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INTERVENTIONAL RADIOLOGY

TECHNICAL NOTE

Percutaneous thrombin injection under contrast-enhanced ultrasound guidance to control active extravasation not associated with pseudoaneurysm

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ABSTRACT

The technique of percutaneous thrombin injection (PTI) under contrast-enhanced ultrasound (CEUS) guidance for control of acute hemorrhage-active extravasation not associated with pseudoaneurysm is demonstrated in three cases: 1) Massive spontaneous retroperitoneal hematoma in a patient with multiple comorbidities. Contrast-enhanced computed tomography (CT) showed extensive active extravasation, which was only partially controlled by transarterial embolization. CEUS was performed in the angiography suite. Contrary to unenhanced US and colour Doppler US (CDUS), CEUS confirmed persistent extravasation; CEUS-guided PTI was performed immediately thereafter. 2) Large rectus sheath hematoma in a patient on anticoagulant therapy. Contrast-enhanced CT and unenhanced US/CD could not definitely diagnose extravasation. CEUS clearly showed extravasation and was used for guidance of PTI. 3) Chest wall hematoma complicating central venous catheter placement in a patient with coronavirus on anticoagulant therapy. CDUS was inconclusive. CEUS was performed at the bedside, clearly showed active extravasation, and was used for guidance of PTI. In all three cases, post-PTI CEUS confirmed the absence of residual enhancement of the hematomas, and the hemodynamic status of the patients improved. PTI appears to be effective in selected cases of hematomas associated with active extravasation. In this context, CEUS may be the most suitable modality for guidance and for an immediate evaluation of the treatment effect.

KEYWORDS

Percutaneous thrombin injection, contrast-enhanced ultrasound, hematoma, active extravasation

Ultrasound (US)-guided percutaneous thrombin injection (PTI) has been used for the treatment of small aneurysms or pseudoaneurysms in several anatomical locations for more than 25 years;[1,2] however, application of PTI for the treatment of active extravasation not associated with pseudoaneurysm is very limited. Additionally, in these cases, localization of the source of bleeding with unenhanced US or colour Doppler US (CDUS) may often be impossible; this may be due to the relatively slow flow or unfavorable location, size, and morphology of extravasation. In this respect, contrast-enhanced US (CEUS) may be superior to the unenhanced US techniques[3] and could replace them as a guiding tool for selected cases of PTI.

CEUS exploits the properties of ultrasound contrast agents (UCAs), which are suspensions of microbubbles composed of an inert fluorinated gas core encapsulated by a phospholipid shell.[4] When insonated at low acoustic power (low mechanical index), microbubbles undergo non-linear oscillation and produce harmonic signals that can be selectively detected and separated from most background tissue signals. Thanks to the appropriate size of the microbubbles (1–5 µm), UCAs are true blood pool agents and do not diffuse in the extravascular space. With modern CEUS techniques, both intravascular circulation (lasting several minutes) and extravasation of the UCA (after vascular injury) can be detected in real time, with extremely high sensitivity.[3,4]

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This report demonstrates the technique of PTI under CEUS guidance for the control of acute hemorrhage associated with active extravasation in the absence of an aneurysm or pseudoaneurysm.

Technique

Case 1

A 70-year-old male, who was a patient in intensive care, developed sudden tachycardia and a drop in blood pressure. Contrast-enhanced computed tomography (CT) revealed a massive right retroperitoneal hematoma with multiple foci of active extravasation (Figure 1a).

