Chapter 25
Intraoperative Coagulopathy

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The patient is a 21-year-old female with past medical history significant for hypertension, idiopathic renal failure, epilepsy, and spina bifida who presents as a recipient of renal transplant with neobladder formation. Her past surgical history involved a number of spine surgeries without any complications. On exam, she weighs 39 kg and is 142 cm in height. Her preoperative labs reveal a potassium of 5 meq/dL, blood urea nitrogen (BUN) of 58 (units), HCO_3 of 23, a hematocrit of 33 %, and platelet count of 147,000. Her coagulation labs were prothrombin time (PT) 10.6 with International Normalized Ratio (INR) 1.1 and partial thromboplastin time (PTT) 27.6 (**L-1**).

Due to difficulty obtaining blood draws as well as placing an IV, the decision was made to utilize one of the ports (red, with 1.3-cc priming volume from port to tip) of her indwelling venous two-lumen hemodialysis vascular catheter (Vas-Cath) for access. Prior to utilizing this port, 5 mL of blood was drawn back, and 10 mL of additional blood was drawn for a repeat set of labs in the preoperative, holding area (**L-2**). After this draw, 3 mL of nonconcentrated 1,000 units/mL of heparin was used to flush and lock the port (**L-6**). After appropriate labs confirmed a match with the kidney, the patient was taken to the operating room some hours after this draw and induced utilizing the red port after the same procedure to flush out the heparin was repeated. An 18-gauge peripheral IV was placed in the left hand after induction. The patient was maintained on one minimum alveolar concentration (MAC) of isoflurane in oxygen and air throughout the case.

Immediately upon skin incision, the surgeon noted excessive oozing of blood in the field and requested that the anesthesiologist prepare to have approximately three units of packed red blood cells brought to the room. This oozing continued persistently throughout the case, and two units of packed red blood cells were

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administered after an estimated blood loss of 400 mL and a hematocrit of 25 %. The patient remained hemodynamically stable throughout the 6-h surgery until closure. Immediately after closure of the abdomen, the patient became hypotensive and an additional unit of packed red blood cells was administered with 1 L of albumin. A discussion between the anesthesiologist and the surgeons regarding re-exploration of the abdomen took place, and the decision to observe the drainage output and resuscitate the patient was made.

The patient was taken to the ICU intubated. In the immediate hour following surgery, the drainage output was 250 mL of frank blood and two additional units of packed red cells were given over the next several hours. After failed attempts at a radial arterial line, a femoral arterial line was placed under ultrasound guidance, and a full lab panel was obtained as well as an activated clotting time (ACT). The ACT was 305 s (normal 120–130). Coagulation panel revealed a PT 13.6 s, INR 1.4, and PTT >300 s. Two units of fresh frozen plasma and 50 mg of protamine were administered and labs were repeated: PT 11.8 s, INR 1.2, PTT 28 s, fibrinogen 171, and D-dimer 2,397 ng/mL (normal <250 ng/mL) (**L-4**). The drain output decreased to minimal over the next 4 h. The patient was extubated later in the day without any other complications (**L-5**).

Lessons Learned

L-1. **What is the volume capacity of the ports on the two-lumen hemodialysis catheter** (**Vas-Cath**)?
Figure 25.1 shows that there are three ports in this catheter, two identical large ports and a smaller proximal port in the middle. In Fig. 25.2, the three lumens are all separated from one another. In Fig. 25.3, the distal lumen has a priming volume of 1.4 mL and the proximal lumen has a priming volume of 1.3 mL. Both of these lumens are self-contained and isolated from each other so that there is no mixing of contents from each lumen.

Figure 25.4 illustrates the heparin dose–response curve. The following procedure is done to construct a dose–response curve for a patient. This dose–response curve is then used to predict the amount of additional heparin to give and to calculate protamine doses for reversal of anticoagulation.

