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Use of N-Butyl Cyanoacrylate in Abdominal and Pelvic Embolotherapy: Indications and Techniques, Complications, and Their Management

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Abstract

The aim of this article is to describe the indications for use of n-butyl cyanoacrylate (NBCA) in abdominal and pelvic embolotherapy, appropriate techniques for NBCA embolotherapy, and NBCA-related complications and their management.

NBCA embolotherapy is a feasible and effective method to treat a variety of abdominal and pelvic vascular lesions or tumors; however, the techniques suitable for each case and knowledge of NBCA-related complications are essential to achieve favorable outcomes.

Keywords

n-butyl cyanoacrylate; NBCA; embolotherapy, transcatheter arterial embolization; abdomen

Introduction

Endovascular embolotherapy is increasingly used to treat various abdominal and pelvic disorders. In such embolotherapy, metallic coils and particles are most commonly used. However, embolotherapy using such agents is not always successful, depending on the anatomy, the size of arterial lesions, and the technical difficulty in superselective placement of the catheter.

N-butyl cyanoacrylate (NBCA, Histoacryl, B. Braun AG, Melsungen, Germany) has been approved by the Food and Drug Administration (FDA) as a preoperative embolic agent for cerebral arteriovenous malformation (AVM) alone. The use of NBCA for abdominal organs is still controversial issue, and there is no world wide consensus. In present time, intravascular use of NBCA has not been approved by Japanese Ministry of Health, Labor and Welfare. However, a growing number of abdominal and pelvic lesions are now effectively treated with NBCA in off-label applications, as described below [1-5]: a. gastrointestinal tract bleeding (ulcer, diverticulum, AVM, etc.), b. peritoneal or intrapelvic bleeding (trauma, pancreatitis, pesudoaneurysm, etc.), c. splanchnic aneurysms and AVMs, d. endoleak after stent grafting, and e. tumors. According to the literature, the viscosity of NBCA is 3.2cP, while that of iodized oil is 17cP to 42cP [6, 7]. Therefore, the viscosity of the mixture of them is low enough to allow its use as an embolic material, although that of the glue mixture increases proportionately with increases in the concentration of ethiodized oil. Because it is liquid, it can be injected via a microcatheter to embolize small arteries and collateral circulations, which are difficult to embolize with coils alone; however, NBCA embolization necessitates considerable experience in its use to achieve optimal results [4, 8]. This article reviews indications and appropriate administration techniques for NBCA, and suggests potential complications of this procedure.

Characteristics of NBCA as an embolic agent

NBCA glue is typically used in combination with iodized oil (Lipiodol, ethyl ester of iodinated poppy-seed oil fatty acid, Guerbe, France) for intravascular embolization to supply radiopacity and achieve a proper polymerization time. The relative concentration of each component influences the setting characteristics of the mixture [9]: the setting time increases as the concentration of NBCA glue decreases. A “slow-setting” glue has a low concentration of adhesive agent; for example, 20% NBCA for 80% iodized oil.

Gounis et al. [7] have, however, recently demonstrated that contrary to a common assumption, the setting characteristics of the acrylate component are not directly altered by the addition of iodized oil. NBCA glue polymerizes when it makes contact with an ionic substance, i.e., blood. Iodized oil thus acts as a buffering agent which delays the contact between NBCA and blood, therefore indirectly delaying the initiation of NBCA polymerization. A "fast-setting" glue is typically used for high-flow lesions, such as arteriovenous shunts or some AVMs. A "slow-setting" glue is preferred for lesions with slower flow or when the microcatheter cannot be placed at the actual site of the lesion. In such instances, slow setting characteristics would in theory allow enough time for the glue to reach distant targets. In reality, however, the increased viscosity of the mixture due to the high content of iodized oil prevents deep distribution of the glue [7].

Advantages of NBCA embolization compared with other embolic materials

A variety of embolic agents such as gelatin sponge particles, microcoils, and polyvinyl alcohol particles have been used in embolization procedures. Among them, coils are usually preferred for embolization of aneurysms, pseudoaneurysms, or bleeding in various organs. Safe release of coils and ideal coil embolization necessitates selective catheterization and stable catheter positioning. However, it is not always feasible to selectively place the catheter close to and beyond the target lesions as a result of small vessel size or tortuous vessel anatomy. Additionally, in cases with many efferent arteries originating from the lesions, the embolization procedure becomes time consuming and technically difficult with coils alone. In cases in which lesions are multiple, distal in location, or supplied by numerous collateral vessels, the use of particulate agents may be indicated. Although particulate agents can be injected from a catheter tip central to a lesion, their site of occlusion is not precise. In addition, the particles themselves are not radiopaque, making exact documentation of their site of occlusion impossible.

Because it is liquid, NBCA injected through a microcatheter into small arteries can reach distant targets through the bloodstream. Consequently, embolization of afferent arteries with simultaneous embolization of efferent arteries which may cause backflow to the lesions can be achieved by a single injection of NBCA. In cases of coil or polyvinyl alcohol particle embolization, occlusion of vessels is dependent on thrombosis rather than the embolic material itself and the coagulation state of the patient is important for the success of the embolization procedure [10]. On the other hand, NBCA can be used effectively even in patients with a coagulopathy because it does not depend on the coagulation process for its therapeutic effect [1, 11]. Finally, unlike coil embolization, NBCA may be used even in an unstable catheter position because of its low viscosity (Fig. 1).

Methods of NBCA embolization

NBCA is mixed with iodized oil in a ratio varying from 1:1 to 1:5. Before injection of the NBCA mixture, the microcatheter is flushed with 5% dextrose solution to prevent premature polymerization of the mixture in contact with residual blood or saline [9]. A small amount of the NBCA mixture (0.1–2 mL) is injected through a 1- or 2-mL syringe under careful DSA guidance. However, if misregistration artifact due to respiration movement is highly predictable in DSA, NBCA glue is injected under careful fluoroscopic monitoring. Immediately after the injection, the microcatheter is retracted to prevent adherence of the catheter tip to the vessel wall and discarded without flushing. The inner lumen of the guiding catheter is aspirated and the next embolization procedure is performed with a new microcatheter. It is not economical that a new microcatheter is needed in each session of NBCA embolization. In some cases, microcatheters can be reused after flush of them with iodized oil as a washer [12]. In critical situation, catheterization of a microcatheter into the same location may be extremely troublesome and time consuming. In such circumstances, advancement of the guiding catheter close to a target point may enable repeated superselective catheterization.

Various techniques in NBCA embolization

Various techniques suitable for each case should be selected to achieve successful outcomes. We categorized NBCA injection techniques into the following four groups: 1) flow-related injection, 2) wedged microcatheter technique, 3) balloon-assisted injection, and 4) combination with coils (Fig. 2).

Flow-related injection

Although the ideal embolization is to exclude both upstream and downstream of the lesion, it is sometimes difficult to selectively place the catheter close to and beyond the lesion in small or severely affected vessels. Even in such situations, NBCA glue injected at a suboptimal proximal position can reach distant targets through the bloodstream, thus enabling embolization of afferent arteries with simultaneous embolization of efferent arteries (Fig. 2 and 3).

Wedged microcatheter technique

When the microcatheter is wedged within the targeted artery and causes flow arrest in its distal distribution, injecting 5% dextrose through the microcatheter provides an adequate “stagnant” nonionic environment that allows excellent distal NBCA progression [9]. This technique also prevents reflux of NBCA around the catheter (Fig.2 and 4), thus enabling the reuse of microcatheters after flush of them with iodized oil as a washer. On the other hands, application of this technique during injection of NBCA has not been well documented, and excessive injection of NBCA under such circumstances may induce subintimal injection of NBCA or nontarget vessel occlusion. Hence, further studies in a large number of series are needed to establish safety and usefulness of this technique.

