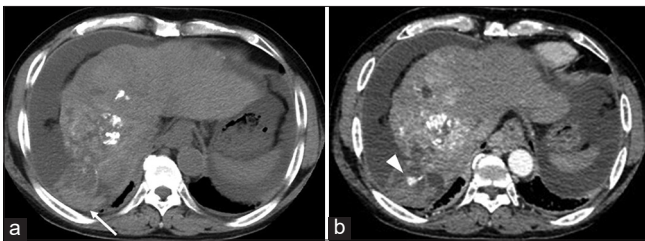


Figure 3: Dynamic contrast-enhanced computed tomography (DCE-CT) performed the next day of the drug-eluting beads transarterial chemoembolization procedure. (a) Pre-contrast images showed a high-density area on the dorsal part of the previously identified segment 8 protruding hepatocellular carcinoma, presumed to be a hematoma (white arrow). (b) A speckled enhancement that seemed to be vascular lake phenomenon was observed within the hematoma in the arterial phase of DCE-CT (white arrowhead).

iodipamidol was selected as the contrast agent for the second procedure. Injection of contrast agent from the anterior segment branch of the right hepatic artery revealed multiple tumor stains in the right lobe, including a tumor protruding from the surface of the S8, which was considered to be the source of the hemorrhage [Figure 4a]. The delayed phase of the angiography revealed extravasation from the surface of the S8 to the abdominal cavity, which was diagnosed as VLP in concordance with the DCE-CT [Figure 4b]. Then, 2 mm porous gelatin particles (Gel-part [Nippon Kayaku, Tokyo, Japan]) dissolved in diluted iodinated contrast agent were injected under fluoroscopic guidance until the blood flow of the anterior segment branch stopped. Finally, the disappearance of tumor stain and extravasation in S8 was confirmed by digital subtraction angiography (DSA) [Figure 4c]. No significant adverse events or complications were

observed during this second procedure.

DISCUSSION

DEB-TACE is a method of embolizing feeding arteries of tumors with beads impregnated with anticancer drugs. It has been in clinical use worldwide since 2004 and has been approved for use in our hospital since 2015. During DEB-TACE, a localized accumulation of contrast agent, similar to extravasation within the tumor, is occasionally observed. This angiographic finding is known as the VLP or pooling phenomenon.^[2,3,5,6] Seki *et al.* hypothesized that the pressure gradient of neovascular vessels within the tumor is associated with the formation of VLPs. There are multiple neovascular vessels with pressure gradients in HCC. The beads used in DEB-TACE first embolize large vessels, thereby increasing the pressure in relatively fine and vulnerable vessels. When a certain constant pressure is exceeded in these vessels, they collapse and form a VLP.^[2] Recent studies have compared treatment outcomes between groups with and without VLP in DEB-TACE and have shown better treatment responses of HCCs in the group with VLP than in the group without VLP.^[1-3] Initially, the rupture of a VLP required re-embolization of the feeding vessels, potentially improving the treatment response. However, the presence of VLP has been reported to be independently associated with a favorable treatment response with or without additional embolization.^[1-3] The previous studies reported that VLP occurs during the DEB-TACE procedure, and even as late as approximately 1 month after the procedure, and the occurrence of VLP should be carefully monitored, especially when incomplete embolization was performed in DEB-TACE.^[7,8]

The cause and management of the shock that occurred during the DEB-TACE in this patient warrant discussion. It is unclear whether the shock during the DEB-TACE procedure was due to an allergy or the rupture of the VLP. It is also unclear whether these two situations result from each other or are coincidental. This represents the most fundamental and crucial limitation of our case report. Although the VLP was identified and re-embolized the day after DEB-TACE, the exact time of VLP onset was unknown. The patient complained of pharyngeal discomfort and sneezing, and treating this patient's reaction as an allergy would be reasonable. We carefully followed up with the patient the next day after DEB-TACE with an abdominal ultrasound and computed tomography (CT) to assess for the presence of a hematoma.

The possible causes of allergy in this case were iodinated contrast agents, cisplatin (IACALL), and beads. The iodinated contrast agents are the most well-known cause of allergy; however, they occur rarely (0.5–3% of patients).^[9] The common symptoms of allergy to the iodinated contrast agents include anaphylaxis, urticaria, angioedema, and in