1. Plot the initial ACT on the *x*-axis (A).
2. Plot the ACT after heparinization (B).
3. Draw the line defined by these two points.
4. If additional anticoagulation is needed, find the desired ACT on that line. The amount of additional heparin needed is the difference on the *y*-axis between the present ACT and the desired ACT.
5. If the third point does not lie on the original line, a new line is drawn originating from the baseline ACT and passing midway between the other two points.
6. For reversal of anticoagulation, the protamine dose is based on the remaining heparin activity, estimated to be the heparin dose corresponding to the latest ACT on the dose–response line.

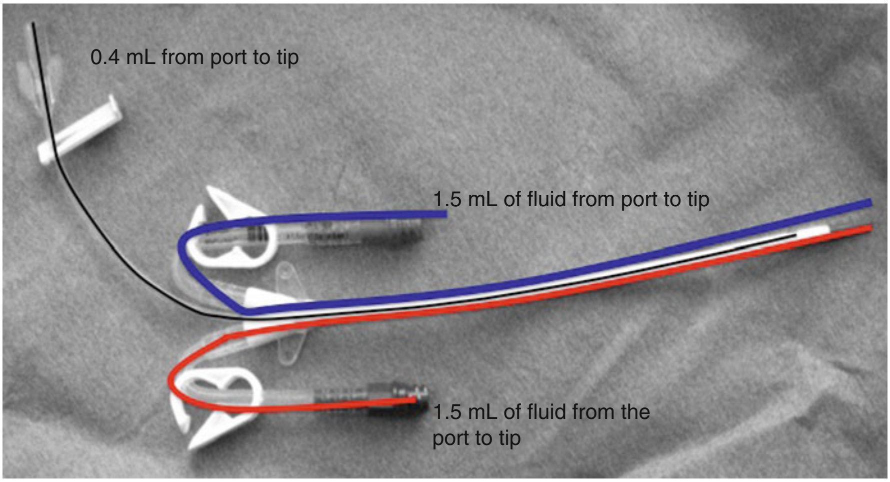

Fig. 25.1 Covidien™ acute triple-lumen dialysis catheter. The volume of dead space (priming volume) from the injection ports to the tip of the catheter is demarcated by the *red and blue lines*. It represents 1.5 mL of fluid through each port which does not mix with any other port's contents along the entire length of the catheter (see Fig. 25.2). The *black line* demarcates the amount of dead space (priming volume) from the port to the tip of the catheter. The priming volume in all three ports is self-contained and isolated from one another (see Fig. 25.2)

L-2. How much fluid should be drawn back when attempting to clear a line of dead-space fluid?

This depends on how much dead space (priming volume) you are trying to clear. For example, in this case, the amount of priming volume in the dialysis catheter to clear starting from the port of the catheter to the tip of the catheter is equal to 1.5 mL of fluid (See Fig. 25.1) for the Covidien catheter. It is 1.3 mL from the red port and 1.4 mL from the blue port of an Arrow Two-Lumen Hemodialysis Catheter. When removing one kind of fluid (heparin) from one small space (one of the lumens of the Vas-Cath) by flushing into it fluid (blood) from a second large space (the vascular system), there is a wash-in (of blood) and washout (of heparin) process that occurs exponentially in the small space (see Table 25.1).

Table 25.2 depicts the exponential decrease in concentration of heparin in the port-to-tip dead space of the catheter as a function of the number of dead-space volumes of blood is aspirated in this dead space by a syringe attached to the dead space. As fluid is aspirated from the catheter, the first 1.5 mL (which represents the total dead-space or priming volume of the catheter) corresponds to removal of 63 % of the dead-space fluid (priming volume), leaving 37 % of the fluid in the catheter. As additional fluid is removed, one can see that the amount of dead-space fluid remaining in the catheter exponentially decreases.

L-3. What coagulopathy should be expected of a patient with renal failure presenting for surgery?

Patients with renal failure, who are receiving regular dialysis, should be expected to have an increase in bleeding time due to chronic uremia and defective platelets.