The patient was transferred to the interventional radiology suite. Emergency digital subtraction angiography showed active extravasation from a right lumbar artery, which was successfully embolized with microspheres (Embozene 900, Varian) followed by gelfoam slurry. Unenhanced US and CDUS were performed on site, immediately post-embolization, with a portable US unit and a convex, 2–5 MHz probe (M8 Mindray, Shenzhen, China). These techniques failed to detect persistent extravasation. CEUS was then performed with the same equipment; the CEUS required a bolus intravenous injection of 1.5 mL of echo-enhancer (stabilized microbubbles of sulfur hexafluoride, "SonoVue"; Bracco, Milan, Italy) followed by 5 mL of normal saline. A contrast-specific, low MI (0.06–0.07) algorithm was applied. CEUS revealed two areas of persistent pooling of the echo-enhancer at the central part of the hematoma, fed by a single, T-shaped source of active extravasation (Figure 1b). Additional attempts were made to angiographically locate the source of bleeding, with catheterization of other arteries (right lumbar, iliolumbar, and ascending branches from the right superior gluteal artery), but they were fruitless. Additionally, this part of the intervention required a change of four angiographic catheters, 30 min of fluoroscopy time, 76 min of operation time, and 250 mL of intravenous iodine contrast agent. The patient showed no hemodynamic improvement. Taking into account the indicative CEUS findings and the projected safe route for a percutaneous approach, it was decided to attempt control of the hemorrhage with PTI under CEUS guidance.

Main points

- Percutaneous thrombin injection (PTI) can be an effective treatment for selected cases of active extravasation not associated with aneurysms or pseudoaneurysms.
- Contrast-enhanced ultrasound (CEUS) is a valuable guiding tool for PTI, when the source of hemorrhage cannot be identified with unenhanced US/colour Doppler US.
- With appropriate portable equipment, CEUS-guided PTI can be performed at the bedside and in the angiography suite, in combination with endovascular procedures.
- Availability of CEUS in the angiography suite and familiarization with this technique could improve the outcome of complex emergency interventional radiology procedures.

The patient remained on the angiography table. His right flank was prepared and draped in sterile fashion, and a sterile cover was placed on the convex US probe. CEUS was repeated (using the same protocol as before). A transverse section through the hematoma (clearly showing the most prominent part of the persistent extravasation) was selected. An entry point, just above the upper border of the probe, to facilitate an in-plane needle approach, was identified. A 20 cm long, 22 gauge Chiba needle was percutaneously advanced under continuous US/CEUS imaging ("dual screen" display mode) into the deepest part of the presumed source of the extravasation. Despite the deep location of the target (10 cm from the skin with an 11.5 cm-long trajectory of the needle), it could be reached with the first attempt. A total of 1,500 international units (IU) of human thrombin (approximately 3/4 of the content of the thrombin vial included in the "Surgiflo" kit; Ethicon Inc., Somerville, New Jersey, USA) were injected during slow withdrawal of the needle for 1.5 cm (Figure 1c, Supplementary Video 1). Immediate cessation of extravasation was noticed on CEUS. The needle was left in place for 2 min; it was then carefully removed, with slow injection into the hematoma of an additional 500 IU of thrombin during needle withdrawal.

Case 2

A 75-year-old man on oral anticoagulants presented with a large painful swelling of the right upper abdominal quadrant (after moderate physical effort) and severely deregulated blood coagulation (international normalized ratio: 7.2). Contrast-enhanced CT revealed a large right rectus sheath hematoma but could not definitely diagnose extravasation (Figure 2a). Unenhanced US and CDUS also failed to accurately locate the source of bleeding. However, CEUS (using the same protocol and equipment as in case 1) clearly showed two areas of pooling of the echo enhancer in the superficial part of the hematoma. After an unsuccessful attempt to control the hemorrhage by direct pressure with the transducer, PTI was performed under CEUS guidance. The larger area was triangular, with contrast emerging from its most proximal (superficial) edge and extending deeper. The proximal edge was targeted and PTI was performed (1,000 IU) with immediate cessation of hemorrhage (Figure 2b, c). The smaller area was a round spot, which was targeted at its center and treated successfully with a smaller thrombin dose (500 IU).

