Patient History:
Female, 18 years old with post primary low transverse cesarean section with idiopathic thrombocytopenic purpura. After consulting with Hematology/Oncology, it was determined the patient would be safe having surgery as long as her platelet count was greater than 100,000/μL. The patient had large amount of vaginal bleeding (600 mL) during her operation, but she recovered without complications.

Laboratory Findings:
CBC: WBC – 12,160/μL, RBC – 3.72 10⁶/μL, HGB – 10.8 g/dL, HCT – 33.6%, PLT – NA, MCV – 90.3 fl, MCH – 29.0 PG, MCHC – 32.1 g/dl, RDW – 15.8%, MPV – NA. Slide estimate determined platelet count to be adequate. Platelet clumping in EDTA and citrate anticoagulants prevented an automated analysis of platelet count. Manual platelet count was performed and reported as 132,000/μL.

Background:
EDTA-Induced Platelet Agglutination (EIPA) is an in vitro phenomenon caused by EDTA-induced agglutination of platelets, leading to an artificially low platelet count on automated analyzers; it may also result in a spurious hyperleukocytosis. A manual platelet count obtained using EDTA-anticoagulated whole blood could also be inaccurate. Careful observation for platelet clumps on hemocytometer is necessary.

EIPA is thought to be the most common cause of pseudothrombocytopenia encountered in clinical laboratories. It occurs in 0.1% to 2% of hospitalized patients and at a lower frequency in healthy outpatients. EIPA can persist for decades in patients without any clinical evidence of abnormal hemostasis and thus has limited clinical significance. However, failure to recognize EIPA can lead to unnecessary and potentially harmful therapeutic interventions.

Pathophysiology:
EIPA is caused by the presence of an antibody against a cryptantigen on the GPIIb portion of the GPIIb/IIIa platelet receptor. Under normal in vivo conditions, this antigen is not accessible for antibody binding, hence the term “crypt” (or hidden) antigen. When EDTA chelates calcium, the GPIIb protein undergoes a structural change that exposes the cryptantigen. The antibody, which is most often of the immunoglobin M (IgM) class and recognizes this cryptantigen, can now bind to the antigen and cause platelet crosslinking to occur. The result is the characteristic platelet clumps observed on peripheral blood smears.

Question:
The occurrence of EIPA is approximately 5% of the general population.  T  or  F
Figures:
Platelet clumps in peripheral blood smear

Commentary:
Various studies on EIPA have offered different preventive approaches. In one study, 10 mg of EDTA-2K and 1 mg citric acid were added to 1 ml blood as anticoagulants (EC method), yielding successful results without affecting any other CBC parameters. (2)

A second study recommended adding 2.5 mL of acid citrate dextrose (ACD) to a plain 5 mL vacutainer tube before blood collection making sure not to break the tube’s vacuum. Dilution corrections were made based on the comparison of hemoglobin values in EDTA and ACD. (3)

A third study concluded that even with the use of sodium citrate or heparin as anticoagulants, they too induced platelet clumping causing spuriously low platelet counts. (4)

A fourth proposed vortexing as the first choice of correcting EIPA, finding success in about 50% of cases. It further recommended that if vortexing corrects the platelet count to a normal range (confirmed by peripheral smear evaluation) that a comment should be added to the result “platelet clumping present but count appears to be normal.” And if it is not corrected by vortexing, “a new specimen should be drawn in a citrate-containing tube.” (5)

References:
Mues, Gabriele MD, et al., EDTA-Induced Pseudo-Gray Platelet Syndrome, (Laboratory Medicine, ASCP, 2002). (1)
Nagata, Tanaka, et al., Anticoagulants Preventing Pseudo-Thrombocytopenia, (Rinsho Byori, pp. 87 – 92, 1992). (2)
Discussion:
EIPA occurs in approximately 0.1% of the general population.

Case Study compiled by:

**Sandra C. Hollensead, M.D.**
Professor of Pathology
Medical Director, Hematology and Coagulation Laboratory
Course Director, Sophomore Pathology Course
Department of Pathology and Laboratory Medicine University of
Louisville Louisville, KY 40292

Marsha B. Cattaneo, MT
Clinical Laboratory
University of Louisville Healthcare