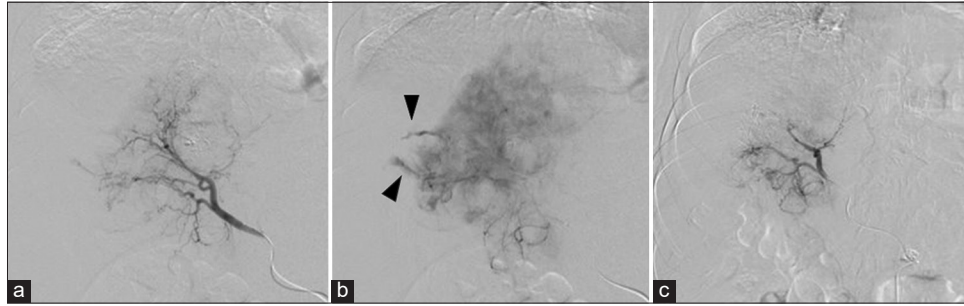


Figure 4: Digital subtraction angiography (DSA) from the anterior segment branch of the right hepatic artery. (a) Multiple tumor stains in the right lobe are observed in the early phase. (b) The delayed phase of the angiography revealed an extravasation from the surface of the segment 8 (S8) to the abdominal cavity (black arrowheads), which was diagnosed as vascular lake phenomenon. (c) Embolization using 2 mm porous gelatin particles were performed and the disappearance of tumor stain and extravasation in S8 was confirmed by DSA.

some cases, gastrointestinal symptoms (such as diarrhea and vomiting), respiratory symptoms (such as dyspnea and bronchospasm), and hypotension that may lead to shock.^[10-12] In this case, the symptoms during the DEB-TACE procedure were consistent with an allergy to the iodinated contrast agents. The frequency of allergic reactions to cisplatin and beads was unknown based on our search. When performing the angiography for patients suspected of having allergies to the iodinated contrast agents, carbon dioxide (CO₂) can be used as a contrast agent, which is only technically available in a limited number of facilities.^[13-15] However, switching to CO₂ angiography may be challenging if an allergy to iodinated contrast agents is suspected during DEB-TACE.

The effectiveness of DEB-TACE in treating tumors has shown inconsistent results in different studies. Some studies found no significant difference in treatment response between c-TACE and DEB-TACE,^[16-18] while others reported better treatment response with DEB-TACE than c-TACE.^[1,17,19] Recently, Ikeda *et al.* showed that cTACE had higher complete response rates for local tumor control as compared to DEB-TACE in the randomized controlled study.^[20] Similarly, the results regarding liver toxicity after embolization are inconsistent. Some studies reported DEB-TACE to have lower liver toxicity than c-TACE,^[18,21] while others found them to be equivalent.^[22] Ikeda *et al.* also reported a significantly higher frequency of post-embolization syndrome in cTACE compared to DEB-TACE.^[20] For patients prioritizing patience with post-embolization syndrome over treatment response, DEB-TACE may be preferred to cTACE. Transarterial chemoembolization (TACE) is generally recommended for patients with four or more tumors, Child-Pugh classification A or B, and the Barcelona Clinic Liver Cancer staging system B with performance status 0.^[23] However, in this case, TACE was not an absolute indication because the Child-Pugh Score was C. Despite this, DEB-TACE, known for its lower liver toxicity, was selected.^[18,21] In addition, considering the patient's liver function, embolization was performed only for the right hepatic artery.

CONCLUSION

We should always be aware that VLP can occur at any time during or after DEB-TACE. It is essential to assess the presence of VLP by DSA before the termination of procedure. In cases where there is a suspected allergy to iodinated contrast agents, careful follow-up with abdominal ultrasound and computed tomography (CT) might be necessary to assess the presence of intra-abdominal hemorrhage associated with VLP.