Case 3

A 76-year-old female patient with a history of atrial fibrillation on oral anticoagulants

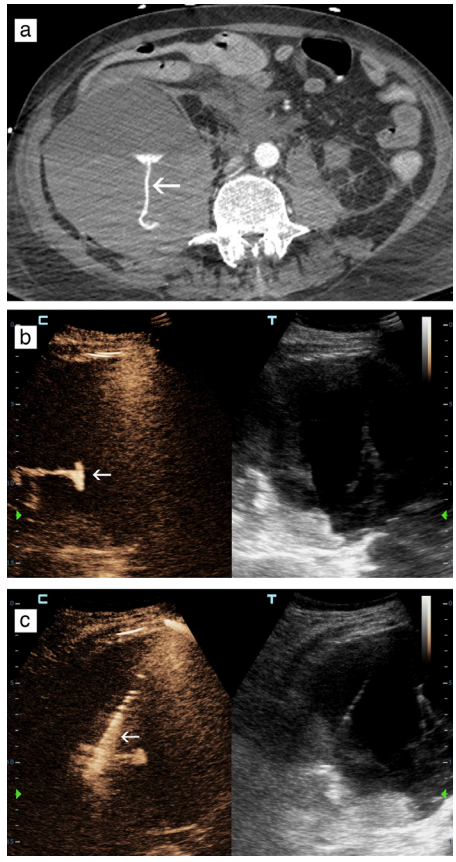

Figure 1. (a-c) Case 1. Axial section of contrast-enhanced CT (arterial phase) pre-intervention: **(a)** shows the large right retroperitoneal hematoma and one of the sites of extravasation (arrow). Sonographic "dual screen" image (unenhanced, reference, gray-scale image on the right; CEUS image on the left) immediately post-transarterial embolization; **(b)** shows a persistent jet of active extravasation (arrow); a close correlation with the CT image is noted. Sonographic image (same configuration as previous image) during PTI; **(c)** shows the Chiba needle, which has reached the proximal part of extravasation, and thrombin injection as linear and punctate echogenicities (arrow). CT, computed tomography; CEUS, contrast-enhanced ultrasound; PTI, percutaneous thrombin injection.

and with coronavirus involving the lungs had a large right chest wall hematoma, which complicated central venous catheter placement. Standard US was performed at the bedside and confirmed the lesion, but CDUS failed to definitely diagnose extravasation. CEUS (also performed at the bedside, using the same protocol and equipment as in the previous cases) clearly showed an ovoid spot of active extravasation. After an unsuccessful attempt to control the hemorrhage by direct pressure with the transducer, PTI (1,000 IU) was performed under CEUS guidance, targeting the center of the lesion.

In all three cases, the hemodynamic status and hematocrit levels of the patients improved after PTI, and follow-up with CEUS one to two days post PTI showed no recurrence of the extravasation. No complications related to PTI were encountered. The patient from Case 1 succumbed to multi-organ failure three days post-PTI, while the other two patients had uneventful recoveries. Additional data for the presented cases are provided in Table 1 and in the Supplementary File.

