Management of Immune Thrombocytopenia in an Unplanned Pregnancy

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Thrombocytopenia

- A deficiency of platelets in the blood below the reference range for a specific laboratory
  - A platelet count <100 x 10^9 /L
    - Defined by International Working Group
      - American Society of Hematology
- It is not a disease but a symptom of an underlying condition

Platelet Count

150,000-450,000 is normal

Minimum of 50,000 or higher

- Bleeding usually not seen with trauma or procedure

10,000-50,000

- Bleeding seen with trauma or procedure

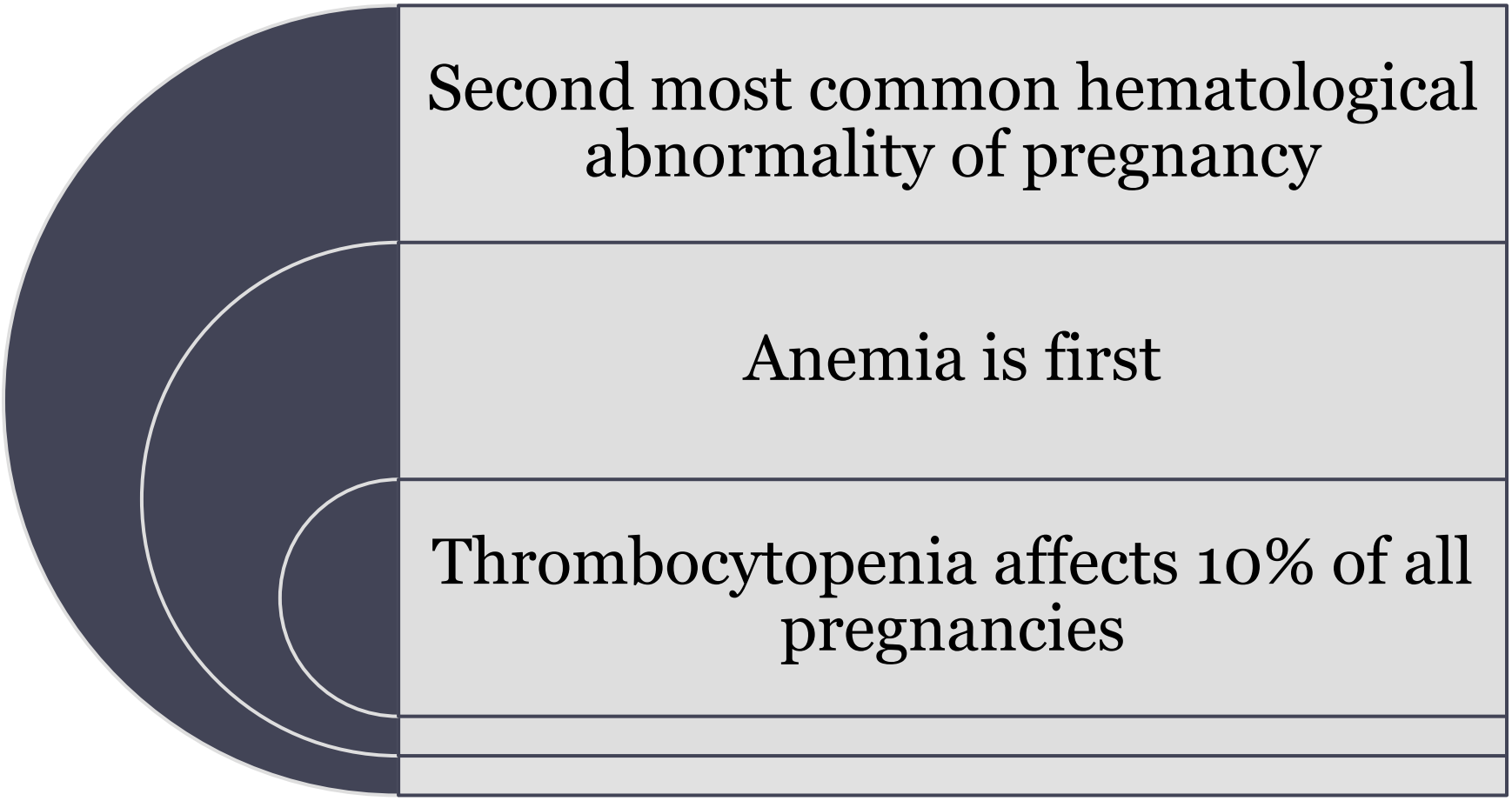
5,000-10,000

- Risk of spontaneous bleed

<5,000

- Very high risk for spontaneous bleed

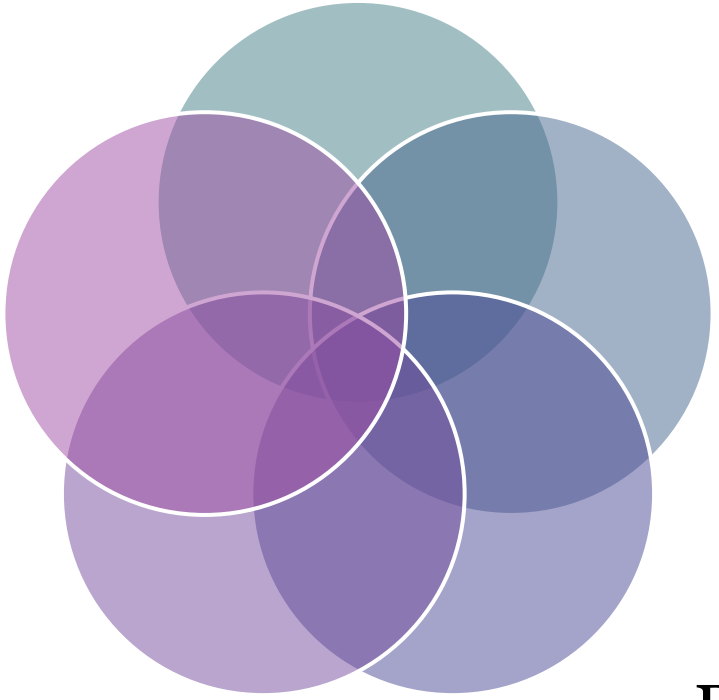
Thrombocytopenia in Pregnancy



Basic Recommended Lab Tests

Complete Blood Count

Viral Screening for HIV, HCV and HBV



Reticulocyte Count

Liver Function Tests

Peripheral Blood Smear

Potential Causes of Thrombocytopenia in Pregnancy

Gestational Thrombocytopenia (5-9%)

- Most common cause of thrombocytopenia in pregnancy 2nd and 3rd trimester
- Diagnosis of exclusion, mechanism unknown
- Hemodilution and accelerated clearance of platelets is suspected as cause

Potential Causes of Thrombocytopenia in Pregnancy

Severe Preeclampsia (5-8%)

- High blood pressure after 20 weeks gestation
- Proteinuria
- Thrombocytopenia is one of the diagnostic criteria for severe preeclampsia