Balloon-assisted injection

Appropriate flow control using a balloon catheter is a useful method for NBCA glue injection, especially in the treatment of high-flow lesions [13] (Fig. 2 and 5); However, optimal flow control using a balloon catheter is usually difficult and the easy usage of this technique may cause adhesion of NBCA glue to a microcatheter or a balloon catheter. Therefore, considerable experience is required to achieve safe and effective usage of this technique.

Combination with coils

This method is used for the following strategies. Firstly, when there are many efferent arteries originating from the lesion or many collateral circulations coming from the adjacent arteries, it is time-consuming and technically difficult to embolize them all with coils alone. In such instances, coil embolization of major branches followed by NBCA embolization of the remaining branches is an alternative method (Fig. 2 and 6).

Secondly, slowing circulation flow with coils before NBCA administration is an alternative technique if it is difficult to reach the optimal position with a balloon catheter (Fig. 2 and 7). Finally, consideration should be given to protective coil occlusion of nontarget branches before NBCA embolization if there is the risk of inadvertent distant embolization of a non-target organ (Fig. 2 and 8).

Complications of NBCA embolization

Several complications related to NBCA embolization have been reported in the literature. Although NBCA can pass through tortuous catheters, it does not necessarily permeate to the capillary level, and therefore does not inevitably result in tissue infarction. However, in some cases, distal embolization and reflux into non-target vessels may cause end-organ ischemia, including liver abscess and infarction after hepatic artery embolization [14], duodenal infarction after gastroduodenal artery embolization [15], and sciatic nerve palsy after internal iliac artery embolization [16]. These complications can be minimized by careful attention to the specific vascular anatomy and the information obtained from test injections with contrast material. According to Ikoma et al. [17], embolization of three or fewer vasa recta with NBCA glue induced no ischemic damage or limited necrosis, whereas embolization of five or more vasa recta with NBCA glue induced extensive necrosis. Additionally, we prefer to use NBCA mixed with iodized oil in a ratio varying from 1:1 to 1:5 to minimize these complications. However, Ogawa et al. have demonstrated no significant difference in the risk of bowel infarction and the success rate of NBCA embolization between mixtures of lower and higher concentration of NBCA [18].

Entrapment of a catheter within an embolized artery is the most serious problem. If a microcatheter is trapped inside the polymer, making it impossible to withdraw, it should never be forcefully pulled as this could induce serious vascular damage. The microcatheter can safely remain inside the vascular lumen with the proximal end cut and left in the subcutaneous tissue in the groin region [19]. Hydrophilically coated microcatheters are known to be less likely to exhibit permanent catheter fixation during NBCA-embolization because of a weaker catheter-NBCA bond and reduced catheter friction [19].

Conclusion

NBCA embolization can be a reasonable and effective therapeutic technique for the treatment of various abdominal and pelvic lesions; however, careful selection of optimal administration methods of NBCA by considering the speed of blood flow, caliber of the parent artery and volume of the embolized area is essential to achieve successful embolization with reducing risk of potential complications.

Fig. 1 81-year-old man with paraanastomotic pseudoaneurysm of right common iliac artery after AAA repair with conventional bifurcated graft

A. Aortography shows a paraanastomotic pseudoaneurysm of right common iliac artery.

B. Using contralateral approach, right internal iliac artery (RIIA) was catheterized with a microcatheter, the tip of which was unstable due to vessel tortuousity. In this case, initially, we attempted to embolize RIIA using IDC coils. However, that was unsuccessful because of bending of a microcatheter in a large aneurysm. Hence, NBCA-embolization of IAA was done. Initially, a stent graft was placed from right iliac leg of the bifurcated graft to right external iliac artery, and NBCA embolization of RIIA was performed via the microcatheter (arrow heads). Curved arrow indicates the balloon catheter for dilating the stent graft. Digital angiography obtained during injection of NBCA-Lipiodol mixture show good accumulation of NBCA glue (arrow) in RIIA. In this case, stent grafting was performed prior to NBCA embolization of RIIA since prior stent grafting prevented migration and reflux of NBCA.

C. Post-procedural angiography shows complete exclusion of the paraanastomotic psudoaneurysm.

Fig. 2

(a) Flow-related injection; NBCA glue injected at suboptimal proximal position can reach distant targets through the bloodstream.

(b) Wedged microcatheter technique; the microcatheter is wedged within the target artery and causes flow arrest in its distal distribution; injecting 5% dextrose through the microcatheter provides an adequate “stagnant” nonionic environment that allows excellent distal NBCA progression. This technique also prevents reflux of NBCA around the catheter.

(c) Balloon-assisted injection; flow control using a balloon catheter is an effective technique especially in treatment of high-flow lesions.

(d) Coil embolization of major branches followed by NBCA embolization of the remaining branches is an effective technique, if there are many efferent arteries originating from the lesion.

(e) Flow control with coils before NBCA administration is effective, if it is difficult to

reach the optimal position with a balloon catheter.
(f) Protective coil occlusion of nontarget branches before NBCA embolization is effective, if there is the risk of inadvertent distant embolization of nontarget organ.

Fig. 3 Technique of flow-related NBCA injection: 39-year-old man with traumatic hepatic injury.

A. Contrast-enhanced CT image shows a traumatic pseudoaneurysm (arrow) in the left lateral lobe of the liver.

B. C. Arteriograms of celiac and hepatic arteries demonstrate the pseudoaneurysm (arrows) in the left segmental branch of the hepatic artery.

D. DSA obtained during flow-related injection of the mixture of NBCA and Lipiodol (ratio 1:3) at the proximal position in the left segment branch of the hepatic artery shows the mixture cast in the pseudoaneurysm, and distal and proximal portions to the pseudoaneurysm.

E. Left hepatic artery arteriography obtained immediately after embolization shows elimination of the pseudoaneurysm.

Fig. 4 Wedged microcatheter technique: 70-year-old man with traumatic renal injury.

A. Contrast-enhanced CT image demonstrates hematoma around left kidney and pseudoaneurysm (arrow) formation.

B. Selective arteriography of the left renal artery shows a pseudoaneurysm (arrow) adjacent to dorsal surface of left kidney. The artery responsible for the pseudoaneurysm is small.

C. A mixture of NBCA and Lipiodol (ratio 1:3) was injected with the wedged microcatheter technique. Arrow indicates NBCA accumulation in the pseudoaneurysm.

D. CT image obtained after embolization shows NBCA accumulation in the pseudoaneurysm (arrow).

E. Left renal artery arteriography obtained immediately after embolization shows elimination of the pseudoaneurysm. The mid to lower pole of the renal parenchyma lacks some vessels as compared with the preprocedure angiogram due to the reflux of a small amount of NBCA into nontarget vessels.

Fig. 5 Balloon-assisted NBCA injection: 56-year-old man with intrapelvic arteriovenous malformation (AVM).
A. CT angiography shows AVM supplied by several branches of right internal iliac artery (arrow).

B. NBCA embolization of feeding arteries was attempted under flow control using a balloon catheter (arrow). Photograph obtained after several sessions of embolization shows excellent accumulation of NBCA and Lipiodol (ratio 1:1-1:2) in feeding arteries.

C. Right internal iliac artery arteriography obtained immediately after embolization shows disappearance of AVM.

Fig. 6 Combination with coils: 76-year-old woman with common and internal iliac artery aneurysms.
A. CT angiography shows the right common and internal iliac artery aneurysms.

B. After introduction of a 5-F catheter into right internal iliac artery (RIIA), main body of Excluder abdominal aortic aneurysm (AAA) graft (arrow) was placed in abdominal aorta to right external iliac artery. Then, two main branches of RIIA were embolized with microcoils (arrowheads) followed by NBCA embolization of RIIA. DSA obtained during NBCA injection shows accumulation of the cast in the remaining branches of RIIA. In this case, CT images (not shown) demonstrated the extension of the aneurysm with a large amount of mural thrombus into the bifurcation of the superior and inferior gluteal arteries. Therefore, embolization of peripheral branches distal to the bifurcation was needed to completely prevent retrograde flow to the aneurysm.