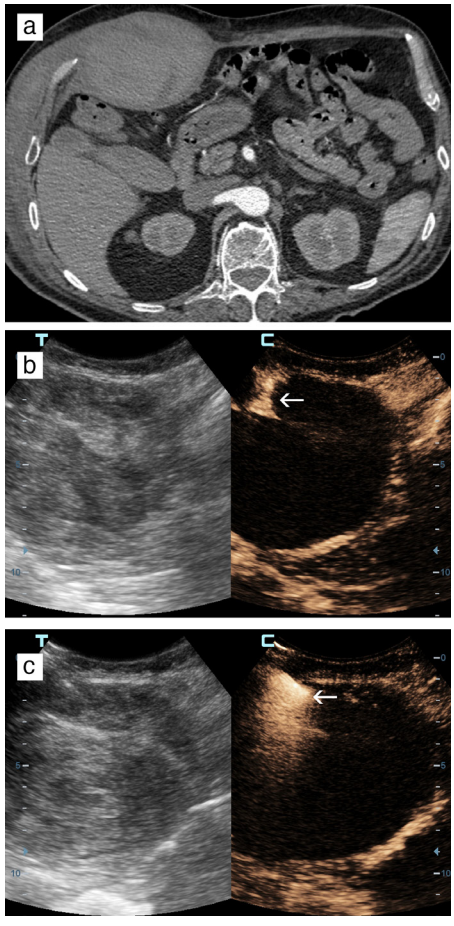

Figure 2. (a-c) Case 2. Axial section of contrast-enhanced CT (arterial phase) pre-intervention: **(a)** shows the right rectus sheath hematoma. No signs of active extravasation. Sonographic "dual screen" image (unenhanced, reference, gray-scale image on the right; CEUS image on the left) pre-intervention; **(b)** shows clearly a triangular-shaped extravasation (arrow). Sonographic image (same configuration as previous image) during PTI; **(c)** shows the Chiba needle, which has reached the proximal part of extravasation, and thrombin injection as linear and punctate echogenicities (arrow). CT, computed tomography; CEUS, contrast-enhanced ultrasound; PTI, percutaneous thrombin injection.

Discussion

As is shown in this report, management of active extravasation with PTI may be more challenging than PTI of pseudoaneurysms, since the former may not be detectable with unenhanced US/CDUS techniques. This emphasizes the role of CEUS, which often is the only sonographic modality that can accurately locate active extravasation and subsequently guide PTI. In an earlier work on CEUS for active abdominal bleeding,[5] two main patterns of leakage of the echo-enhancer were distinguished: the first was a round or oval spot of pooling of the echo-enhancer, and the second a fountain-like hyperechoic jet. The latter was associated with more severe hemorrhage and is very similar to the pattern that prevailed in the first two cases presented in this study. To control this type of extravasation, it was empirically decided to target the most proximal part of the detectable leakage to block the source of extravasation more effectively. This is at variance with a previously reported application of PTI for extravasation post-renal biopsy, where the injection was performed with the needle tip placed 2 mm superficial to the origin of the arterial jet.[6] Nevertheless, the maneuver presented herein proved effective, with complete and immediate cessation of UCA leakage and with no need to cover the entire area of extravasation. In addition, there were no complications. We speculate that, even if this approach to the source of extravasation eventually resulted in intravascular injection of thrombin, it would only occlude minor muscular branches with no clinical consequences. Contrary to the first two cases, the ovoid area of extravasation in the third case resembled the first of the aforementioned patterns ("pooling" instead of "fountain") and was associated with less dramatic hemorrhage. A proximal, narrow source of extravasation could not be clearly identified in this case. It was therefore preferred to target the center of the "pool" and fill it with thrombin.

The availability and portability of CEUS greatly facilitates application of PTI in the emergency setting and in combined interventional radiology (IR) procedures. If CEUS had not been available during the intervention for case 1 and after the inconclusive angiograms, the search for persistent hemorrhage would have required the application of cone-beam CT (CBCT) after bolus intravenous (and perhaps even intra-arterial) iodine contrast injection. Compared to CEUS, CBCT is much more cumbersome, time consuming, and difficult to perform in critically ill patients who are connected to tubes, vascular lines, and monitoring equipment. In case 3, CEUS enabled the operator to control the hemorrhage at the bedside, immediately after diagnosis and with no patient transfer. An additional advantage of US/CEUS as guiding tools for PTI is that they are free from metal artifacts, which appear on CT/CBCT during needle placement. These artifacts may obscure contrast extravasation and interfere with targeting.

