

Retiform Purpura After Transcatheter Arterial Chemoembolization: A Case Report

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CASE PRESENTATION

A 66-year-old man with chronic hepatitis C and newly diagnosed HCC presented for a conventional TACE procedure and workup for Yttrium-90 (Y-90) radioembolization. Previous imaging had shown a 10.8-cm mass consistent with HCC in the right dome of the liver on magnetic resonance imaging. Laboratory values obtained previously were as follows: aspartate aminotransferase 100 U/L, alanine aminotransferase 30 U/L, alkaline phosphatase 120 U/L, total bilirubin 0.7 mg/dL, and alpha-fetoprotein tumor marker 56,662 ng/mL. Two vials of 100u Embozene microspheres were injected into the right inferior phrenic artery for embolization. Angiography after embolization demonstrated decreased perfusion to the tumor blush but preserved perfusion in branches of the right inferior phrenic artery. This was followed by the administration of a dose of Tc-99m labeled macroaggregated albumin into the posterior division of the patient's right hepatic artery. The procedure was completed without any immediate complications.

Abstract: Cutaneous complications secondary to transcatheter arterial chemoembolization (TACE) are exceptionally rare and may occur because of nontarget embolization of terminal vessels supplying the skin. We present a patient who developed painful retiform purpura on the right flank shortly after TACE for treatment of hepatocellular carcinoma. Biopsy revealed intravascular tan to yellow amorphous spherical structures within the dermis, confirming the presence of foreign material within these vessels. The authors review the literature and discuss previous cases of skin lesions manifesting after TACE, as well as potential factors influencing the probability of cutaneous complications. Histopathologic findings described in similar cases are presented. Prophylactic measures and attempted treatments to reduce likelihood of long-term injury are also reviewed. An awareness that cutaneous injury is a rare, but potential complication of transcatheter arterial embolization, as well as an understanding of management options is important for any provider using this procedure.

Key Words: retiform purpura, transcatheter arterial chemoembolization, cutaneous complication

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INTRODUCTION

Transcatheter arterial chemoembolization (TACE) and more recent incorporation of transcatheter arterial radioembolization (TARE) are currently standards of treatment for unresectable hepatocellular carcinoma (HCC). Transcatheter arterial chemoembolization (TACE) and more recent incorporation of radioembolization (TARE) are currently standards of treatment for unresectable hepatocellular carcinoma (HCC).¹ This minimally invasive approach has been shown to be effective and is associated with far fewer complications than invasive surgery.² However, adverse outcomes secondary to arterial embolization are well documented, including hepatic, biliary, gastrointestinal, and pulmonary injury.^{3,4} Rare cutaneous complications after TACE have also been reported. We present a patient who developed retiform purpura on the flank shortly after chemoembolization, with subsequent discovery of intravascular foreign material on histopathologic examination.

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FIGURE 1. Retiform purpura on the right flank of the patient a few hours after the procedure.

Within hours after the procedure, he developed increasing pain in the right flank, followed by the subsequent appearance of a rash on the skin localized over the area of pain. The patient had a previous episode of idiopathic thrombocytopenic purpura and a history of acute myeloid leukemia in remission but had no history of blood clotting. His pain worsened over the next several hours and dermatology was consulted. On examination, he exhibited a large, well-defined area of reticulate erythema and retiform purpura on the right flank (Fig. 1). Two 8-mm punch biopsies were taken from white zones interspersed within the reticulate erythema of the patient's right upper and lower flank.

Microscopic analysis of each specimen revealed sparse perivascular infiltrate of lymphocytes, with the lower flank specimen exhibiting a focally dilated vessel within the mid and deeper dermis containing tan to yellow amorphous spherical structures and associated neutrophils, confirming the presence of intravascular foreign material (Fig. 2).

The patient was admitted for observation and started on pentoxifylline 400 mg 3 times daily, with petrolatum ointment applied liberally to the areas of skin breakdown and application of a topical ice pack to his flank. The patient was admitted for observation and started on pentoxifylline 400 mg TID, with petrolatum ointment applied liberally to the areas of skin breakdown and application of a topical ice pack to his flank. In addition, hematology was consulted for additional therapeutic options, such as warfarin. They ultimately recommended that he not begin systemic anticoagulation. In addition, hematology was consulted and recommended that he not begin systemic anticoagulation. His pain gradually improved over the next several hours and was discharged the following day with recommended follow-up for wound care. Our patient reported a persistent but improving deep flank pain at 3 months and exhibited signs of ongoing healing of his skin necrosis.

