

A Case of Acute Intravascular Hemolysis During Dialysis: A Quiz

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Clinical Presentation

A woman in her 70s with kidney failure was referred to the emergency room for abdominal pain, nausea, and headache that appeared 10 minutes before the end of an otherwise routine hemodialysis (HD) session. For the past 7 years, she had been coming to a dialysis unit thrice weekly to perform self-care HD via a right internal jugular catheter. She used a Baxter AK98 dialysis machine fitted with a remote operator's panel, which is a model approved by the European Medicine Agency for self-care HD.¹ Her medications included acenocoumarol, aspirin, amiodarone, bisoprolol, calcium acetate, magnesium carbonate, sevelamer, etelcalcetide, and darbepoetin alfa. Immediately after the dialysis session concluded, the patient experienced sudden onset of skin darkening (Fig 1A). When the patient first urinated after completion of the dialysis treatment, she noted a red color to her urine. Blood tests performed 24 hours after the dialysis treatment revealed a normocytic normochromic anemia with a hemoglobin drop from 10.9 g/dL (the value obtained 10 days earlier during routine laboratory testing) to 8.7 g/dL, platelet and leukocyte counts within reference ranges, markedly elevated lactate dehydrogenase (LDH) level of 6,690 IU/L, and concentrations of total and unconjugated bilirubin of 4.6 mg/dL and 3.7 mg/dL, respectively. Peripheral blood smear showed no schistocytes and serum haptoglobin was undetectable. Coombs test was negative. Laboratory values are presented in Table 1.

Based on the clinical presentation and the laboratory findings, the patient was diagnosed with acute intravascular hemolysis. Two units of packed red blood cells were transfused in the following days and the skin pigmentation progressively cleared within 5 days (Fig 1B).

- What is the clinical presentation of acute intravascular hemolysis?
- What is the differential diagnosis of acute intravascular hemolysis during dialysis?
- How should intravascular hemolysis be managed?
- What is the cause of this patient's acute intravascular hemolysis?

Discussion

What is the clinical presentation of acute intravascular hemolysis?

The symptoms of acute intravascular hemolysis are nonspecific and may include nausea, abdominal/back

Table 1. Laboratory Data

Parameter	Value	Reference Range
Hemoglobin, g/dL	8.7	12.2-15
Reticulocyte count, $\times 10^3/\mu\text{L}$	120	30-100
Platelet count, $\times 10^3/\mu\text{L}$	165	150-400
WBC count, $/\mu\text{L}$	7,040	4,000-10,000
Lactate dehydrogenase, IU/L	6,690	<250
Haptoglobin, g/L	<0.1	0.3-2
Total bilirubin, mg/dL	4.6	<1.2
Unconjugated bilirubin, mg/dL	3.7	<0.3
AST, IU/L	465	9-36
ALT, IU/L	38	7-35
Coombs test	Negative	
Schistocytes	Not detected	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell.

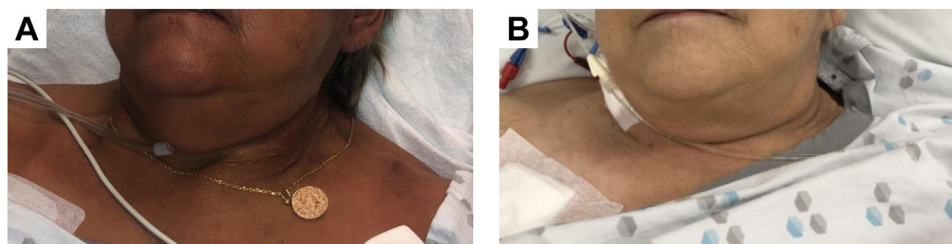


Figure 1. Photographs showing (A) sudden skin hyperpigmentation at the end of the HD session, and (B) complete restoration of the patient's usual skin pigmentation after 5 days.

pain, shortness of breath, headache, dark urine, and chills.² Laboratory findings include anemia, elevated LDH level, and low serum haptoglobin concentration. Sometimes patients may present with sudden darkening of skin pigmentation due to the generation of free hemoglobin, methemoglobin, methemalbumin, and/or hemopexin-heme-containing complexes. Rarely, severe intravascular hemolysis may lead to the release of a large amount of hemoglobin into the urine (hemoglobinuria), which causes the urine to become red colored. Visual inspection of the dialysis circuit may reveal blood that is port wine or cherry colored.