In the first case in this report, the deep location of extravasation represented an additional challenge. It should be recognized that

Table 1. Additional data for the presented cases (n = 3)

Case	Hematoma size (mm)	Comorbidities/ predisposing factors	Ht prior to PTI	Shape of dominant extravasation	Additional treatments	Ht 2 days post PTI
1	158 × 88 × 201	Sepsis possible vasculitis (investigation incomplete)	15	T-shaped/ fountain-like	Embolization blood transfusions	22.5
2	114 × 89 × 204	Cardiac surgery acenocoumarol	12.3	Triangular/ fountain-like	Blood transfusions FFP transfusions direct pressure	22.3
3	92 × 43 × 47	Atrial fibrillation rivaroxaban	18.4	Teardrop-/ pool-shaped	Direct pressure blood transfusions	23.4

Ht, hematocrit; PTI, percutaneous thrombin injection; FFP, fresh frozen plasma.

CEUS guidance is more complex than unenhanced US guidance. Good coordination with the injection of the echo-enhancer and some degree of expertise are therefore required to perform CEUS-guided PTI of deeply seated extravasations. It should also be emphasized that CEUS-guided PTI for control of active extravasation has not been tested in large-scale, prospective studies and that its long-term efficacy is not known. Therefore, the approach presented herein should be considered as a rescue technique that should be performed only if embolization (a well-established endovascular treatment for control of hemorrhage) is not feasible.

In conclusion, CEUS-guided PTI appears to be a promising alternative to more complex procedures for the treatment of selected cases of active extravasation, even when this extravasation is not associated with pseudoaneurysms and is undetectable with unenhanced sonographic techniques.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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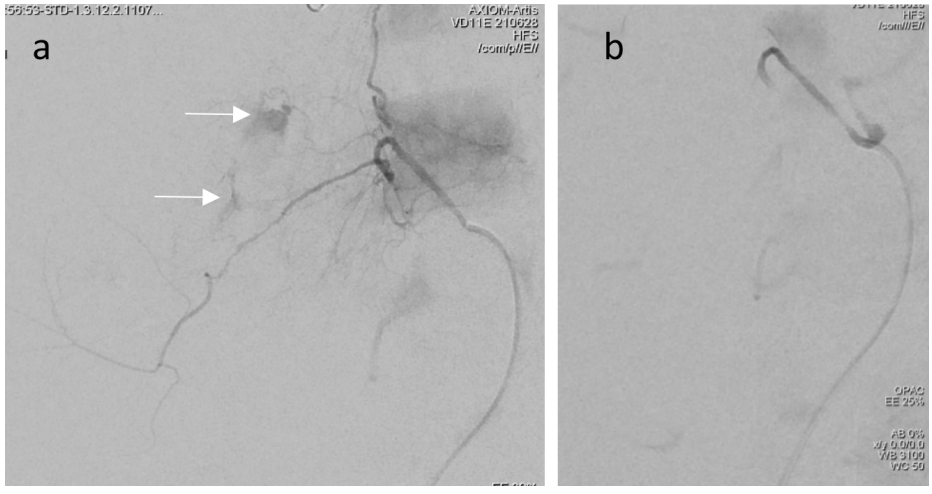
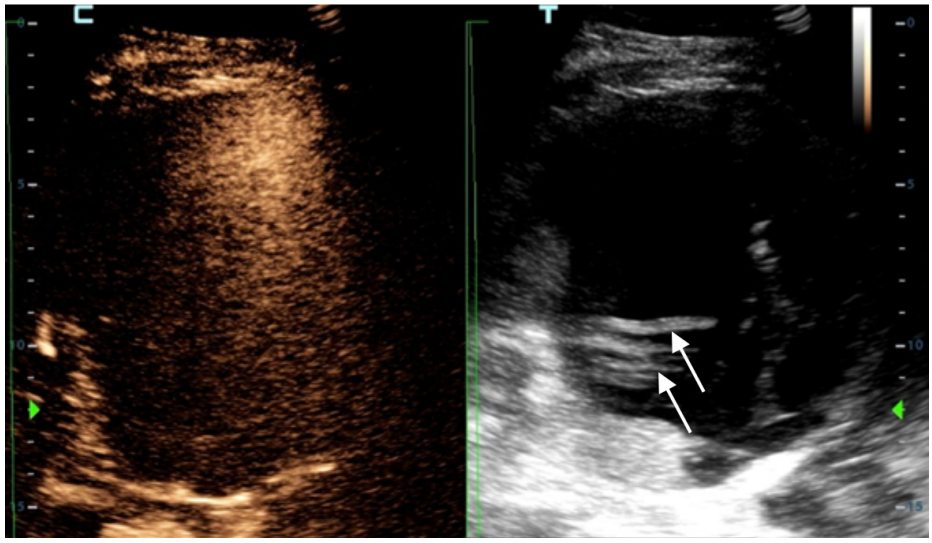
Supplementary Video 1: https://youtu.be/LblHGXn_MTg