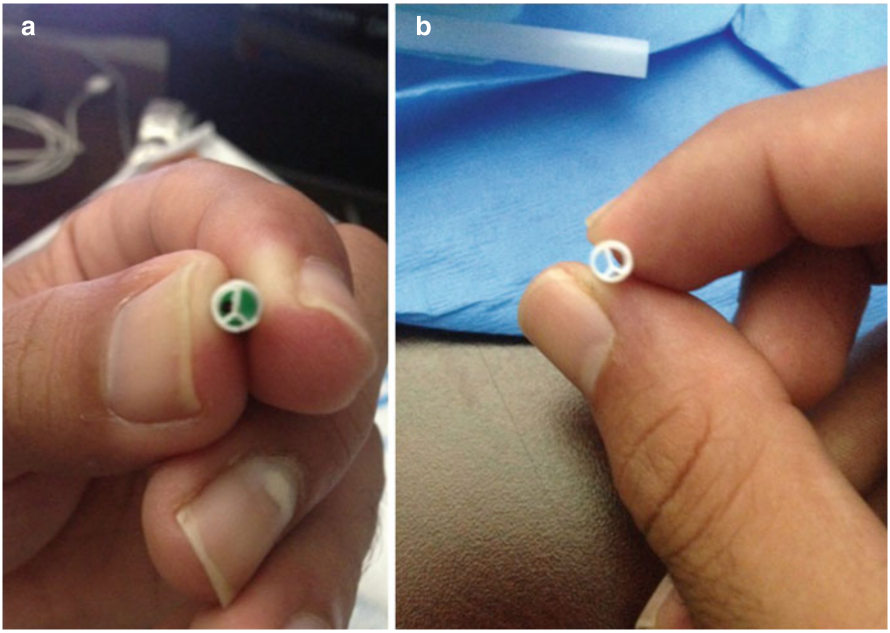

Fig. 25.2 Cross-section view of the Covidien™ acute triple-lumen hemodialysis catheter. (**a**) This view is a cross section near the distal tip of the catheter. There is a green obturator (plastic block) near the tip which blocks off the flow in two of the three lumens. Therefore, fluid exits on the side of the catheter through orifices that are just proximal to the obturator block in these two lumens. The fluid in the lumen on the left, the remaining third lumen at the 9 o'clock position, flows through the distal tip. (**b**) This is the cross section of the middle of the catheter showing the segregation of the priming volume in the three lumens along the length of the catheter

Also, they may have low levels of von Willebrand factor (VWF), which reduces the half-life of factor VIII. Moreover, since they are receiving dialysis through catheters that may be indwelling for long periods of time, the patients are predisposed to iatrogenic heparinization from the "locking" of their access catheters with heparin; in other words, a caregiver may make a mistake at any time and inject something through a heparin-filled ("locked") Vas-Cath lumen [1].

L-4. **What is the significance of the D-dimer level**?

A D-dimer level is a measure of thrombus formation and breakdown (fibrin split products). A value above normal limits means that the patient is forming clot and lysing the clot faster than any normal process would allow for. It is often drawn to confirm a diagnosis of thrombosis or DIC. If the probability of thrombosis (pulmonary embolus or deep venous thrombosis) is low to intermediate, then a D-dimer of zero rules the diagnosis of thrombosis out. In this regard, it is a sensitive test. If the probability is high and the D-dimer is greater than normal limits (250 ng/mL), another confirmatory test will need to be done (such as pulmonary angiography or lower-extremity ultrasound) since it is not a very specific test. It only tells the