Ethical approval

The research/study was approved by the Institutional Review Board at Akita University Graduate School of Medicine, number 2986, dated May 26, 2023.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Kong J, Jiang X, Zhang Y, Wang W, Li Y, Shen X, *et al.* Clinical management of vascular lake during transarterial chemoembolization with Calli-Spheres drug-eluting beads (DEBs) for the treatment of hepatocellular carcinoma. *Transl Cancer Res TCR* 2020;9:2895-903.
2. Seki A, Hori S, Shimono C. Management of vascular lake phenomenon on angiography during chemoembolization with superabsorbent polymer microspheres. *Jpn J Radiol* 2015;33:741-8.
3. Cavalcante RN, Nasser F, Motta-Leal-Filho JM, Affonso BB, Galastri FL, De Fina B, *et al.* Occurrence of vascular lake phenomenon as a predictor of improved tumor response in HCC patients that underwent DEB-TACE. *Cardiovasc Intervent Radiol* 2017;40:1044-51.
4. Li H, Wang M, Chen P, Li F, Kuang D, Han X, *et al.* Occurrence, related factors and prognostic value of vascular lake in hepatocellular carcinoma patients treated with drug-eluting bead transarterial chemoembolization. *Onco Targets Ther* 2021;14:4659-70.
5. Osuga K, Hori S, Hiraishi K, Sugiura T, Hata Y, Higashihara H, *et al.* Bland embolization of hepatocellular carcinoma using superabsorbent polymer microspheres. *Cardiovasc Intervent Radiol* 2008;31:1108-16.
6. Seki A, Hori S, Kobayashi K, Narumiya S. Transcatheter arterial chemoembolization with epirubicin-loaded superabsorbent polymer microspheres for 135 hepatocellular carcinoma patients: Single-center experience. *Cardiovasc Intervent Radiol* 2011;34:557-65.
7. Shiozawa K, Watanabe M, Ikehara T, Ogino Y, Umakoshi T, Matsukiyo Y, *et al.* Delayed intratumoral hemorrhage after drug-eluting bead transarterial chemoembolization for hepatocellular carcinoma. *Case Rep Oncol* 2014;7:739-45.
8. Ritter CO, Wartenberg M, Mottok A, Steger U, Goltz JP, Hahn D, *et al.* Spontaneous liver rupture after treatment with drug-eluting beads. *Cardiovasc Intervent Radiol* 2012;35:198-202.
9. Brockow K, Christiansen C, Kanny G, Clément O, Barbaud A, Bircher A, *et al.* Management of hypersensitivity reactions to iodinated contrast media. *Allergy* 2005;60:150-8.
10. Torres MJ, Trautmann A, Böhm I, Scherer K, Barbaud A, Bavbek S, *et al.* Practice parameters for diagnosing and managing iodinated contrast media hypersensitivity. *Allergy* 2021;76:1325-39.
11. Brockow K, Romano A, Aberer W, Bircher AJ, Barbaud A, Bonadonna P, *et al.* Skin testing in patients with hypersensitivity reactions to iodinated contrast media - a European multicenter study. *Allergy* 2009;64:234-41.
12. Böhm I, Heverhagen JT, Klose KJ. Classification of acute and delayed contrast media-induced reactions: Proposal of a three-step system. *Contrast Media Mol Imaging* 2012;7:537-41.
13. Caridi JG, Stavropoulos SW, Hawkins IF. Carbon dioxide digital subtraction angiography for renal artery stent placement. *J Vasc Interv Radiol* 1999;10:635-40.
14. Krasny R, Hollmann JP, Günther RW. Initial experiences with CO₂ as a gaseous contrast medium in digital subtraction angiography. *Rofo* 1987;146:450-4.
15. Young M, Mohan J. Carbon dioxide angiography. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2023. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK534244> [Last accessed on 2023 Dec 29].
16. Chang Y, Jeong SW, Jang JY, Kim YJ. Recent updates of transarterial chemoembolization in hepatocellular carcinoma. *Int J Mol Sci* 2020;21:8165.
17. Golfieri R, Giampalma E, Renzulli M, Cioni R, Bargellini I, Bartolozzi C, *et al.* Randomised controlled trial of doxorubicin-eluting beads vs conventional chemoembolisation for hepatocellular carcinoma. *Br J Cancer* 2014;111:255-64.
18. Bzeizi KI, Arabi M, Jamshidi N, Albenmoussa A, Sanai FM, Al-Hamoudi W, *et al.* Conventional transarterial chemoembolization versus drug-eluting beads in patients with hepatocellular carcinoma: A systematic review and meta-analysis. *Cancers (Basel)* 2021;13:6172.
19. Bargellini I, Lorenzoni V, Lorenzoni G, Scalise P, Andreozzi G, Bozzi E, *et al.* Duration of response after DEB-TACE compared to lipiodol-TACE in HCC-naïve patients: A propensity score matching analysis. *Eur Radiol* 2021;31:7512-22.
20. Ikeda M, Arai Y, Inaba Y, Tanaka T, Sugawara S, Kodama Y, *et al.* Conventional or drug-eluting beads? randomized controlled study of chemoembolization for hepatocellular carcinoma: JIVROSG-1302. *Liver Cancer* 2022;11:440-50.
21. Arabi M, BenMoussa A, Bzeizi K, Garad F, Ahmed I, Al-Otaibi M. Doxorubicin-loaded drug-eluting beads versus conventional transarterial chemoembolization for nonresectable hepatocellular carcinoma. *Saudi J Gastroenterol* 2015;21:175-80.
22. Zhang ZS, Li HZ, Ma C, Xiao YD. Conventional versus drug-eluting beads chemoembolization for infiltrative hepatocellular carcinoma: A comparison of efficacy and safety. *BMC Cancer* 2019;19:1162.
23. Bruix J, Sherman M. Management of hepatocellular carcinoma: An update. *Hepatology* 2011;53:1020-2.

How to cite this article: Ogawa A, Wada Y, Iijima K, Mori N. Interruption during drug-eluting beads transarterial chemoembolization procedure by presumed allergic shock requires careful follow-up on the development of vascular lake phenomenon. *J Clin Imaging Sci.* 2024;14:27. doi: 10.25259/JCIS_47_2024