Supplementary images for case 1

Coronal maximum intensity projection of contrast-enhanced computed tomography pre-intervention, shows the large right retroperitoneal hematoma and multiple foci of extravasation.

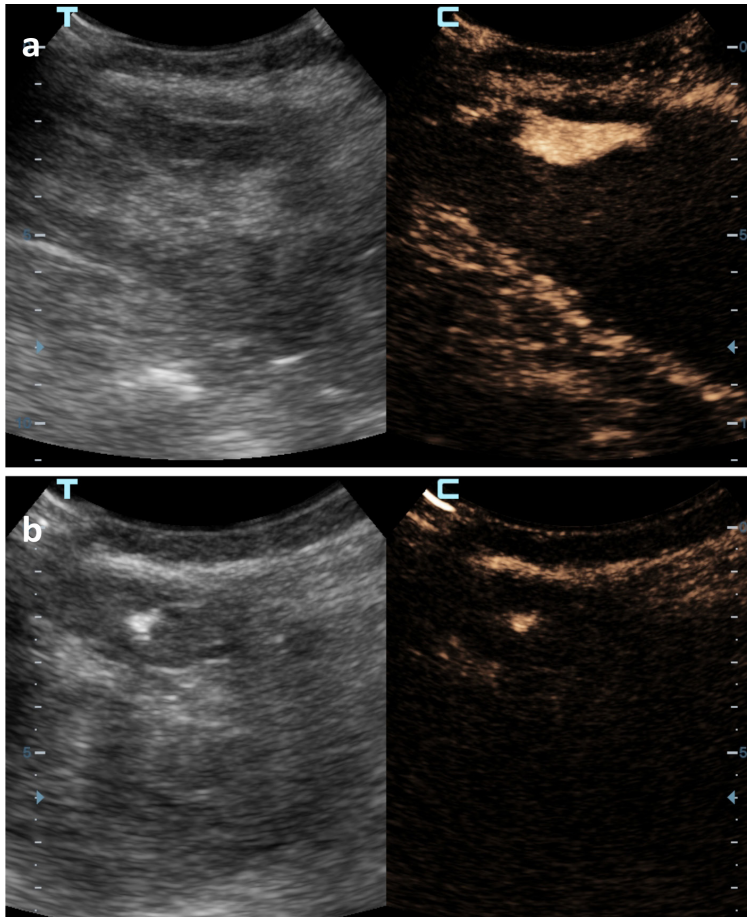


(a) Digital subtraction angiography (DSA) at baseline shows active extravasation from a right superior lumbar artery. **(b)** DSA post embolization shows complete occlusion of this artery.



Sonographic image (unenhanced, reference gray-scale image on the right, CEUS image on the left) immediately post percutaneous thrombin injection shows no enhancement of the hematoma and newly appearing echogenic thrombotic material (arrows).

Supplementary images for case 3



Sonographic images (unenhanced, reference gray-scale image on the right, contrast-enhanced ultrasound image on the left) before **(a)** and immediately post PTI **(b)**.