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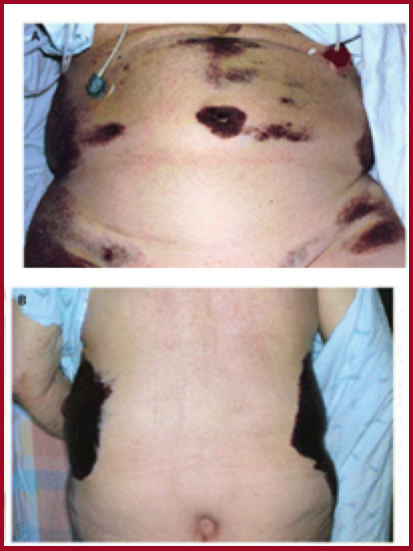
EM CASE OF THE WEEK

BROWARD HEALTH MEDICAL CENTER DEPARTMENT OF EMERGENCY MEDICINE



The above pictures show Cullen's sign and Grey-Turner's sign, findings that suggest possible abdominal bleeding. It is important to recognize these signs and work quickly to manage the patient's bleeding, especially if they are anticoagulated.

EM CASE OF THE WEEK

EM Case of the Month is a monthly "pop quiz" for ED staff. The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

Abdominal Bleeding on Warfarin

A 67 year old female with a history of hypertension and on Warfarin for a mechanical mitral valve replacement presents to the North Broward ER with abdominal pain after coughing. The abdominal pain has been present for two days, is constant and crampy, and located in the left lower quadrant and flank area. On exam she is calm and cooperative, with a positive Cullen's sign and tenderness to palpation in the LUQ and LLQ over a palpable mass. A CT scan shows extensive left rectus abdominal wall extraperitoneal hematoma and a pancreatic tail mass. She is afebrile with a HR of 70 in atrial fibrillation, and a blood pressure of 111/53. Her INR is 2.7 and her hemoglobin is 10.3.

What is your next step in management?

a) Book an OR; she needs emergency surgery.
b) Begin gently reversing her Warfarin with fresh frozen plasma and a slow vitamin K infusion.
c) Hold her Warfarin for a few days while monitoring daily INR.
d) Continue her Warfarin, get a type and cross to prepare for a blood transfusion.
e) Check a lipase, start fluids and IV pain meds.

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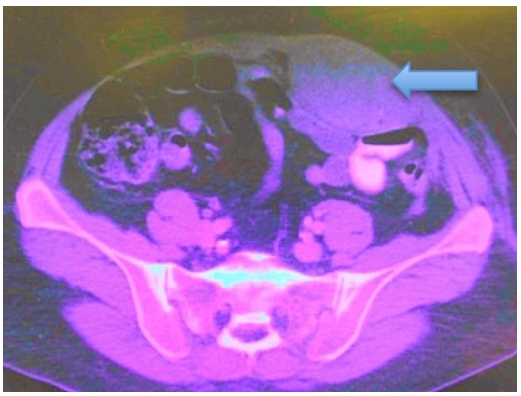

CT showing L rectus abdominus hematoma

Take Home Points

- Cullen's sign (periumbilical ecchymosis) and Grey-Turner's sign (flank ecchymosis) are physical exam findings that can indicate an abdominal bleed or a necrotizing pancreatitis.

- Life threatening differential diagnoses include ruptured aortic aneurysm, ruptured ectopic pregnancy, necrotizing pancreatitis, or other serious abdominal bleed.

- When correcting INR in a patient who is bleeding or has a supratherapeutic INR: If the INR is **<5 with no bleeding**, decrease or hold Warfarin dose. If the INR is **5-9 with no bleeding**, hold the next dose. If the INR is **>9 with no or little bleeding**, give FFP 2u and oral vitamin K. If there **is serious bleeding**, give FFP 4u and vitamin K 10mg slow IV infusion. If there **is life-threatening bleeding** regardless of INR, consider recombinant factor VIIa or PCC.

Abdominal Bleeding

The correct answer is C. Our patient was bleeding into her rectus abdominus muscle quite extensively, but it appeared to be a slow process; her vitals were stable and her hemoglobin had not dropped significantly. Because she was on Warfarin checking her INR was a very important step. As it was still in the therapeutic range (2-3) according to the American College of Chest Physicians guidelines there was no need to actively reverse her anticoagulation, but merely to decrease or pause her dose until the bleeding stopped.

What happened?

- She was admitted and remained stable. She was given a unit of blood and her warfarin dose was held for the next three days; her INR decreased to 1.2.
- She was not considered a surgical candidate and was observed for a few days before being sent home back on warfarin with a lovenox bridge, with instructions to follow up promptly with her cardiologist for adjustment of her warfarin dose, and for the pancreatic mass.

Cullen Sign and Grey-Turner Sign:

- This bruising along the flanks represents blood tracking from a retroperitoneal or intraperitoneal bleed.
- Grey-turner sign was first recognized as a sign of acute pancreatitis in 1920. The pancreatic inflammation spreads from the fascia behind the kidneys to the edge of the quadratus lumborum. Grey-Turner sign in acute pancreatitis confers a very poor prognosis. Cullen's sign in pancreatitis is caused by extension of fluid and inflammation from the gastrohepatic ligament and across the falciform ligament.
- Other signs of retroperitoneal hematoma include Fox's sign (ecchymosis of the proximal thigh) and Bryant's sign (discoloration of the scrotum).