C. DSA obtained after placement of Excluder iliac legs shows complete obliteration of iliac artery aneurysm.

Fig. 7 Combination with coils: 70-year-old man with intestinal bleeding.
A. Selective arteriography of iliocolic artery show an AVM (arrow) supplied by a branch of the iliocolic artery.

B. Initially, coil (arrow head) embolization was performed to slow circulation flow. Then, an NBCA-Lipiodol mixture (ratio 1:1) was injected. Post-embolization arteriography shows disappearance of the AVM.

Fig. 8 Combination with coils: 59-year-old man with duodenal bleeding.
A, B. Superior mesenteric artery arteriography (A) and superselective arteriography of the first jejunal branch (B) show extravasation (arrows) from a small branch of the inferior pancreaticoduodenal artery, which has the same origin as the first jejunal branch (arrow heads).

C. Before NBCA injection, the first jejunal branch was embolized with microcoils (arrow head) to prevent migration of NBCA into the nontarget branch. NBCA accumulates in the vessel responsible for extravasation. Post-embolization arteriography shows disappearance of extravasation.

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Fig. 1A

Fig. 1B

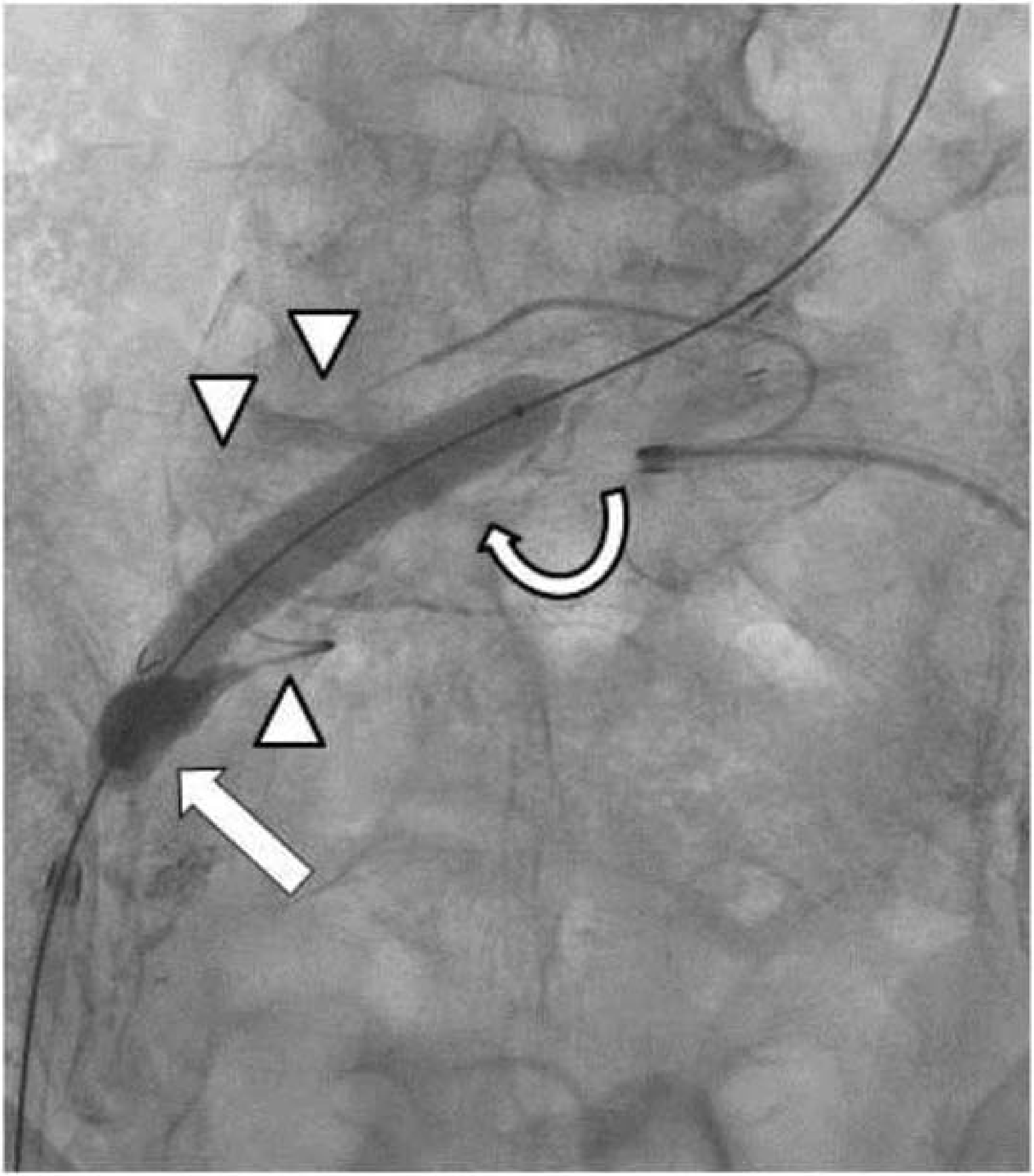
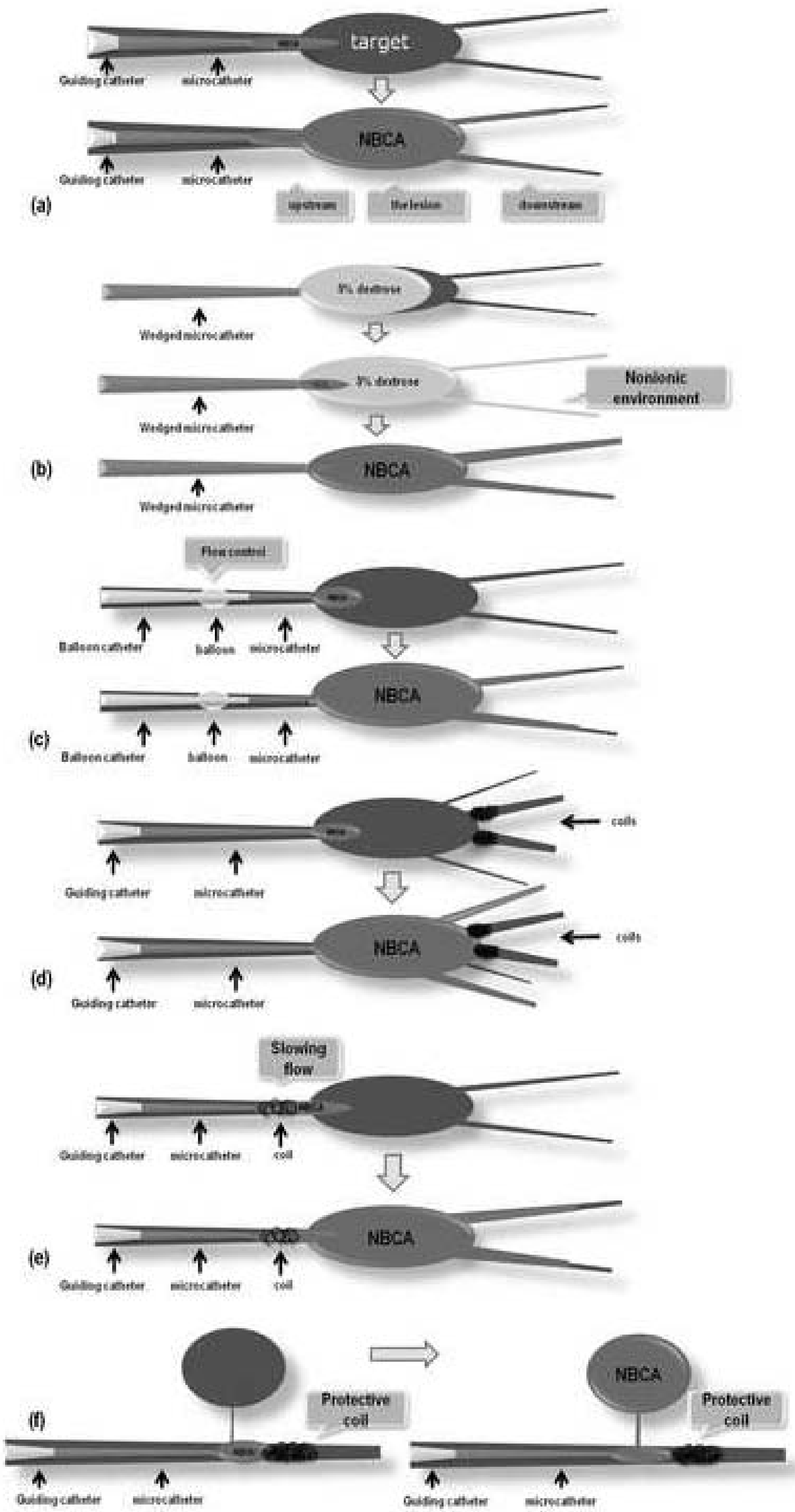