Potential Causes of Thrombocytopenia in Pregnancy

HELLP Syndrome (0.6%)

- Hemolysis, Elevated Liver enzymes and Low Platelets
- Distinguished from preeclampsia by the presence of hemolysis and elevated liver enzymes
- Microangiopathic Hemolytic Anemia
- 3rd Trimester
- Treatment is corticosteroid therapy

Potential Causes of Thrombocytopenia in Pregnancy

AFLP (<0.01%)

- Acute Fatty Liver of Pregnancy
- Elevated liver enzymes and conjugated bilirubin
- Overlapping symptoms with HELLP but thrombocytopenia is present less than half of the time
- 3rd trimester

Potential Causes of Thrombocytopenia in Pregnancy

TTP(<0.01%)

- Thrombotic Thrombocytopenia Purpura
  - Congenital deficiency/inhibitor of ADAMTS13 gene
- Microangiopathic Hemolytic Anemia may be pre-existing condition
- Most common onset second trimester
- Therapeutic plasma exchanges can improve outcomes

Potential Causes of Thrombocytopenia in Pregnancy

aHUS (<0.01%)

- Atypical Hemolytic Uremic Syndrome
  - Complement dysregulation
- Microangiopathic Hemolytic Anemia
- Most common onset postpartum
- Therapeutic plasma exchanges can improve outcomes

Potential Causes of Thrombocytopenia in Pregnancy

ITP (<1%)

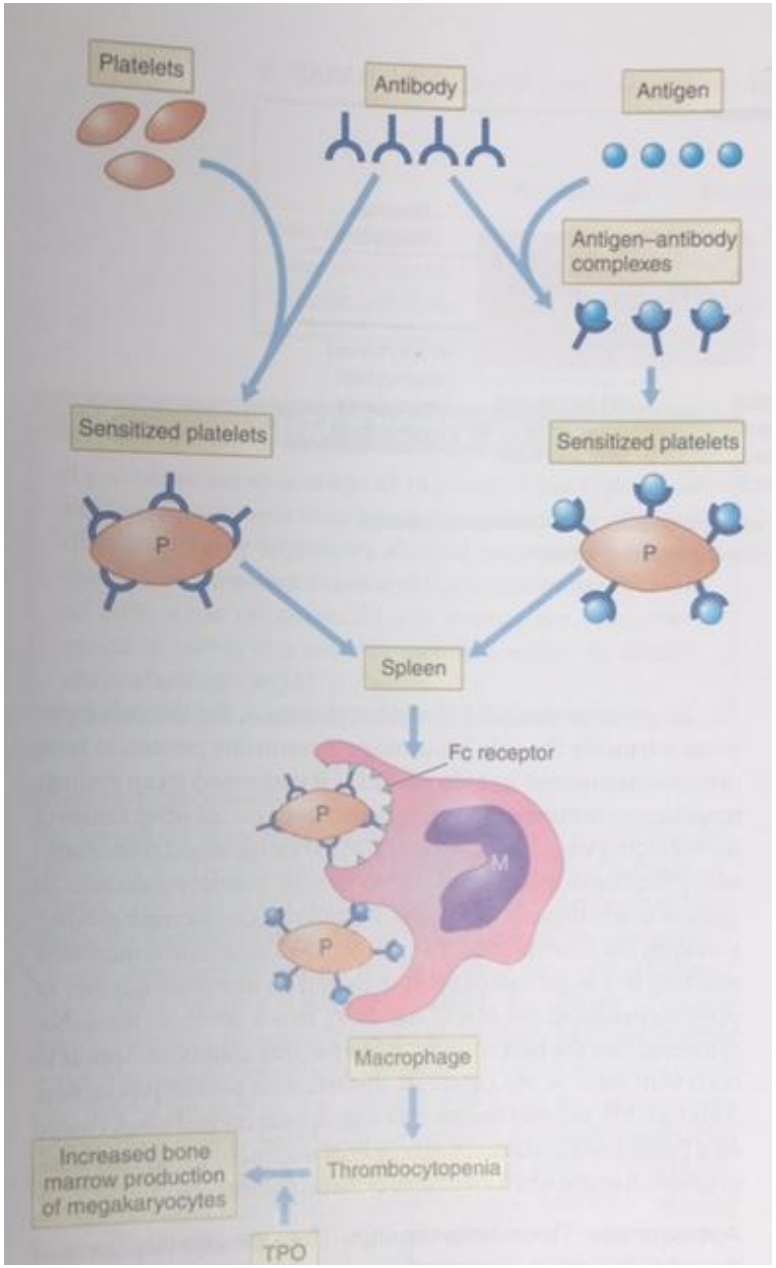
- Idiopathic Thrombocytopenia Purpura
- Immune Thrombocytopenia
- Pre-existing condition diagnosed by exclusion or onset occurs most commonly in the first trimester