What is the differential diagnosis of acute intravascular hemolysis during dialysis?

Several mechanisms capable of inducing hemolysis during HD have been recognized and these include dialysate contamination with trace metals (copper or zinc) or toxins (eg, chloramine, nitrates), hypo-osmolar dialysate, overheated dialysate, or kinked dialysis blood lines (Box 1). Attempting a high dialysis blood flow with a small gauge needle may also induce hemolysis.³ Several outbreaks of acute intravascular hemolysis attributed to chloramine contamination of dialysis fluid have been reported.^{4–6} Chloramines are the preferred disinfectant for city water supplies owing to long half-life in water and strong bactericidal properties. As neutral, low-molecular-weight compounds, chloramines are not removed by reverse osmosis or deionization. Chloramine is ordinarily removed by adsorption via passage through carbon filters in the water treatment systems.² However,

Box 1. Causes of hemolysis during hemodialysis

•Mechanical/shear stress

- ◊ Kinked tubing, faulty blood tubing
- ◊ High rates of blood flow through smaller gauge needles
- ◊ Partial occlusion of hemodialysis catheter
- ◊ Excessively negative arterial pressures

•Dialysate factors

- ◊ Contamination with zinc, copper, nitrate, formaldehyde, or chloramine
- ◊ Hypotonic dialysate
- ◊ High dialysate temperature

•Patient-specific factors

- ◊ Sickle-cell anemia
- ◊ Hereditary spherocytosis
- ◊ Autoimmune hemolysis
- ◊ Electrolyte abnormalities such as hypophosphatemia

traditional carbon filters may be inadequate when chloramine concentrations are abnormally high, or in the case of an exhausted carbon filter. For this reason, carbon filters are usually connected in series.²

Inadvertent use of hypotonic or deionized dialysate and faulty conductivity monitoring may also lead to fatal hemolysis owing to osmotic injury. Use of hypotonic dialysate will lead to a sudden drop in serum osmolar concentration, which causes a shift of water into red blood cells and their subsequent lysis.⁵ When acute intravascular hemolysis occurs in an individual patient within a dialysis unit, kinked dialysis blood lines or dialysis with a small gauge needle should be considered.

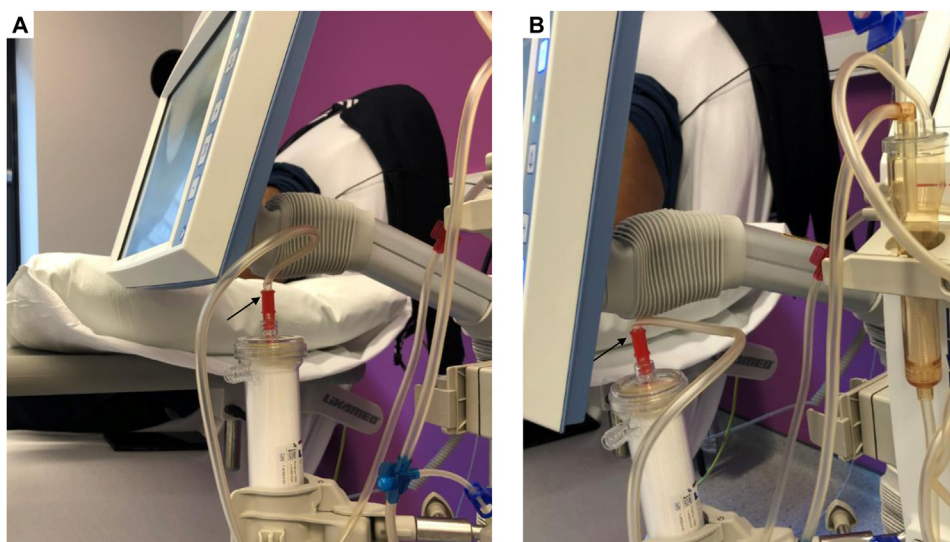


Figure 2. Demonstrations of kinking introduced to the blood lines when the remote operator's panel is positioned adjacent to the dialysis cartridge. Note that the remote operator's panel has been installed on the same side of the HD machine as the cartridge.