Fig. 1C

Fig. 2



target
Guiding catheter
microcatheter
NBCA
(a)
upstream
the lesion
downstream
5% dextrose
Wedged microcatheter
Nonionic environment
(b)
Flow control
Balloon catheter
balloon
(c)
coils
(d)
Slowing flow
coil
(e)
(f)
Protective coil

Fig. 3A

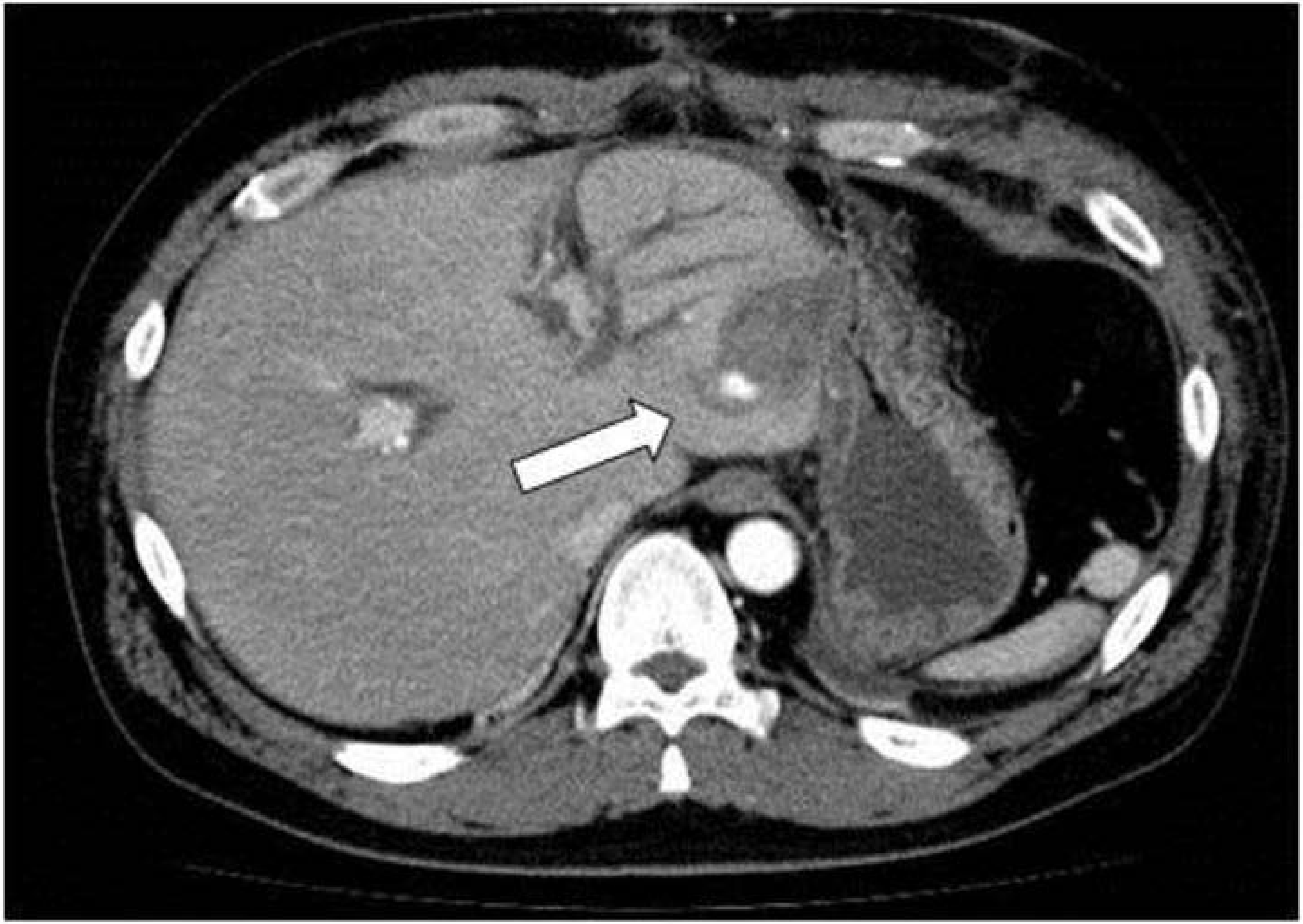
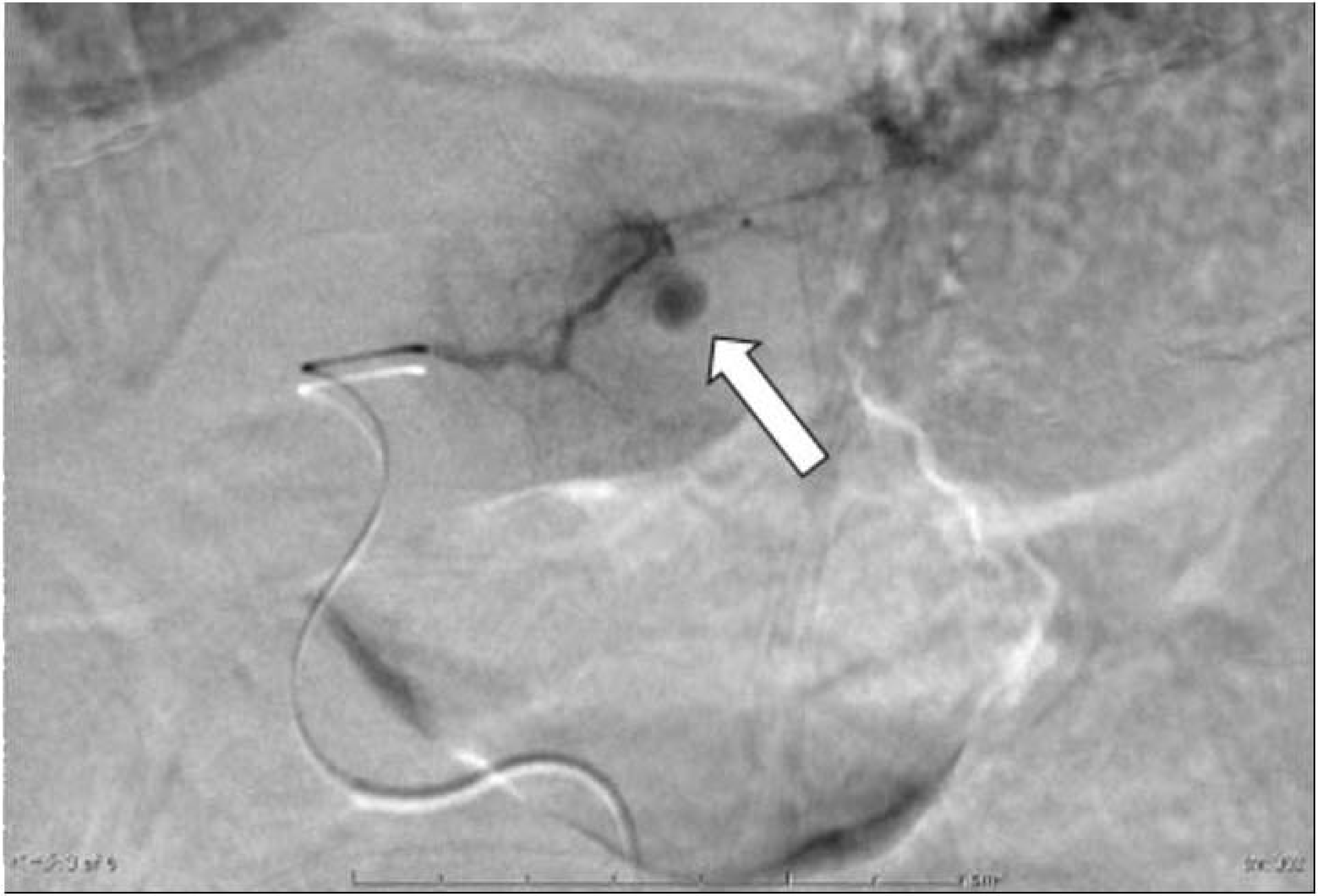