Immune Thrombocytopenia in Pregnancy

Autoimmune disease

IgG anti-platelet auto-antibodies	Decreased platelet production	Abnormal regulatory T cells	Loss of T cell tolerance to platelet antigens

Antibody coated platelets are removed by binding to splenic macrophages via the Fcγ receptor



ITP and Complications to Fetus/Neonate

Risk of Fetal Thrombocytopenia

Intracranial hemorrhage during delivery (Rare)

Maternal IgG cross placenta and may bind to fetal platelets

Mothers platelet count and antiplatelet IgG levels are not predictive of platelet count of fetus

Fetal scalp sampling or percutaneous umbilical blood sampling is not predictive of neonatal thrombocytopenia and is not recommended

Case Study

Historical Lab Data Pre-pregnancy

- At ~ age 8 yrs platelet count was 398,000
- Initial diagnosis of ITP was ~ age 13yrs
- At ~16yrs went to specialist, platelet count was 16,000

  HBG: 10.8g/dL (Low)
  HCT: 30.9% (Low)
  Smear indicated insufficient platelets
  LDH minimally elevated
  Remainder of CBC was normal
  CMP was normal
  Physical was normal, obesity was noted
- Treatment was IVIG 1gram/kg for Chronic ITP
- Patient is O positive

Treatment of ITP

Corticosteroids

- Inhibits the phagocytosis of opsonized platelets
- Impairs autoantibody production
- Prednisone 1 mg/kg/day; reduced to lowest effective dose

IVIG

- Works by overwhelming the spleen with antibody to the point where it stops targeting antibody coated platelets
- Rapid short term increases in platelet count seen

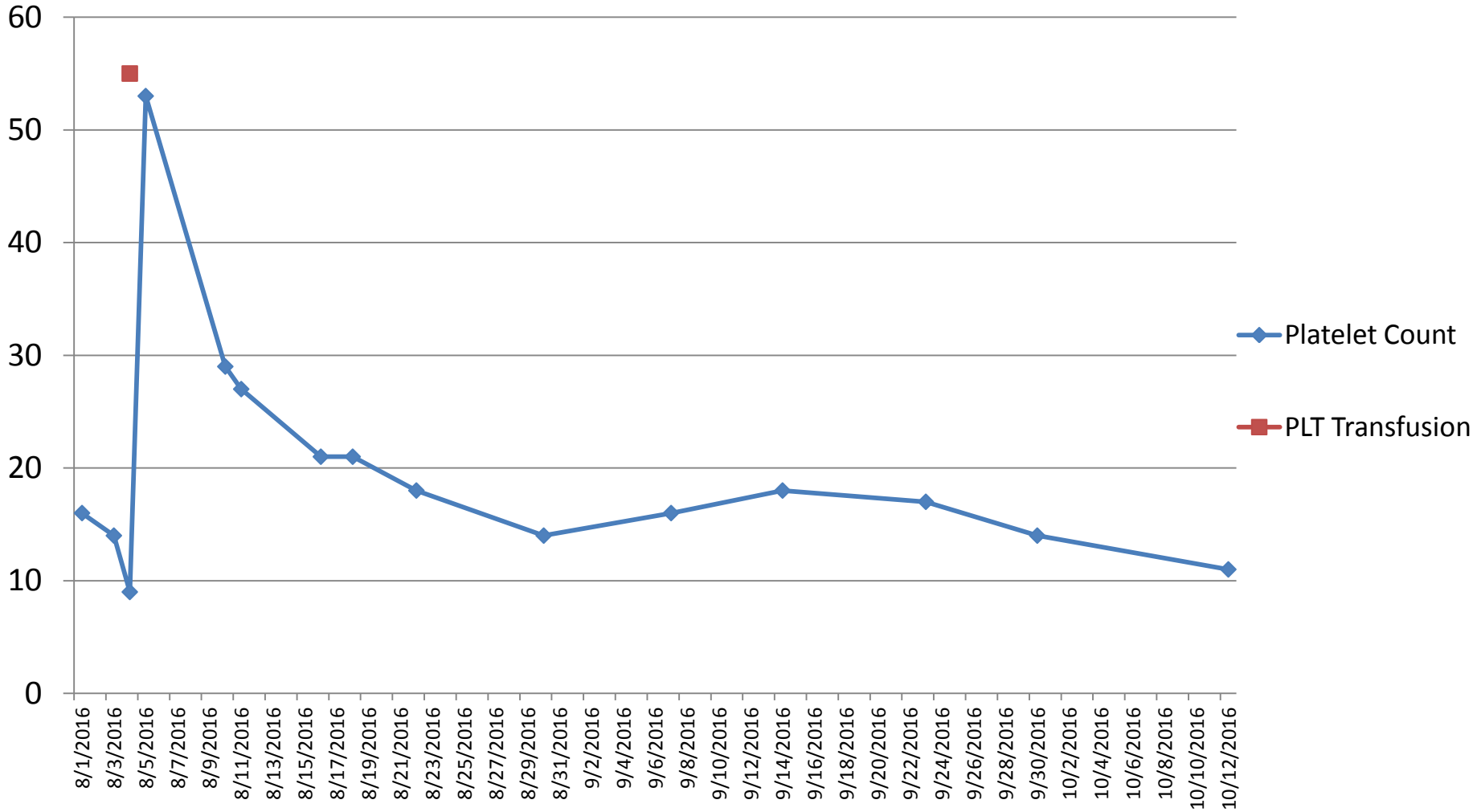
Drugs

- Rituximab, Cyclosporine, Azathioprine etc.