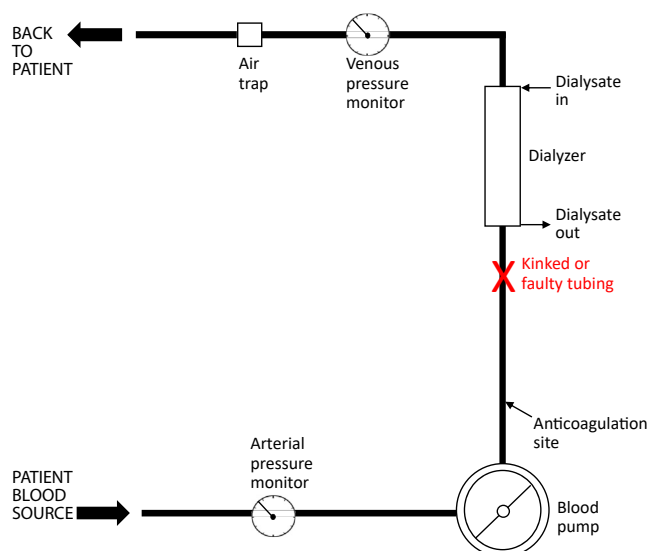


Figure 3. Schematic representation of the dialysis circuit. When a kink occurs between the pump and the cartridge, the increased pressure in the tubing is transmitted to the blood pump but not to the pre-pump arterial pressure monitor. If the blood pump does not have an alarm, a kink in the tubing immediately after the blood pump may not trigger an alarm. [Video S1](#) provides a demonstration of this behavior. When the remote operator's panel of the Baxter AK98 dialysis machine is positioned to create a kink in the line after the blood pump, the alarm from the arterial pressure monitor is not triggered. By contrast, when the line is clamped before the blood pump, the arterial pressure monitor alarm is triggered.

How should intravascular hemolysis be managed?

When hemolysis is suspected, the HD session should immediately be interrupted and blood from the circuit discarded. Returning the blood to the patient can lead to severe hyperkalemia by infusing potassium released from hemolyzed erythrocytes. To confirm the diagnosis, laboratory tests including a hemolytic panel (LDH, haptoglobin, reticulocyte count, bilirubin, schistocytes count, Coombs test) should be ordered. Massive hemolysis can be complicated by arrhythmias, acute coronary syndromes, profound anemia, severe necrotizing pancreatitis (thought to be due to a release of proinflammatory cytokines), and death.² Depending on the severity of symptoms, referral should be made to the emergency room or intensive care unit for close monitoring. In our case, laboratory values returned to reference ranges and skin pigmentation resolved within a few days without further intervention.

What is the cause of this patient's acute intravascular hemolysis?

Because no other patient in the dialysis unit experienced acute intravascular hemolysis during the dialysis session, chloramine contamination of dialysate water or hypotonic dialysate use was unlikely. Use of a small gauge needle was also ruled out as a cause of acute intravascular hemolysis because the patient was dialyzed through a catheter. We hypothesized that the acute intravascular hemolysis was due to kinking in the

dialysis circuit blood lines caused by the positioning of the remote operator's panel, a movable screen that can be maneuvered near to the patient to allow control of self-care dialysis settings. [Fig 2](#) shows how this might occur, and the schematic in [Fig 3](#) illustrates that severe kinking in the blood line just after the pump segment would be expected to cause a back pressure without triggering the pressure alarms.⁶ Currently, the manufacturer's instructions state the remote operator's panel may be installed on either side of the HD machine. However, a kink at this location in the blood lines is only possible when the panel is installed on same side of the machine as the dialysis cartridge. Although we did not witness a kink in the blood line and cannot prove that the intravascular hemolysis in this case was due to this proposed mechanism, we suggest that the remote operator's panel should be installed on the side of the machine opposite to the dialysis cartridge.

Final Diagnosis

Intravascular hemolysis during dialysis owing to a kink in the dialysis line.

Supplementary Material

Supplementary File (MP4)

Video S1: Demonstration of differing alarm behavior of Baxter AK98 dialysis machine depending on whether kink is before or after the blood pump.

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