June 2018 Critical Care Case of the Month

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History of Present Illness
A 60-year-old native American man presented to an outside hospital with several days of nausea, vomiting and diarrhea. The patient felt weak and called emergency medical services and was taken to the emergency department.

Past Medical History
He has a history of end stage renal disease secondary to diabetes mellitus and hypertension. He received a cadaveric renal transplant in 2008 which was complicated with acute on chronic rejection and symptomatic hyponatremia.

Physical Examination
His pulse was recorded as 28 beats/min and his blood pressure was 90/60.

Which of the following ***should be done***?

1. Administer atropine
2. Begin transcutaneous pacing
3. Obtain a drug history
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

An electrocardiogram was obtained which showed sinus bradycardia. Atropine is the first drug of choice for symptomatic bradycardia (1). The dose is 0.5mg IV push and may repeat up to a total dose of 3 mg. He responded with an increased in both heart rate and blood pressure. A review of his drugs revealed that he had been prescribed carvedilol, valsartan, prednisone, and tacrolimus. Initial laboratory revealed a Na+ 115 mEq/L, K+ 6.4 mEq/L, HCO3- 12 mEq/L, blood urea nitrogen (BUN) 70 mg/dL, and serum creatinine (SCr) of 3.16 mg/dL. His baseline Na+ was 120-130s mg/dL and SCr ~2 mg/dL.

He was transferred to Banner University Medical Center Phoenix for further care.

Which of the following ***should be done***?

1. Administer normal saline
2. Administration of an AVP receptor antagonist with rapid correction of his hyponatremia to 135 mEq/L
3. Hold his beta blocker
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

The most likely cause of his bradycardia is the beta blocker. This was held and his symptomatic bradycardia resolved over several hours. His hyponatremia should not be rapidly corrected because rapid correction can result in osmotic demyelination syndrome (ODS) (2). His hyponatremia should be corrected slowly at 4-8 mEq/L per day. Vasopressin receptor antagonists (vaptans) should not be used in hypovolemic hyponatremia, or in conjunction with other treatments for hyponatremia (2). One could administer limited amounts of 3% saline with careful monitoring of his serum sodium but that is not given as one of the options.

He is monitored in the intensive care unit and his serum sodium slowly rises. However, over several days his platelet count slowly decreased (Figure 1).