Fig. 3B

Fig. 3C



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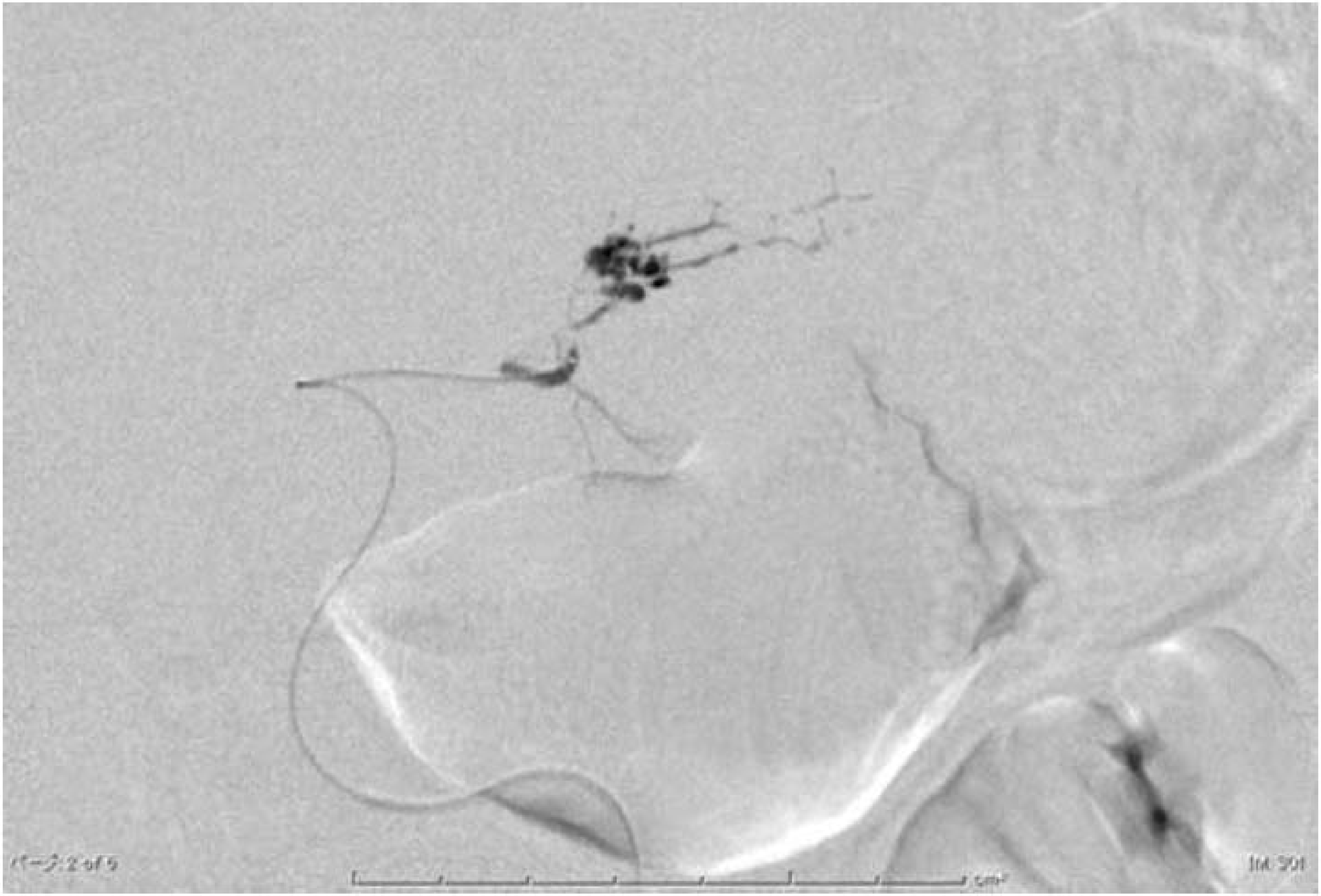

