VOLUME - 11, ISSUE - 10, OCTOBER - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Hematology

PSEUDOTHROMBOCYTOPENIA A CLINICAL UPDATE

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ABSTRACT Pseudothrombocytopenia is a complex phenomenon common finding in clinical laboratory error, misdiagnosis, inappropriate analysis caused due to various factors like time, temperature, technique, anticoagulants used for collecting samples, and few disease conditions the underlying mechanism is autoantibodies forming the clumping of the platelets which is interpretive as low platelet count, the present article discuss on various factors, mechanism and measures to correct the error and management of the pseudothrombocytopenia.

KEYWORDS :

INTRODUCTION

Pseudothrombocytopenia (PTCP) is the not a clinical condition, it can be due variety of disorders like autoimmune disease, chronic inflammatory disease, viral, bacterial infection, metabolic syndromes, neoplastic diseases, allogenic stem cell transplantation, use of drugs like valproic acid, olanzapine, insulin, levofloxacin. However, the patients with PTCP do not need clinical evaluation, laboratory monitoring or therapeutic management however most of the time PTCP is finding that lead to diagnostic errors, overtreatment, unnecessary testing results in inappropriate platelet transfusion, diagnosis technique and therapeutic procedures.[1,2]

On other hand, PTCP is result of in-vitro sampling error, which misleads diagnosis as low platelet count, can be due to sample collection, anticoagulant used.

Prevalence of Pseudothrombocytopenia

The PTCP has incidence of 0.03-0.27% in outpatient population, 15.3% in inpatient population, 17% patient with EDTA dependent PTCP, prevalence of PTCP in blood and platelet apheresis with 0.01%-0.2% rate, and platelet satellitism is 1 in every 12000 blood counts.[5,6,7]

Factors lead to Pseudothrombocytopenia in laboratory

Collection of blood sample

The specimen collected from venipuncture, overfilled blood specimen, blood drawn from indwelling catheter can cause invitro coagulation, clumping. So specimen collected for testing should be fresh blood drawn with actable size needle.[3]

Anticoagulants and other compounds

The anticoagulants used for sample should be such that the platelet clumping should be minimized, and prevent dissociate platelet aggregation.

Ethylene diamine tetra acid EDTA is common anticoagulant used in sample collection, the possibility of platelet aggregation, clumping is high leads to wrong diagnosis. Hence EDTA with aminoglycosides like amikacin, kanamycin, potassium azide, calcium chloride, antiplatelet agents like GpIIbIIIa inhibitors, thromboxane inhibitor, cyclooxygenase inhibitor, apyrase are added as additive supplement to have effective against platelet clumping.[4]

Temperature

The temperature to be maintained at 37 degree Celsius till the completion of analysis of the blood, the temperature prevents platelet clumping.[8]

Time

From the time of blood sample collection one minute after till four hours.

Technique for analysis

The technique for the analysis is selected as the facility availability, any diagnostic technique used should be calibrated, standardized and affordable with better results and minimal errors.[9]

Alternative anticoagulant

The anticoagulant such as sodium citrate, heparin, sodium fluoride, trisodium citrate, pyridoxal phosphate and tris, CTAD (citrate, theophylline, adenosine, dipyridamole), magnesium sulfate prevent the platelet binding and better the diagnosis.[18]

Pseudothrombocytopenia with clinical impact

The anticoagulant (EDTA, Heparin and Citrates) induce PTCP when used for medical condition like systematic lupus Edematous, lupus nephritis, paroxysmal atrial fibrillation, sepsis, viral infection-gastroenteritis, COVID with clinical implication such as unnecessary platelet transfusion, delayed cardiac care management, use of steroids in management.[10]

Mechanism and Causes of Pseudothrombocytopenia

- The auto antibodies are directed against fibrinogen receptors, responsible for in vitro platelet agglutination after activation by tyrosine kinase, platelets from the patients with deficit GPIIbIIIa a fibrinogen receptor fails to bind autoantibodies.
- Patients with bleeding diathesis, identified citrate anticoagulated blood caused IgM class agglutinin against collagen receptor GPVI and trigger platelet activation.
- Further immune complex interacting with fibrinogen receptors on platelet surface implicate in PTCP.
- In spurious thrombocytopenia, the IgG autoantibodies target GpIIbIIIa receptors bind to neutrophil Fibrinogen gamma receptors. And proteins from alpha granules expressed on platelet membrane leads to adhesion to neutrophils, this invitro process agglutinates the platelets in large quantity.[11,12]
- The use of Ethylene Diamine Tetra Acid as anticoagulant, platelet col d agglutinins, multiple myeloma. The in-vitro agglutination of platelets, platelet clumping reports as low platelet count.
- The automated platelet counting device results as false positive result.[20]

These are the possible mechanism and causes for the PTCP.

Diagnosis of PTCP

- On diagnosis of PTCP, patients blood sample is examined under microscope, visible clumping of platelets and normal platelet count PSPT is concluded.[13]
- Different anticoagulant citrate is used for sample instead of EDTA, confirm PSPT.
- Anti platelet- Antibody activity based on immunofluorescence test.[19]
- Hematology flow cytometry
- Fluorescent dye staining
- Platelet counting.

Management of PTCP in laboratory

- A careful management in laboratory includes the identification, confirmation and prevention of error in analysis of the test. On identification of the clot initially inspection of histogram and scatter gram of RBC's platelets and white blood cells done along with May-Grunwald Giemsa Smear, suggest the platelet satellitism, giant platelets or aggregation confirmed on PBS.[14]
- The fluorescence and optical measurements are used for next level confirmation the histograms of these methods are used for analysis.[15,16] On difficulty in interference the anticoagulant method is used where in the EDTA, magnesium sulfate are recommended.
- Even after the failure of above method the manual counting of platelets is the confirmation of the PTCP.[17]

CONCLUSION

PTCP is a complex concept, influenced by the count of thrombocytes. There is no particular cause or specific disease cause the PTCP, the condition is due to misdiagnosis, that leads to impaired management, and therapeutic decision which reduces the benefit of treatment and harm the patients. The risk of PTCP is higher in people over 50 years, male, diseases and on treatment for coagulation disorders who are on low molecular weight heparin. New technologies like fluorescence, optical platelet counting and use of additional supplement like magnesium, amikacin, kanamycin is effective method for accurate results of thrombocytes. This can prevent the error occur due to misdiagnosis at laboratory and further prevent burden to the patient.

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