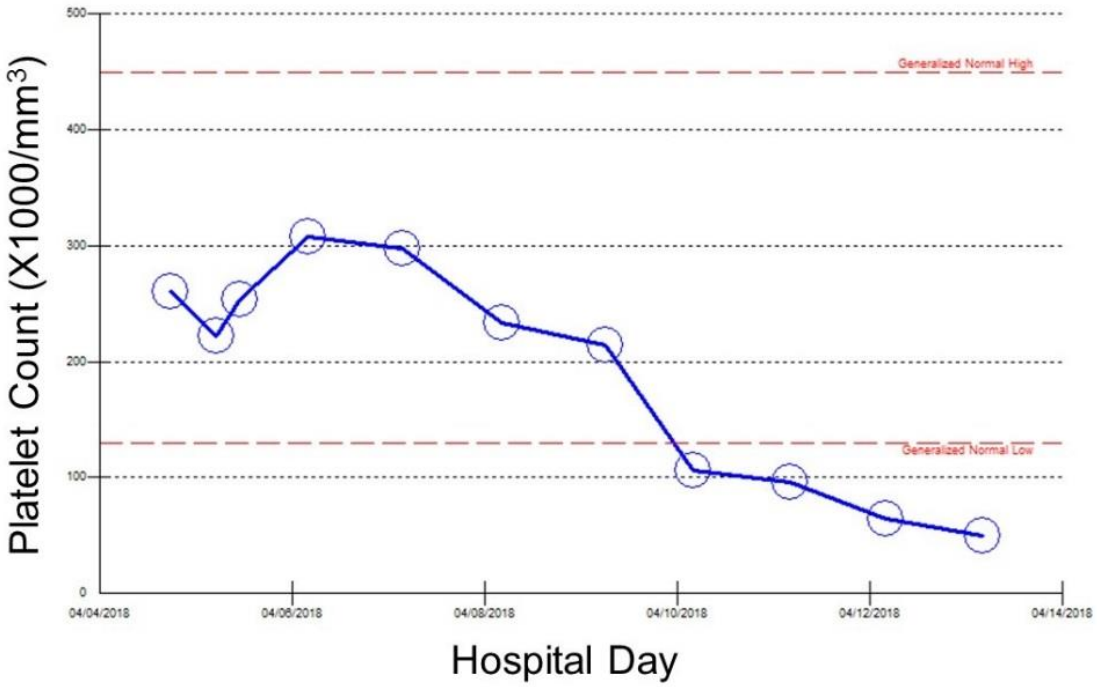

Figure 1. Platelet count over initial days of hospital admission.

Accompanying the decrease in platelets was an increase in the white blood cell count to over 30,000 cells/mm^3.

What should be ***done at this time***?

1. Examine the peripheral smear
2. Stool sample for *H. pylori*
3. Stop any heparin administration
4. 1 and 3
5. All of the above

Correct!
5. All of the above

Thrombocytopenia is common in the ICU and is associated with many severe illnesses (3). Most agree that examining the peripheral smear is important in evaluating thrombocytopenia. One algorithm which has been proposed to work up thrombocytopenia is shown in Figure 2.

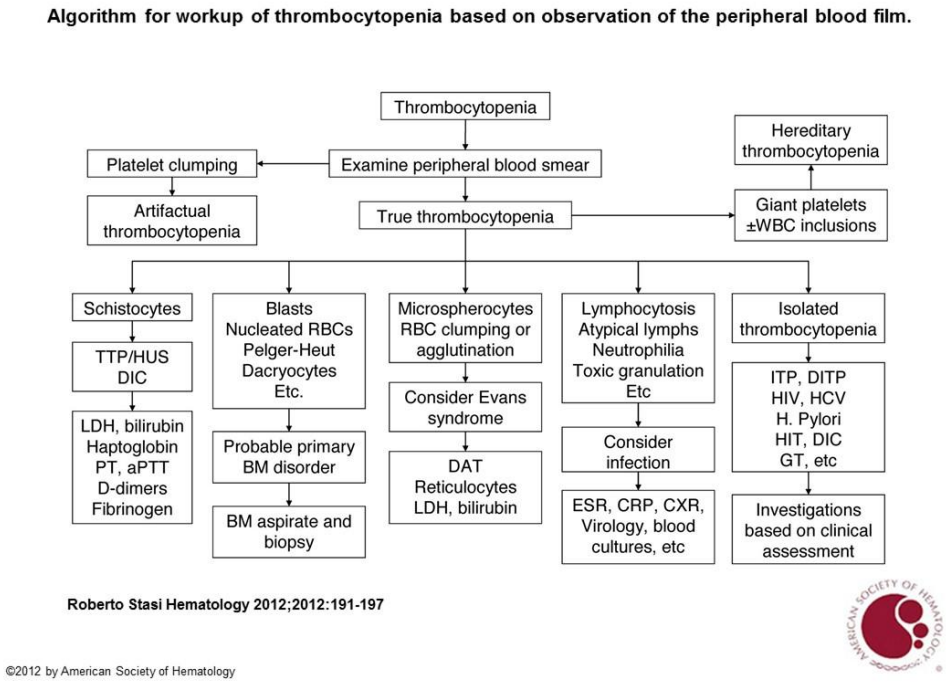

Figure 2. Algorithm for thrombocytopenia workup. See article for abbreviation definitions.

H. pylori has been associated with thrombocytopenia and our patient presented with diarrhea, although this had largely resolved. In addition, heparin-induced thrombocytopenia (HIT) is fairly common in the ICU and a true medical emergency. Our patient's *H. pylori* was negative and his immunoassay for antibodies against heparin/platelet factor 4 (PF4) complexes were also negative.

His peripheral smear showed the presence of 1+ schistocytes.

Which of the following ***should be done next***?