Fig. 3E

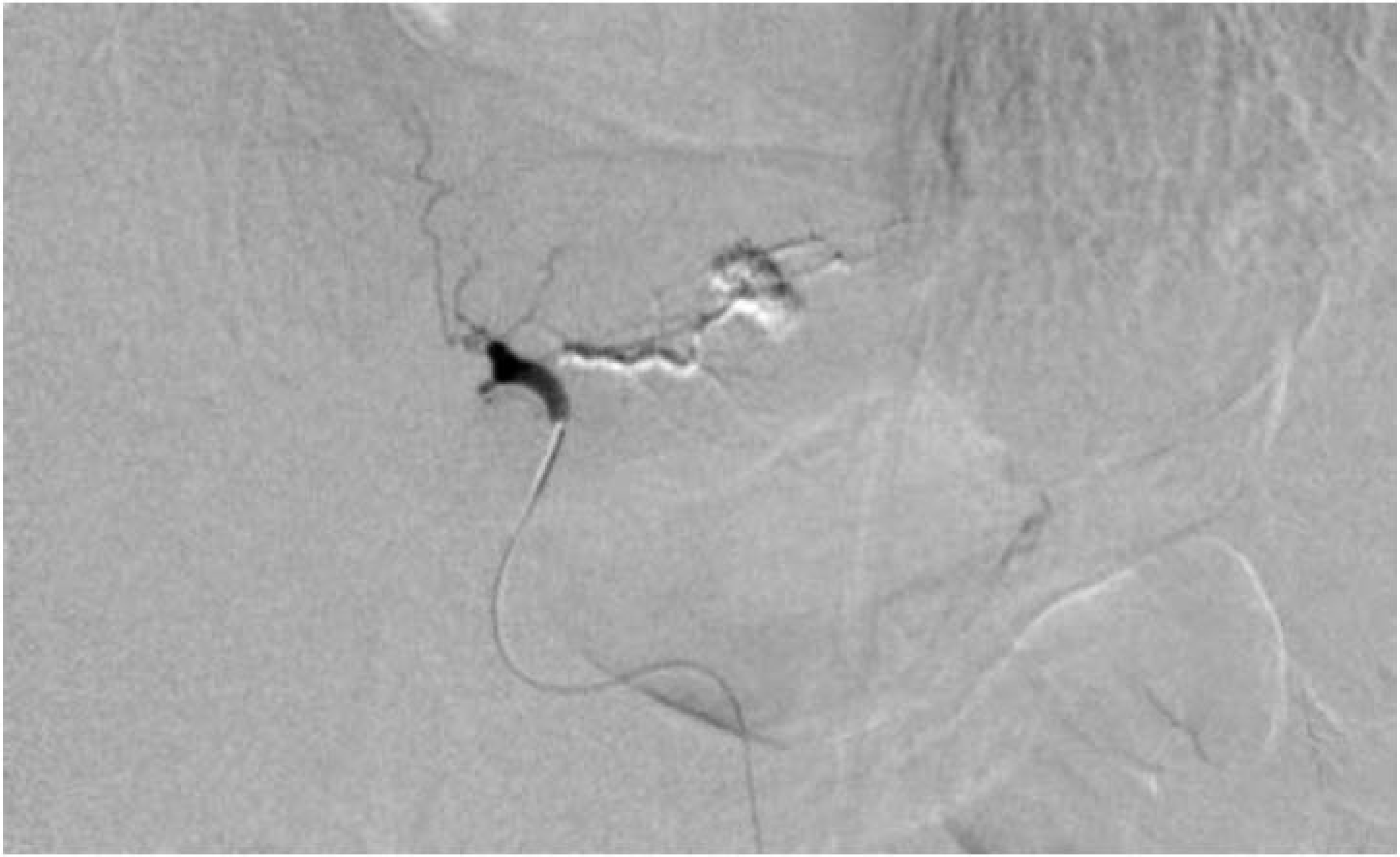

Fig. 4A

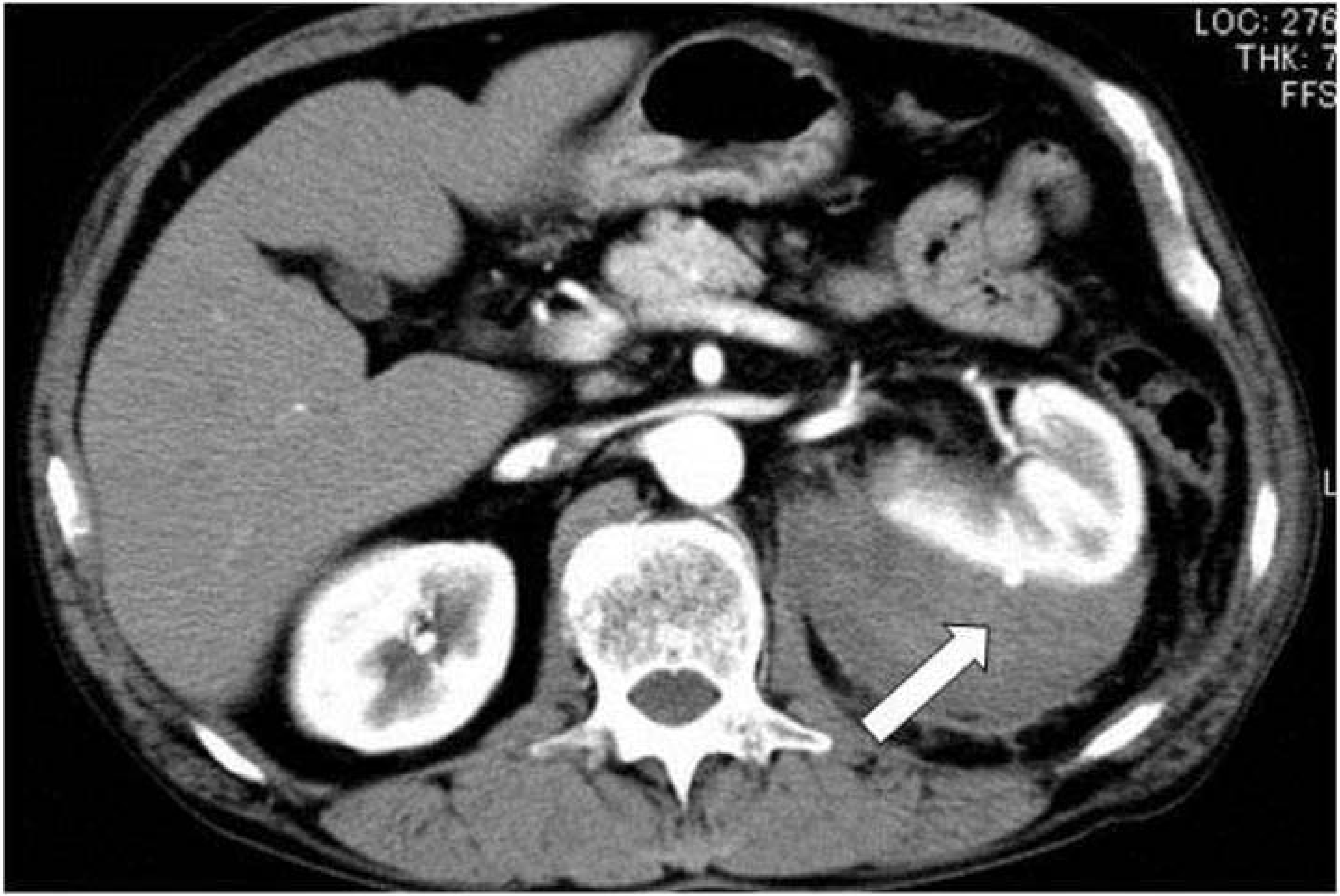

Fig. 4B

Fig. 4C

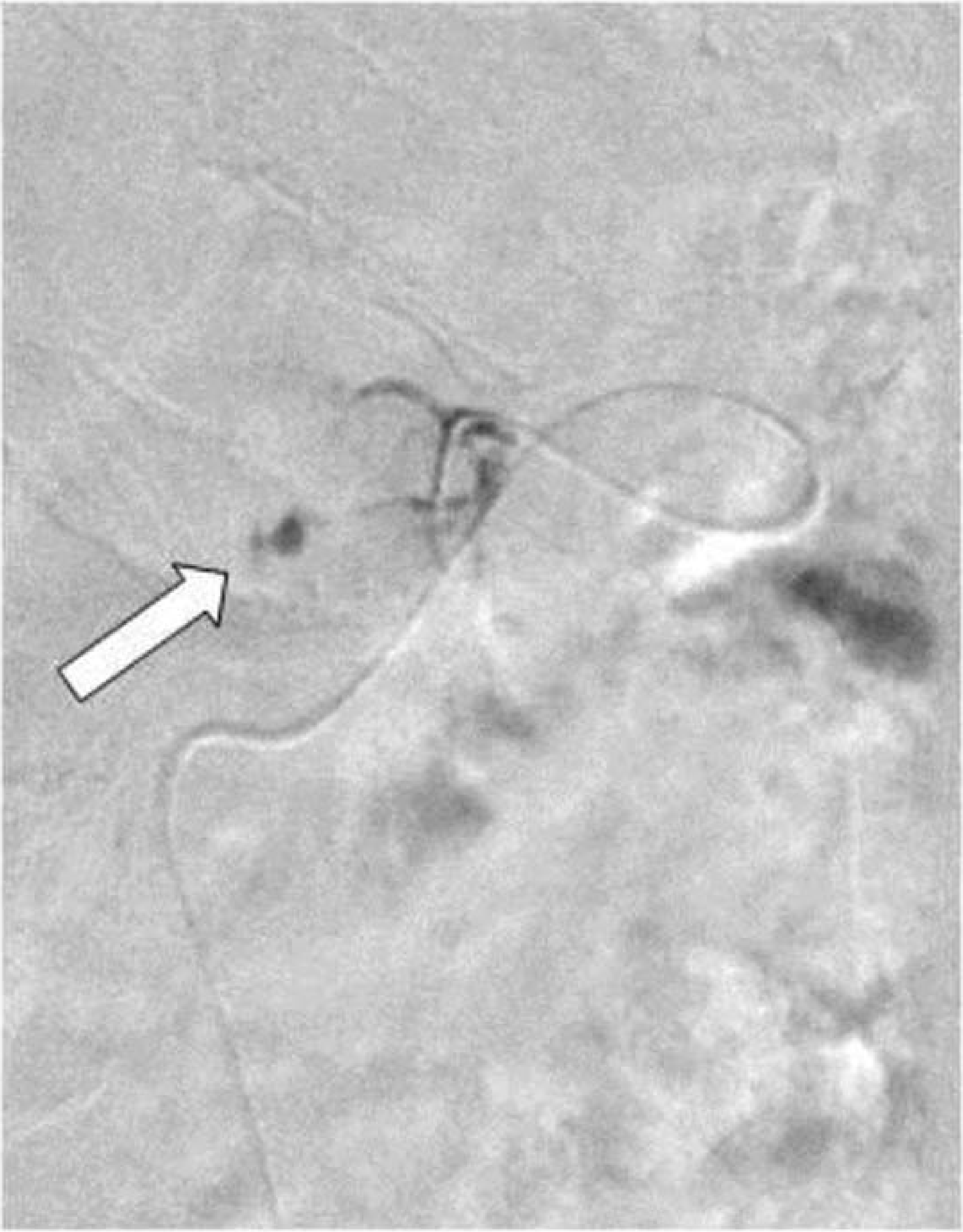