Surgery

- Splenectomy or partial embolic splenectomy

Pre-Pregnancy Platelet Counts



Initial Pregnancy Consultation

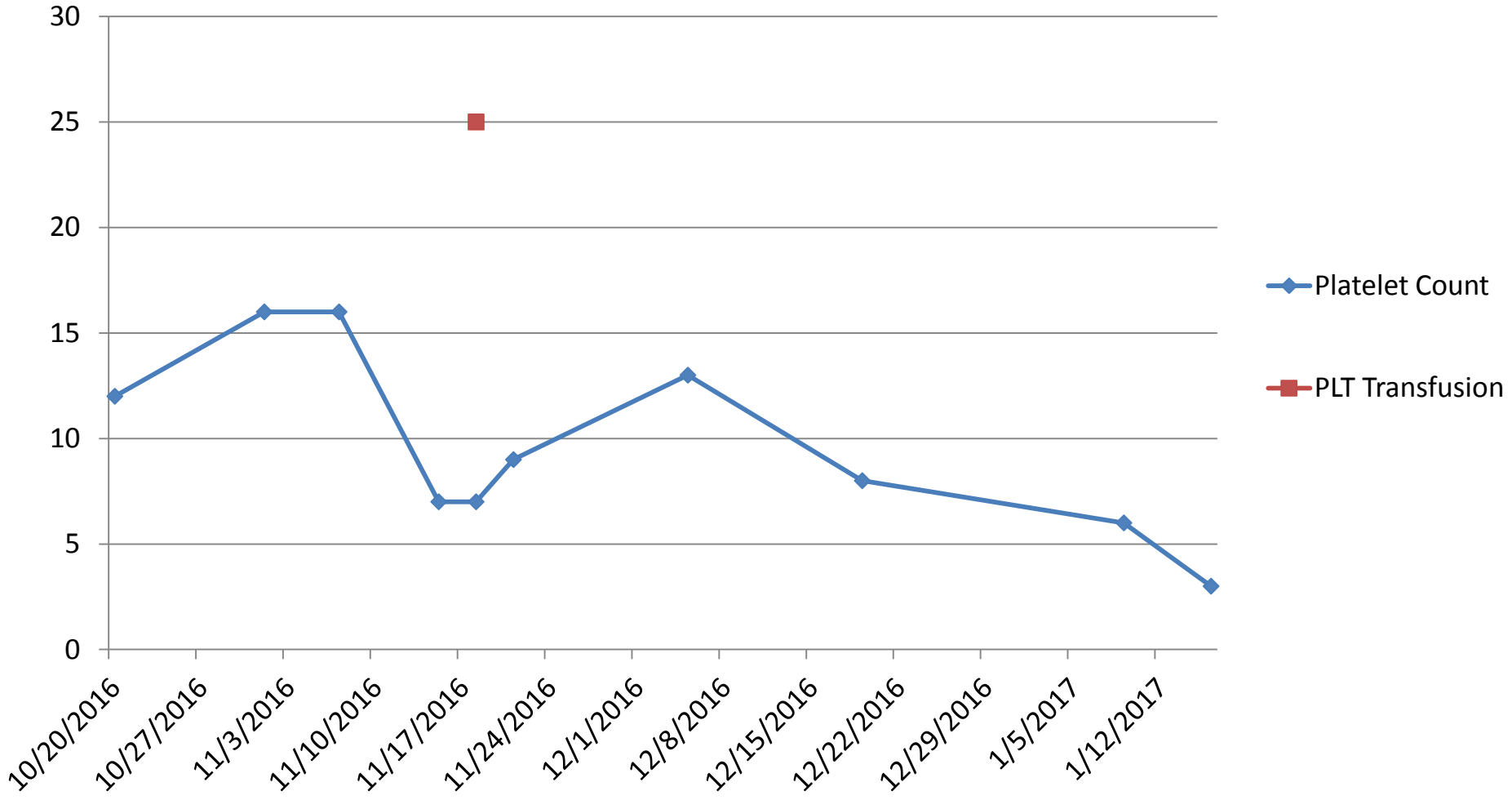
Unplanned pregnancy at age 16yr

Consulted about the high risk nature of teenage pregnancy

Consulted about high risk nature of pregnancy with ITP

Was advised to seek prenatal care in St. Louis due to the delays in transport, >2hrs, for platelets to arrive at smaller hospital in an emergency

3 Months post Dx of Pregnancy



Treatment Recommendations

- Treatment has been recommended for pregnant women with platelet counts 10,000/uL anytime during the pregnancy or below 30,000/uL in 2nd trimester
  - **Corticosteroids and IVIG**
    - **Corticosteroids have been linked to congenital anomalies such as orofacial clefts**
- Splenectomy 2nd trimester for patients who fail to respond to Steroids and IVIG
  - **75% experience remission after splenectomy**
- Some drugs such as danazol, cyclophosphamide and vinca alkaloids are potential teratogens