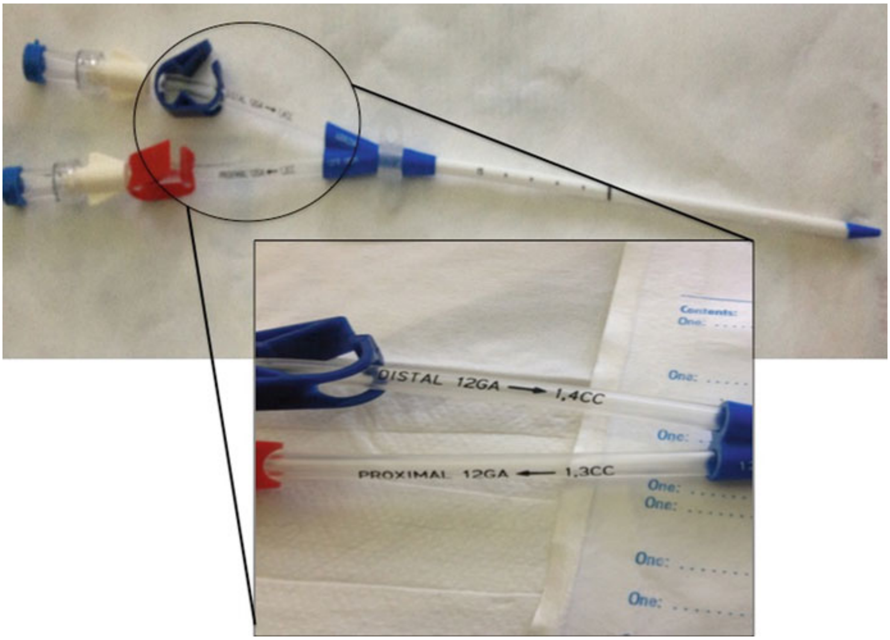

Fig. 25.3 Arrow® two-lumen hemodialysis catheter showing the priming volume in the two ports

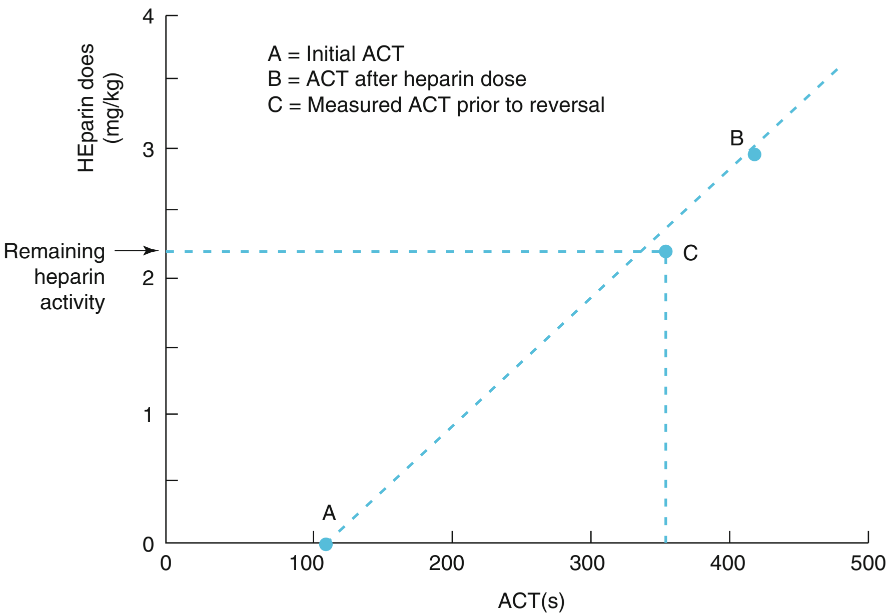

Fig. 25.4 Heparin dose–response curve. Activated clotting time (*ACT*) in seconds versus total heparin dose in milligrams per kilogram (Adapted from [3])

Table 25.1 Wash-in of blood and washout of heparin process

Flush of blood from the vascular system into a lumen of the Vas-Cath in increments of 1 port-to-tip dead space = 1.5 mL	Concentration (% of original) of heparin in a port-to-tip lumen of the Vas-Cath
0	100
1.5	37
3	13.5
4.5	5
6	1.8
7.5	0.7

Table 25.2 The different heparin preparations at UCSD

Heparin concentration (units/mL)	Total volume available (mL)	Uses/locations found
10,000	0.5	Thromboprophylaxis
10,000	10	Infusion center
1,000	10	Operating room cat
100	5	IV line flush
50	500	Therapeutic anticoagulation
2	500	Arterial line bags

physician that there is abnormal thrombus formation and breakdown. Its utility in this case was as a measure of fibrin split products to assess for a disseminated intravascular coagulation (DIC) or a consumptive coagulopathy. D-dimer level should be interpreted with caution since recent surgery, trauma, infection, pregnancy, and liver disease can all raise D-dimer levels. An appropriate use for it would be to monitor the effectiveness of therapy after suspected DIC. At the University of Southern California San Diego (UCSD) Medical Center, the upper limit for normal is 250 ng/mL. In this case, only one value was drawn, and since it was elevated nearly ten times the upper limit of normal, it is plausible to entertain the diagnosis of DIC in this patient [2].