Fig. 4D

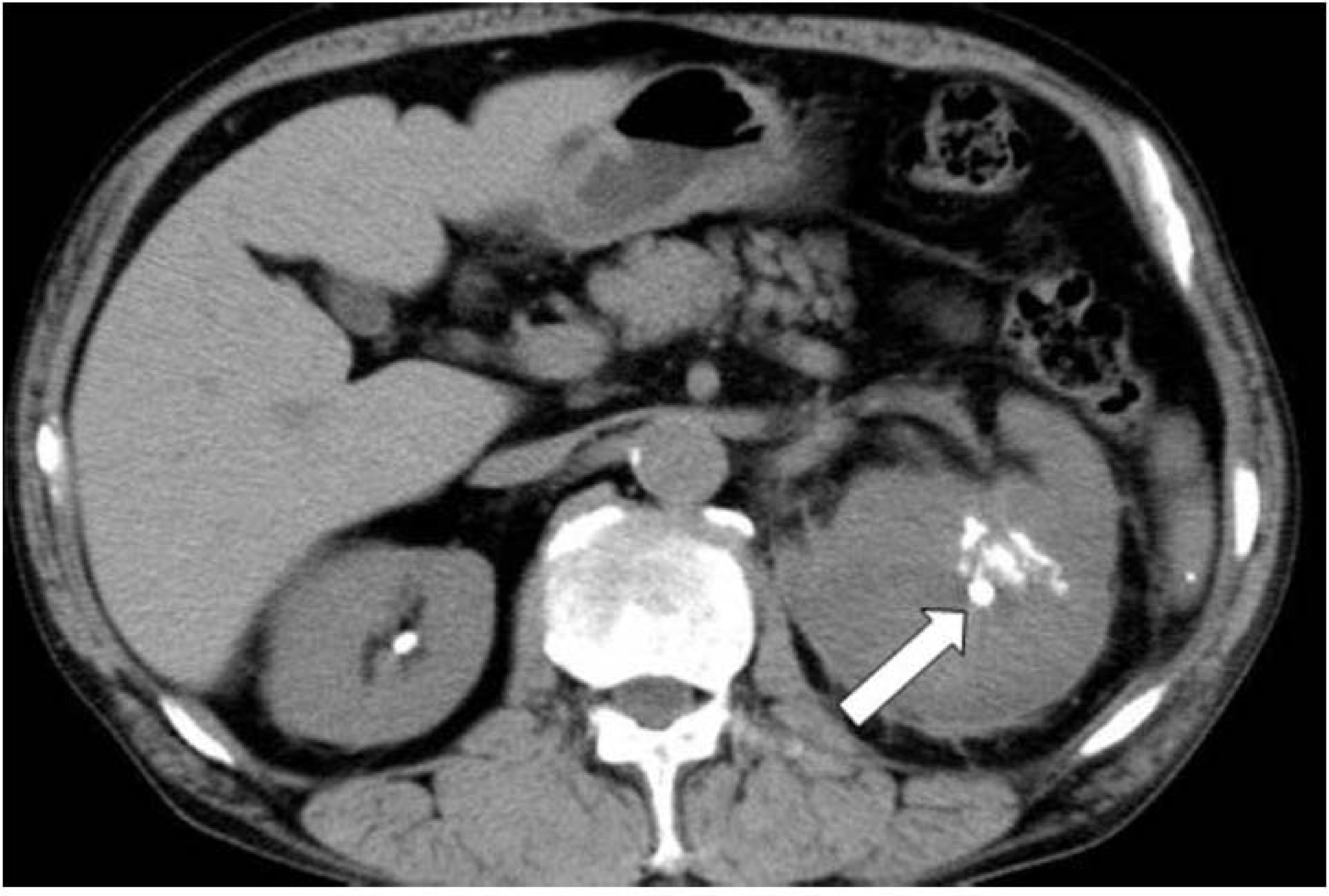

Fig. 4E

Fig. 5A

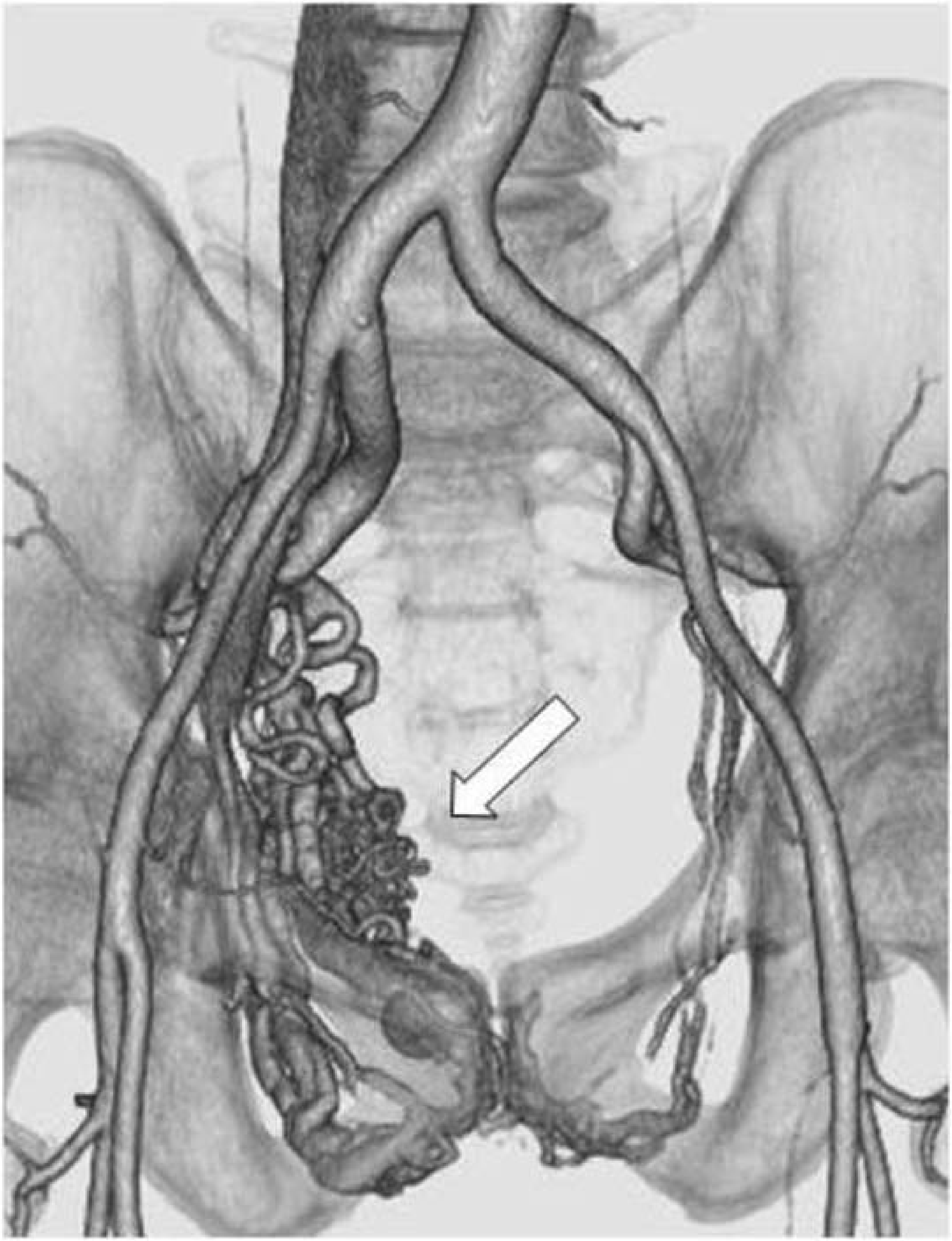

Fig. 5B

Fig. 5C

Fig. 6A