2nd Trimester Partial Embolic Splenectomy

Now 17 yrs old

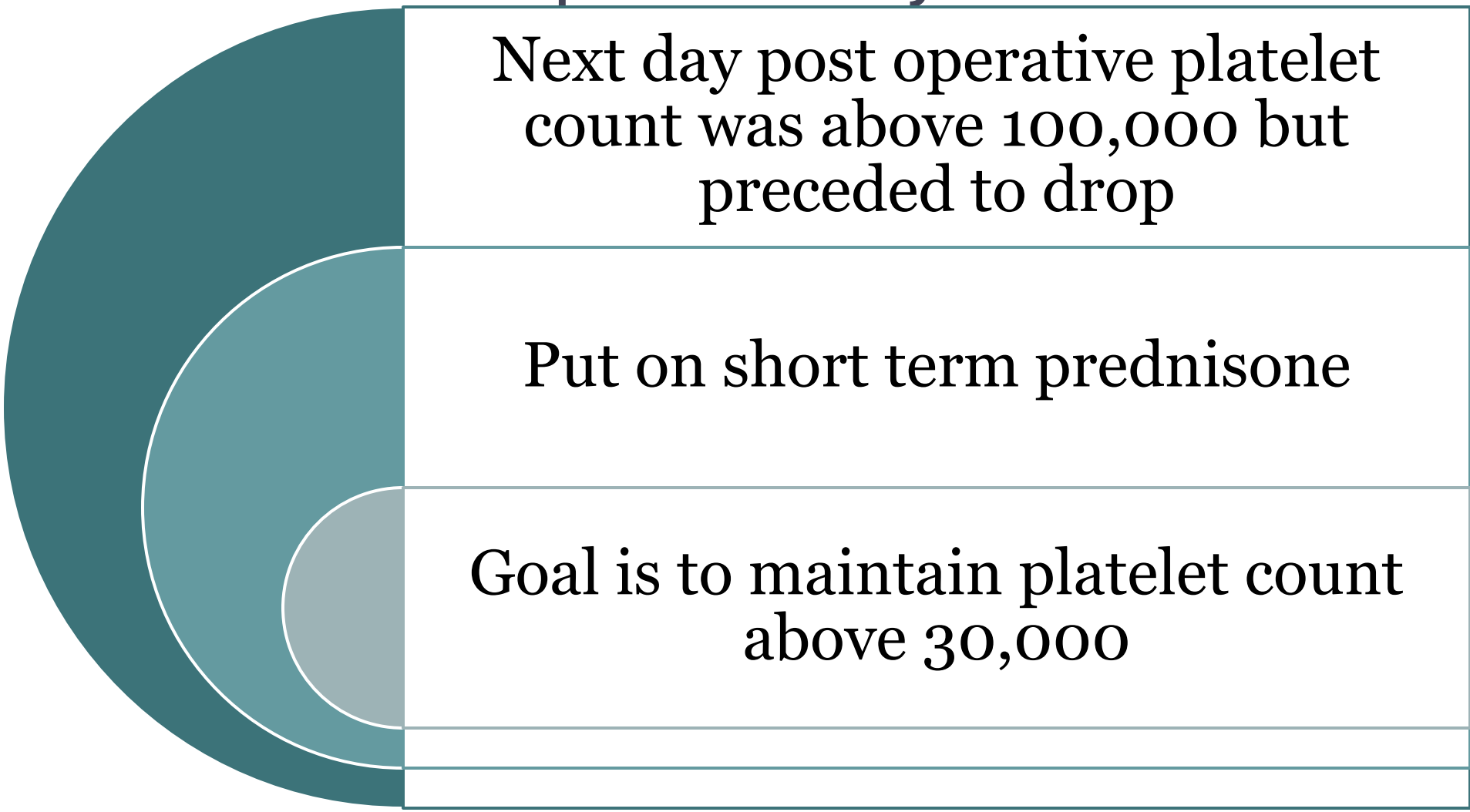
Persistent platelet counts less than 10,000