L-5. **What conclusions can be drawn from this case**?

The data available in the narrative of this case do not permit a clear explanation of what caused the very high ACT and bleeding at surgery. Of course, it is important to clearly aspirate any preexisting residual heparin (or any drug) out of a catheter that is going to be used for the induction of anesthesia or for bolusing medications. It is clear that the problem was not caused by accidental entrainment of heparin from one port by a forceful injection into the other port during induction via the Venturi effect, which was the original clinical hypothesis. After careful study of the design of the hemodialysis catheters used in this institution, this is not likely since the lumens are physically separated. In this case, the total amount of heparin that could have been injected into the patient is 1,500 units of heparin because 3 mL of heparin (1,000 units/mL) was used to flush a 1.3-mL space. This would mean that a 3-mL injection into either port of the lumen would clear the catheter completely and deliver 1.7 mL (1,700 units) of heparin into the patient and leaving the other 1.3 mL in the lumen (assuming the Arrow double-lumen catheter). A similar heparin dose would have been delivered to the patient if the Covidien™ catheter was used. Since several hours seemed to have elapsed between this flush and the start of surgery, the ensuing coagulopathy cannot be explained by this alone, unless there was a higher concentration of heparin used to flush the ports (drug swap error) based on the typical dose–response curves for heparin (see Fig. 25.2) [3]. There are various different concentrations of heparin available. The available preparations at UCSD are summarized in Table 25.2. Since heparin dose–response curves are individualized for each patient, Fig. 25.4 should be interpreted as a typical example of heparin's effect on a patient. It is clear from this curve that 1,500 units of heparin should not result in an ACT of 300 s as was seen in this case.

In Table 25.2, the unit per mL value is in the left-hand column, the total amount available in mL is in the middle column, and the typical uses or locations that these preparations are found in the hospital are listed in the right-hand column. Of the different heparin preparations at UCSD, only the 10,000-unit/mL preparation available from the infusion center, which is the site where chemotherapy is performed at UCSD (second row), would have been enough to accidentally heparinize the patient enough to bring the ACT to 300.

This case has an interesting differential for the unexpected coagulopathy that was encountered. It is not clear if the patient underwent dialysis prior to the case, but this could be a source for unintentional heparinization that occurred after the initial labs were drawn. More importantly, the anesthesiologist should be aware that a uremic patient with thrombocytopenia is a setup for bleeding and the coagulation parameter that may be abnormal is the bleeding time. This is not a routinely measured lab preoperatively, but it may be over 30 min in patients with uremic platelets [1]. It is the author's opinion that this patient was bleeding from uremic platelets and low VWF and factor VIII levels which led to the initial oozing of blood after incision. This prompted blood transfusion, which led to a coagulopathy resembling DIC from an adverse reaction to the transfusion. DIC has a very broad differential diagnosis and the mainstay of therapy is to treat the underlying cause.

Another possibility is a dilutional coagulopathy that may take place after packed red blood cells are administered without platelets or fresh frozen plasma (FFP). In this case four units of packed red cells were given before any FFP or platelets were given. Factors V and VIII can become diluted when plasma-poor blood is transfused. A dilutional thrombocytopenia may develop; however, it is more common after at least ten units of packed red blood cells has been given.

Finally, the simplest and least complex explanation is that a high concentration of heparin was wrongly used to lock one of the lumens of the Vas-Cath and then flushed into the patient during the induction of anesthesia.

L-6. If the port-to-tip volume = 1.3 and 3 mL of heparin was put in this port, then 1.7 mL (1,700 units) of heparin entered the patient at this point in time. Is this significant?

Since the half-life of heparin is 1 h, there should be very little heparin active in the patient's body several hours later.

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