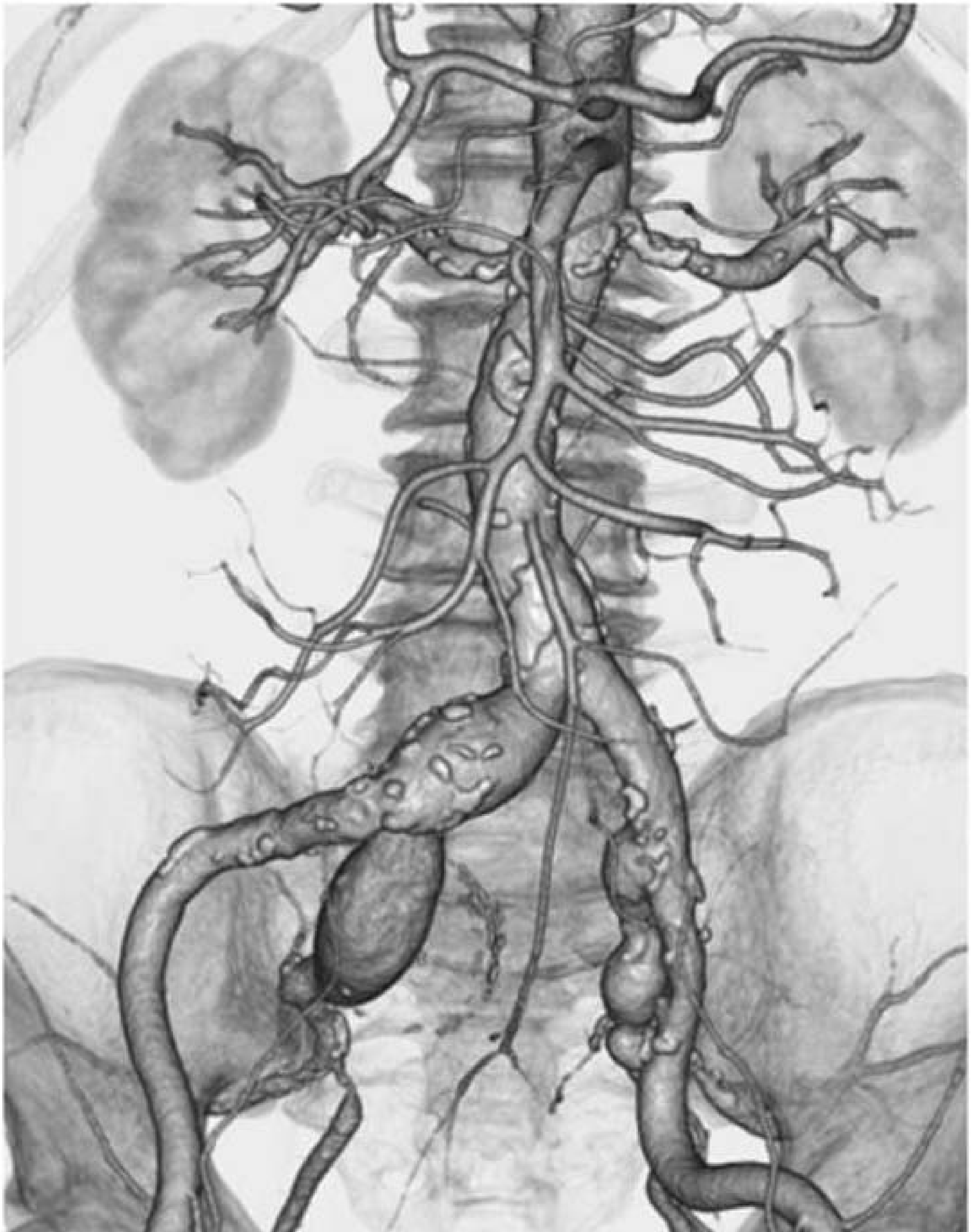

Fig. 6B

Fig. 6C

Fig. 7A

Fig. 7B

Fig. 8A

Fig. 8B

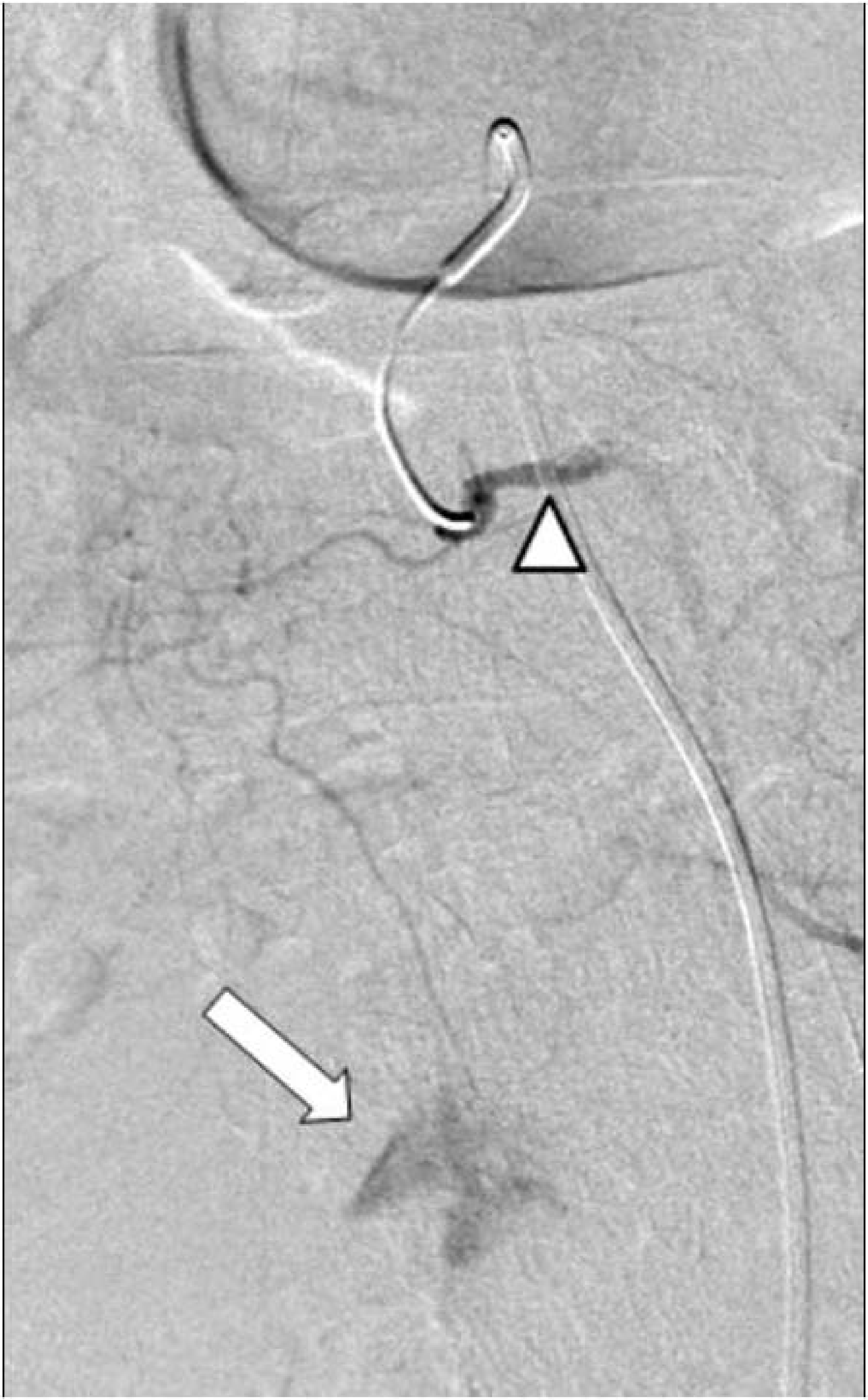

Fig. 8C