Completely refractory to oral steroids and IVIG

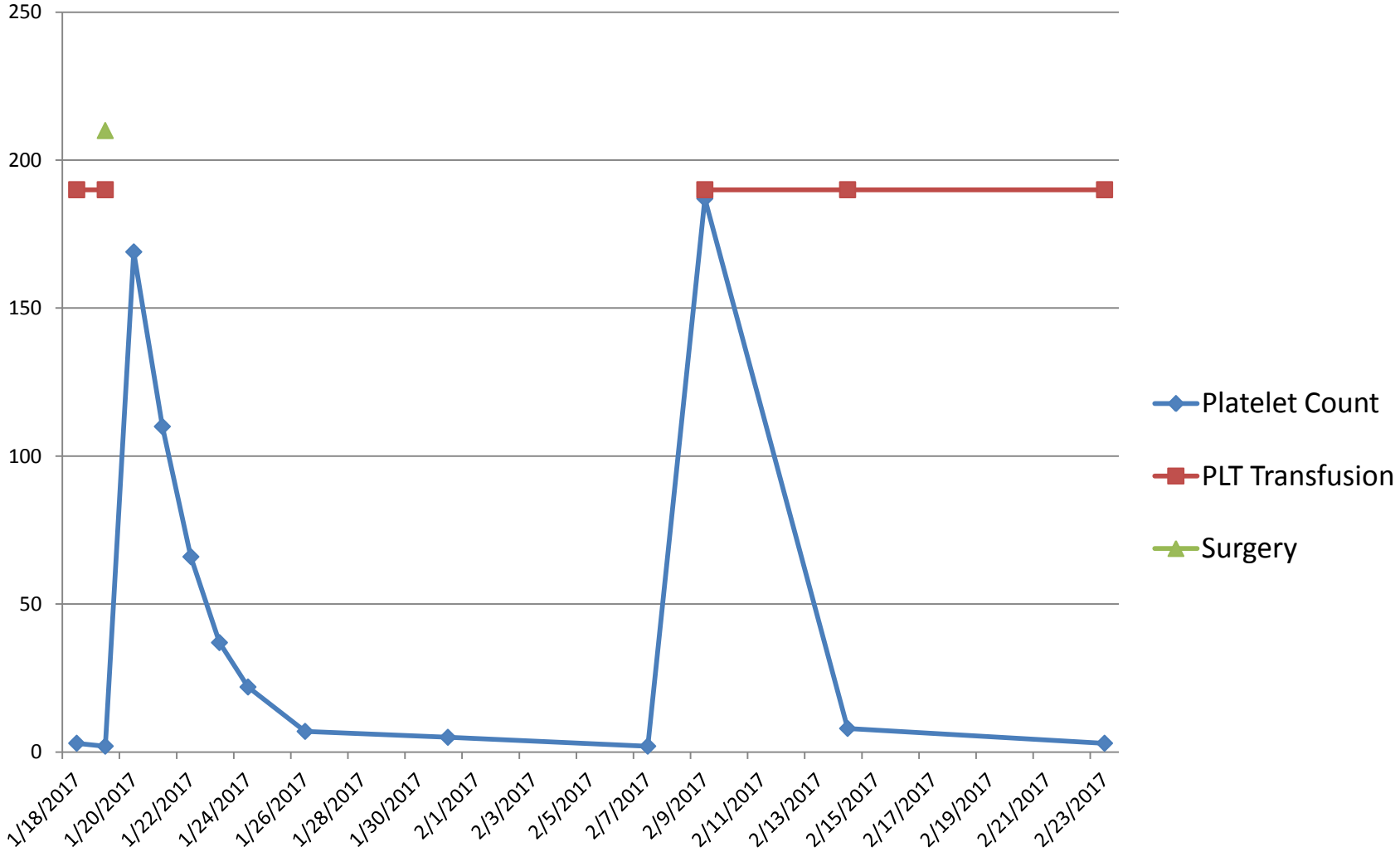
Started on a continuous platelet infusion