1. Fibrinogen level
2. Measure (ADAMTS13) activity
3. Tacrolimus level
4. 1 and 3
5. All of the above

Correct!
5. All of the above

The presence of schistocytes suggests a microangiopathic process with intravascular hemolysis. In this clinical situation this suggests disseminated intravascular coagulation (DIC) or thrombotic thrombocytopenic purpura (TTP). The pathogenesis in DIC is a thrombin excess with evidence of diffuse consumptive coagulation (elevated PT, PTT, fibrin degradation products, D-dimers but decreased fibrinogen). In contrast, the pathogenesis in TTP is an endothelial defect and most of the parameters that are grossly abnormal in DIC are either normal or only slightly abnormal. Additional diagnoses that should be considered in patients presenting with an acute thrombotic microangiopathy (TMA), especially in those in whom levels of ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) activity are nondeficient (>10%) including drug-induced thrombotic microangiopathy (4).

Our patient had an ADAMTS13 above 10% (40%), a normal fibrinogen level but a slightly elevated tacrolimus level of 16.2 ng/ml (usual preferred range 5-15 ng/ml).

What should be ***done next***?

1. Begin cyclosporine for prevention of rejection
2. Begin vincristine
3. Discontinue the tacrolimus
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

The patient's course was most consistent with drug-induced microangiopathy secondary to tacrolimus (5). His tacrolimus was stopped and his immunosuppression switched to prednisone and cyclosporine. However, his platelet count did not increase within two days. Since there have been some anecdotal reports of drug-induced thrombotic microangiopathic thrombocytopenia improving with plasma exchange, this was initiated (5). The platelet count slowly rose over several days and a dose of rituximab was administered when the progress seemed slow (Figure 3).

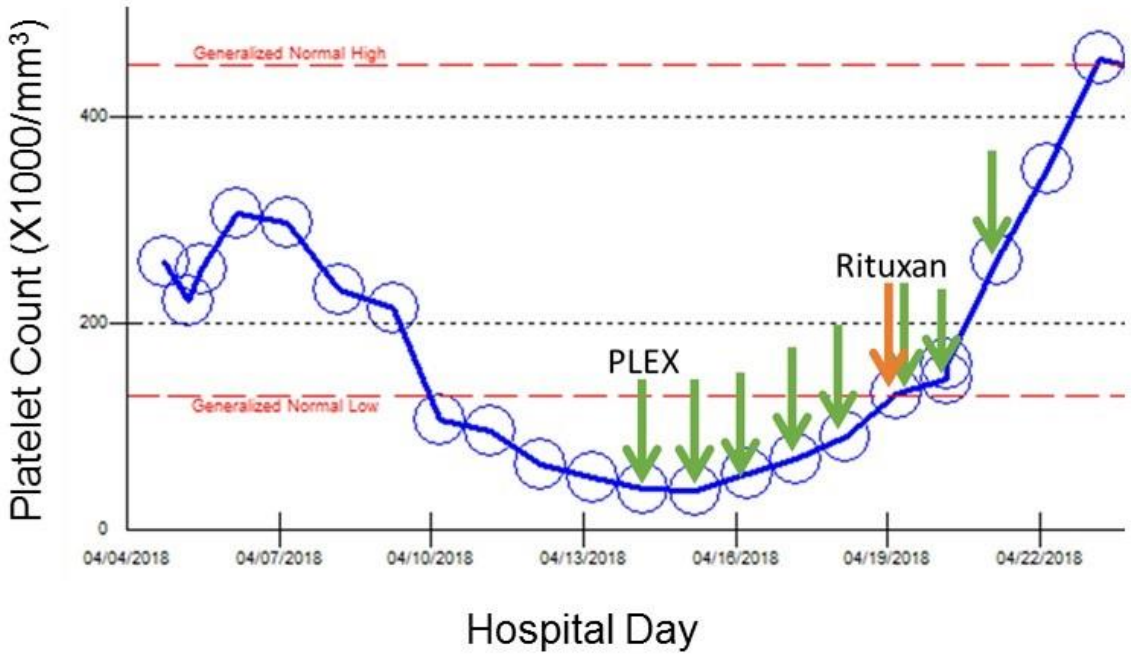

Figure 3. Platelet counts over hospital course. Plasma exchange (PLEX) was performed at the green arrows and a dose of rituximab given at the orange arrow.

The patient had no recurrence of his thrombocytopenia and was discharged on prednisone and cyclosporine in addition to an angiotensin receptor blocker and a lower dose of beta blocker.

References

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