Differential:

- Necrosis of the pancreas during acute necrotizing pancreatitis can present with a retroperitoneal bleed represented by Cullen's or Grey-Turner's sign.
- Ovarian cyst rupture with significant intraabdominal hemorrhage can also present with these signs.
- A splenic rupture is also a possibility; to be considered during a mononucleosis infection.
- Ruptured ectopic pregnancy is an important differential not to overlook in women of childbearing age.

Warfarin Basics:

- Vitamin K antagonist used commonly for the treatment of atrial fibrillation, mechanical valves, and clotting disorders.
- After beginning warfarin its anticoagulation should be effective within 2-7 days.
- If INR is stable, it can be checked as infrequently as every month.
- Risk of clot increases as INR <2, and risk of bleeding increases as INR increases >4 and 5.
- Patients that employ more frequent self-testing were more successful with INR management than those managed by physicians less frequently, and roughly the same as those managed at a Warfarin clinic.

Warfarin Reversal:

- The American College of Chest Physicians published the basic guidelines of reversal in the state of supratherapeutic INR.
- The three steps are decreasing or holding the Warfarin dose, giving vitamin K oral or IV, and giving fresh frozen plasma (FFP).
- Physicians are often too eager to reverse the anticoagulation, when in fact the chance of bleeding with a supratherapeutic INR is relatively low (1% chance in 30 days with INR of 5-9).
- A high dose of vitamin K can take up to a week to reverse, putting the patient at risk for clotting.
- In urgent situations like a brain bleed, 4-factor or 3-factor prothrombin concentrate complex (PCC) can be given. 4-factor is preferred (contains factors II, VII, IX, and X). 3-factor contains II, IX, and X, and should be given with FFP or recombinant factor VII.

A Brief Note on TSOACs

- Target Specific Oral Anticoagulants (TSOACs): dabigatran and the Xa inhibitors (rivaroxaban, apixaban, edoxaban).
- Dabigatran level can be assessed sometimes by thrombin time; Xa inhibitor activity is measured for the others. Levels in general are estimated based on the time of the last dose and renal and hepatic clearance ability.

TSOAC (cont.)

- There is no immediate reversal agent for these medications.
- If the last dose was within a few hours, activated charcoal can be used for both dabigatran and the Xa inhibitors.
- Options for reversal during serious bleeding include PCC, anti-fibrinolytic agents, and hemodialysis (dabigatran only).

TABLE 1: Vitamin K Dosing for Elevated INRs OR BLEEDING in Patients on Warfarin (1-7)

Condition	Intervention
INR > goal but < 5 **No significant bleeding or risk of bleeding**	• Lower dose or omit next dose
INR ≥ 5 or < 9 **AND** **No significant bleeding or risk of bleeding**	• **Preferred:** Omit next 1-2 doses • Alternatively, omit 1-2 doses and give Vitamin K (1-2.5 mg po) • Alternatively for patients at high risk of thrombosis (i.e. valves), omit 1-2 doses and use FFP 2 units IV – DO NOT use Vitamin K
INR ≥ 9 **No significant bleeding** **AND/OR** **Low-moderate risk of bleeding**	• Hold warfarin therapy • Give FFP 2 units IV • Give Vitamin K (2.5-5 mg po) • In patients with prosthetic heart valves, give FFP 2 units IV and lower dose of Vitamin K (1-2.5mg po)
Serious bleeding at any elevation of INR **AND/OR** **High risk of bleeding**	• Hold warfarin therapy. • Give FFP 4 units IV • Vitamin K 10mg by slow IV infusion • May repeat FFP and Vitamin K as needed • In patients with prosthetic heart valves, FFP is *preferred* over Vitamin K; use only very low doses of Vitamin K (1mg by slow IV infusion).
Life-threatening bleeding	• Hold warfarin therapy. • Give FFP 4 units IV • Vitamin K 10mg by slow IV infusion • Consider recombinant Factor VIIa for unresolved coagulopathy • Repeat FFP and Vitamin K as needed

INR = international normalized ratio FFP = fresh frozen plasma

References:

1. Mookadam, F.Cikes, M. Cullen's and Turner's signs. *N Engl J Med*. 2005;353:1386.
2. Chhabra, P et al. Grey-Turner's sign in acute necrotizing pancreatitis. *Annals of Gastroenterology.* 2015; 28(1): 147.
3. Sugimoto, M et al. MPR-hCT imaging of the pancreatic fluid pathway to Grey-Turner's and Cullen's sign in acute pancreatitis. *Hepatogastroenterology.* 2005; 52(65): 1613-6.
4. Jim, J; Thompson, R. Clinical features and diagnosis of abdominal aortic aneurysm. Aug 20, 2014. UpToDate.
5. Hirsch, J et al. American Heart Association/American College of Cardiology Foundation Guide to Warfarin Therapy. *Circulation*; 2003; 107; 1692-1711.
6. Garcia, D;Crowther, M. Management of bleeding in patients receiving target-spcific oral anticoagulants. UpTodDate.

This week's case was prepared by Avalon Mertens. Avalon rotated at the Broward North ER in February, 2015, and is pursuing a combined residency in medicine and pediatrics in July.