Underwent partial embolic splenectomy

2nd Trimester Partial Embolic Splenectomy



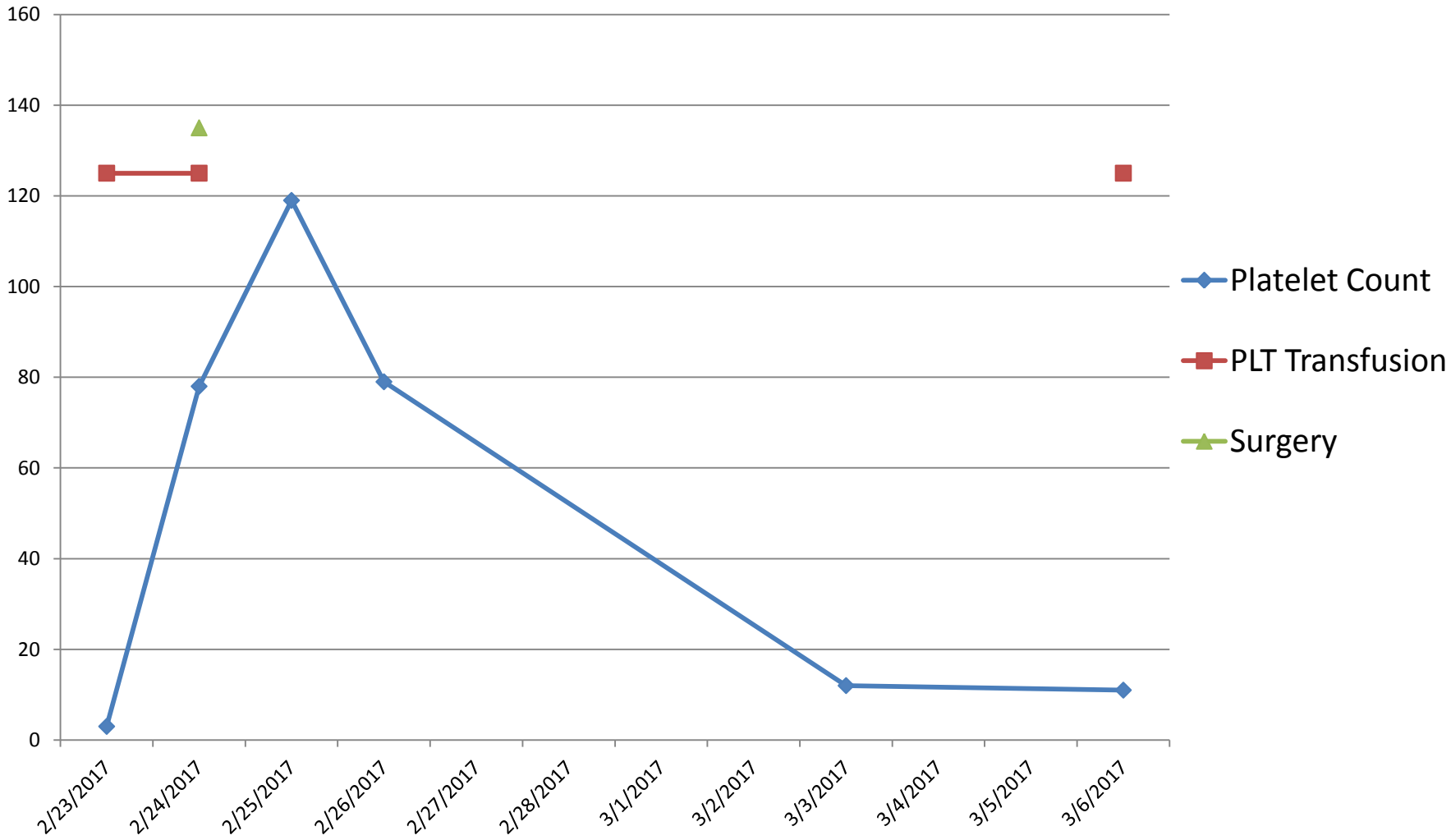
Post Partial Embolic Splenectomy



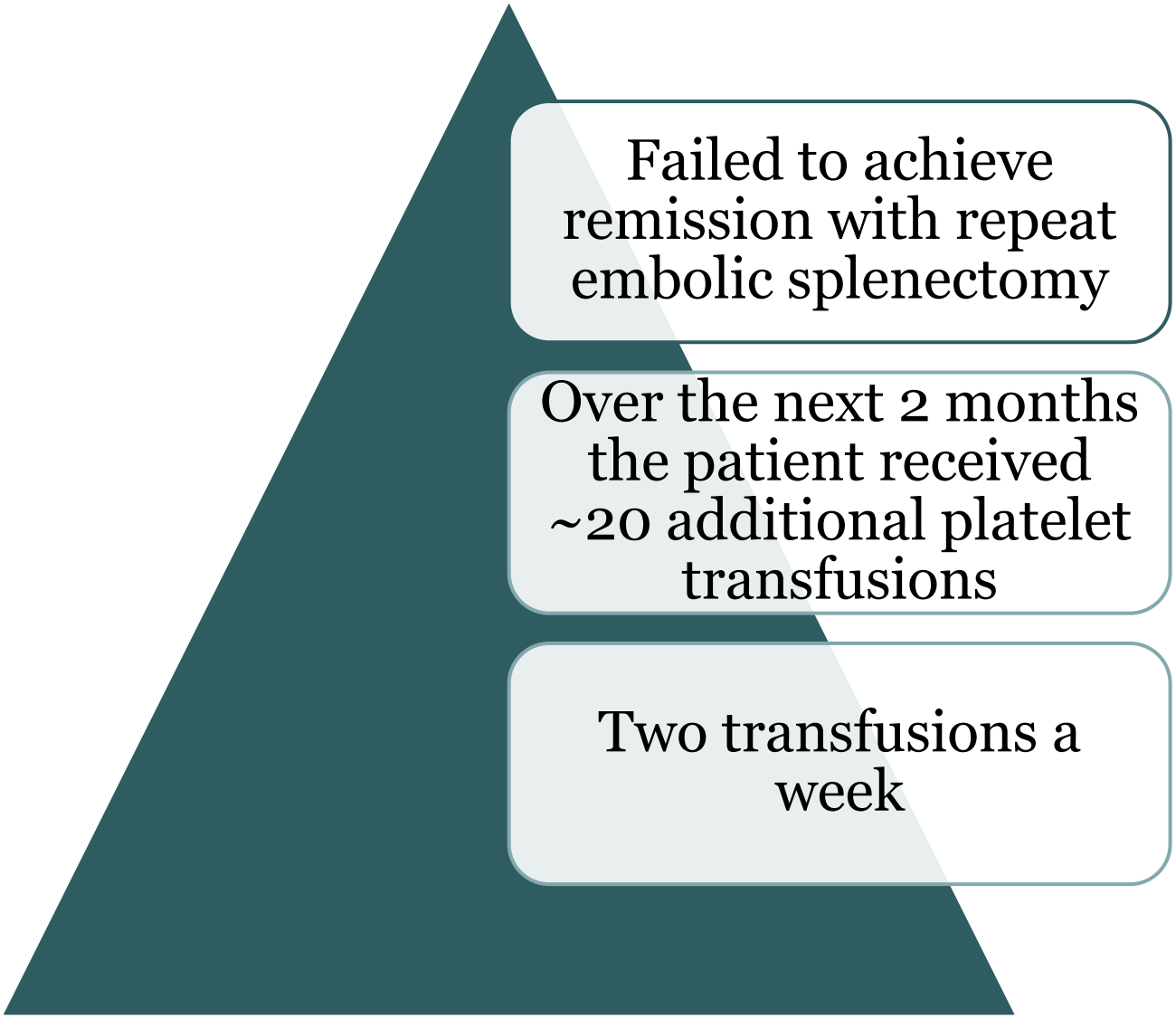
Readmitted for Complete Embolic Splenectomy

- Platelet count had fallen to 3,000
- Received platelet transfusion before and after surgery
- Late 2nd Trimester
- If second splenectomy is unsuccessful will plan on platelet transfusions 1-2X per week for the remainder of the pregnancy
- Stopping prednisone