DISCUSSION

TACE has represented a minimally invasive treatment option for advanced HCC for several decades and involves catheterization of the right or left hepatic arteries followed

by injection of microspheres containing a chemotherapeutic drug in addition to an embolizing agent. This method occludes the vascular supply to the tumor and produces a local chemotherapeutic effect.¹ Radioembolization is a more recent alternative, performed by the same method, but containing a radioisotope (eg Y-90) instead of a chemotherapy agent.⁵ Inadvertent embolization of nontarget branches can result in potentially severe complications depending on location, including gastrointestinal ulceration, cholecystitis, pancreatic disease, and pulmonary embolism.³ It has been suggested that portal hypertension leads to the development of portal collateral vessels, which may generally increase the risk of these complications.⁶

Terminal cutaneous branch embolization, though exceptionally rare, has also been reported and can be associated with skin erythema, pruritus, pain, and even necrosis with ulceration.^{4,7} Superficial lesions secondary to TACE have been described most frequently as just superior to the umbilicus through supply from the hepatic falciform artery, a condition termed supraumbilical skin rash.^{6,8–11} Cutaneous complications have been reported after embolization of other extrahepatic collaterals such as the internal mammary artery, intercostal arteries, or the inferior phrenic artery, as seen in our patient.^{12–14} Two chief factors influencing likelihood of skin injury because of transcatheter therapies have been suggested. The first is the size of the occlusion material, with smaller particles exhibiting a higher risk of complete embolization to the area of perfusion. The second is the agent's duration of use; cutaneous injury has been documented with continuous arterial injection of chemotherapeutic medications.⁶

Suspicion for cutaneous vessel embolization after TACE can be greatly aided by the timeline of rash appearance within hours after the procedure, although cases of fixed drug eruption

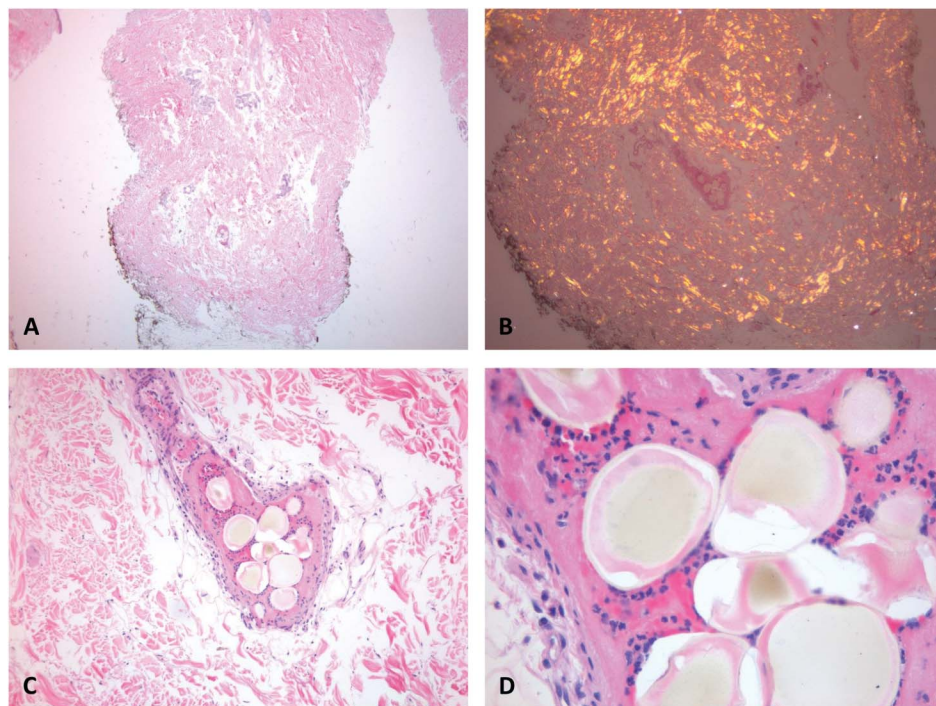


FIGURE 2. Skin biopsy from the right flank showing a focally dilated vessel within the reticular dermis, within which are yellow amorphous spherical structures, and associated neutrophils. A, $\times 12.5$. B, The foreign material does not polarize $\times 25$. C, $\times 50$. D, $\times 400$.

mimicking supraumbilical skin rash have been reported.¹⁵ Regardless of suspicion, biopsy is essential in the workup of any case of retiform purpura presenting in hospitalized patients, as this finding signifies infarction and complete blockage of vascular flow and usually requires intervention.¹⁶ Microscopic evaluation in cases of cutaneous injury after chemoembolization has shown a nonspecific focal eosinophilic necrosis, collagen thickening, and eccrine gland necrosis in the dermis, indicating hypoxic damage. One author likened their histological findings as similar to carbon monoxide poisoning or coma-associated bullae.⁸ Others have also described histology of necrosis and the presence of intraluminal thrombotic material of an arterial vessel in the hypodermis.¹¹

Treatment modalities have thus far been experimental and case based. The ideal approach is to prevent these complications by placing the catheter tip as close as possible to the particular vessel supplying the tumor to avoid nontarget embolization.¹³ Wang et al¹⁷ suggested topical application of ice packs as an additional prophylactic measure to allow vasoconstriction of superficial arterial branches. Steroid injections have also been performed with reportedly quick resolution of rash and pain.⁶ However, application of topical steroids has also been reported to further aggravate skin lesions and result in blistering.¹³ Treatment with pentoxifylline, a vasodilatory drug with antithrombotic effects, has been described with successful reduction in pain and induration, prompting the use of this agent in our patient.⁸ Pentoxifylline is presumed to increase blood flow and tissue oxygenation, and has been shown to alter blood viscosity, inhibit platelet aggregation, and exhibit antifibrinolytic effects.¹⁸

In conclusion, it is important to be aware that cutaneous injury and necrosis are potential sequelae of transarterial embolization for HCC and that measures can be taken to reduce the likelihood of developing such complications.

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