Platelet Count Post 2nd Splenectomy



Summary of Outcomes Post 2nd Splenectomy



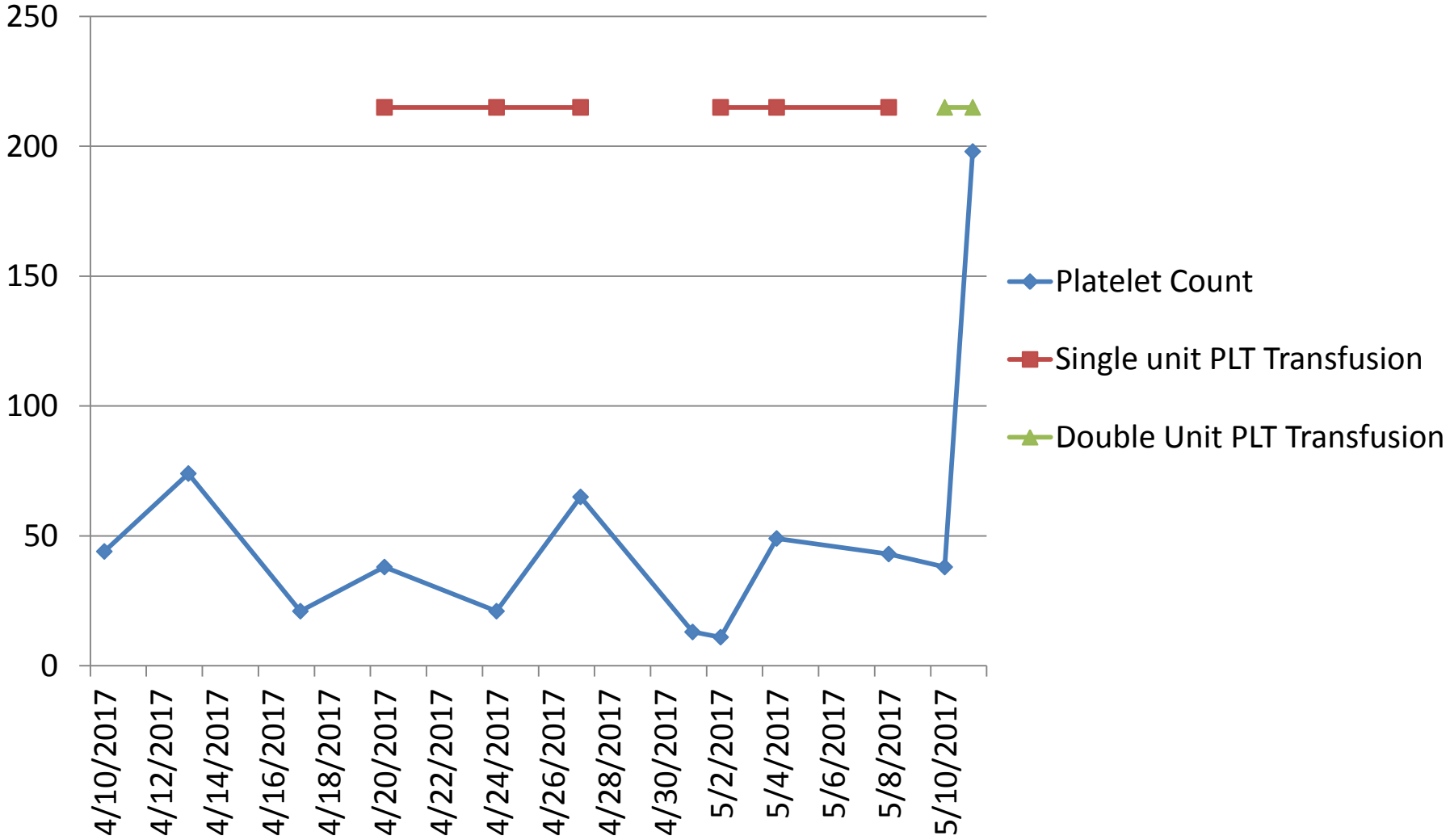
Abnormal lab results at 30 wks and 4 days gestation

- RBC 2.44 M/uL (L)
- HGB 8.5 g/dL (L)
- HCT 25% (L)
- MCV 102.5 fL (H)
- MCH 34.8 pg (H)
- Platelet 21 K/uL (L)

Results of 2nd Trimester Fetal Growth Ultrasound

- 2nd percentile for overall growth
- Abdominal circumference less than 1st percentile
- Normal amniotic fluid, umbilical and MAC Doppler
- Adequate fetal movement
- Fetal growth restriction most likely due to complications related to ITP but cannot exclude other causes

Platelet Count up to Delivery on 5/11/2017



Delivery

- Cesarean delivery at 35 weeks gestation after 29 hours of labor at 5 cm dilated with no changes
- Gestational hypertension and PROM (premature rupture of membranes)
- Patient received 2 units of platelets and 2 units of packed red cells
- Baby boy was delivered at 4 pounds 2 ounces
- Infant O positive with negative Coombs test

Remember the Possible Affects of ITP on the Infant

Risk of Fetal Thrombocytopenia

Intracranial hemorrhage during delivery (Rare)

Maternal IgG cross placenta and may bind to fetal platelets

Infant Platelet Counts Show No Thrombocytopenia

Complications for Infant Included

- Low birth weight (4-10%tile)
- Hyperbilirubinemia prematurity
- Low resting heart rate (80-90s)
- Bedside EKG showed sinus bradycardia
- Apnea was noted on 5/25/2017
- Was in ICU for 19 days (5/30/2017) before being sent home

Conclusions

Platelet transfusions were instrumental in managing refractory ITP in this pregnancy

Not all chronic ITP responds to splenectomy

ITP is an autoimmune disease with a continuum of symptoms

Conclusions

The infant did not suffer from thrombocytopenia or intracranial hemorrhage associated with ITP

The patient continues to have chronically low platelet counts between 15,000-33,000 up to three months post delivery

Are donors aware that platelets could be used to treat complications with pregnancy?

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