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Understanding the Impact of Medications on Blood Platelet Levels: Navigating Drug-Induced Thrombocytopenia for Better Health

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ABSTRACT:
Drug-induced thrombocytopenia (DIT) is a significant health concern characterized by a drastic reduction in platelet count, resulting from certain medication use. The most common culprits include heparin, quinine, and various antibiotics, which can trigger the body's immune system to produce antibodies that mistakenly identify platelets as threats, destroying them.Diagnosis of DIT can be challenging due to its symptom similarity with other conditions. It is primarily based on patient history, including recent drug intake, signs of bleeding, and sudden drop in platelet count. Laboratory tests, such as a complete blood count (CBC) and tests for specific antibodies, can provide additional confirmation.The primary treatment for DIT involves immediate discontinuation of the suspected drug. In severe cases, treatments may include corticosteroids, intravenous immunoglobulin (IVIG), and platelet transfusions to control bleeding and hasten recovery.Recent advancements in diagnostic techniques and a better understanding of DIT pathogenesis promise improved patient outcomes. However, increased healthcare provider awareness and vigilance in monitoring patient responses to medications remain crucial for early detection and management of DIT.
Keywords: Thrombocytopenia, Immune response, Antibody, Splenectomy

I. INTRODUCTION:

Thrombocytopenia, a condition characterized by an abnormally low count of platelets in the blood, plays a critical role in hemostasis and thrombosis. It is a common hematological disorder that can lead to a high risk of bleeding in affected patients. While various causes can lead to thrombocytopenia, one of the less-known but highly impactful sources is drug-induced thrombocytopenia (DIT). This form of thrombocytopenia is a significant clinical problem and is often underdiagnosed, leading to unnecessary tests, treatments, and hospitalizations.

Drug-induced thrombocytopenia occurs when certain drugs trigger the immune system to destroy platelets, the tiny fragments in our blood that form clots to stop bleeding. The result is a decrease in platelet count, leading to an increased risk of bleeding. This can range from minor bruises and nosebleeds to life-threatening hemorrhages in the brain or digestive tract. Despite the potential seriousness of this condition, our understanding of its causes, mechanisms, and management is still evolving.[1]

Understanding the intricacies of drug-induced thrombocytopenia is critical for physicians and healthcare providers. It is a condition that can be induced by a wide variety of medications, including common over-the-counter drugs, prescription medications, and certain types of food and dietary supplements. This wide range of potential causes, combined with the lack of specific diagnostic tests, makes DIT a challenging condition to diagnose and manage effectively.

The mechanism by which these drugs induce thrombocytopenia is complex and not entirely understood. It is believed that certain drugs may cause an immune response that leads to the accelerated removal of platelets from the bloodstream. Other drugs may interfere with the production of platelets in the bone marrow. Furthermore, some drugs may cause a combination of these effects. The development of drug-induced thrombocytopenia can occur quickly, within hours of drug exposure, or it may take several days or even weeks.[2]

Platelets, small in size and plate-like in shape, are not actual cells but fragments of cells that circulate in the blood. Despite being fragments, they are crucial in preventing bleeding. They have proteins enabling them to attach to any damage in the blood vessel walls and to each other, forming a

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plug. These proteins also allow platelets to change shape for better adhesion. Their size is around 2-3 µm, about a quarter of red blood cells. With a lifespan of 9 to 10 days, our bodies produce between 15,000 to 45,000 platelets daily to maintain stability.

Normal values for platelet count are 150,000 to 400,000 cells/mm^3.Platelets, first identified by Addison in 1841, were described as "extremely minute granules" present in clotting blood. These tiny components were named "platelets" by Bizzozero, who noted their "increased stickiness" particularly when a vascular wall was damaged. This observation shed light on their adhesive properties, which play a crucial role in blood clotting. The identification of these elements continued with microscopic examinations of blood smears by Schaefer and Hayem in the late 19th century. By 1906, James Homer Wright hypothesized that blood platelets originated from the cytoplasm of megakaryocytes, effectively establishing the basic elements of thrombopoiesis or platelet production. [3,4]

Thrombopoiesis refers to the process of generating platelets within the bone marrow. The principal controller of this mechanism is thrombopoietin. This element influences a multitude of features associated with platelet creation, such as the self-regeneration and multiplication of hematopoietic stem cells. It also boosts the growth of precursor cells of megakaryocytes and aids in their maturation into cells that are responsible for the production of platelets, which is further detailed below.

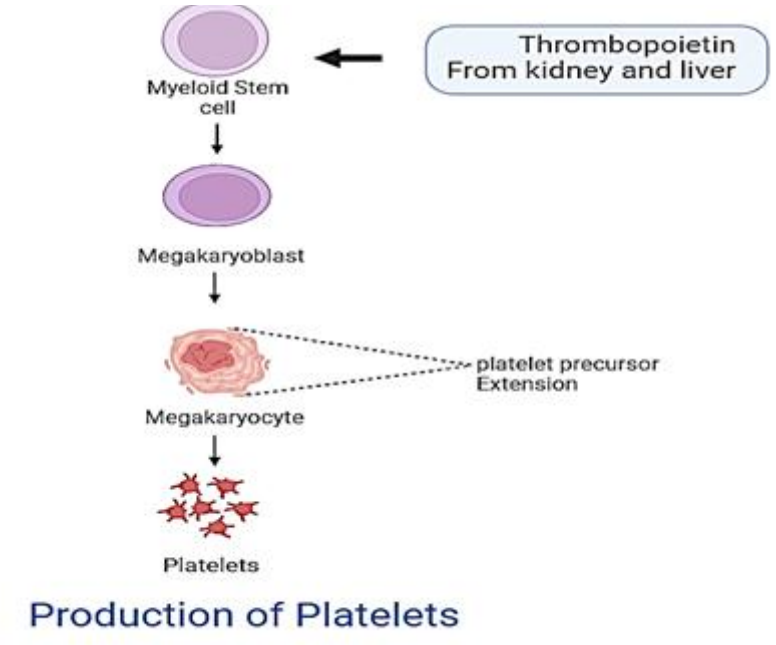

Fig 1 Production of platelets

II. FUNCTIONS OF THROMBOCYTES:

Hemostasis: Platelets play a crucial role in hemostasis, the process of stopping bleeding. They aggregate at the site of injury, forming a plug that prevents further blood loss. They also release chemicals that trigger the coagulation cascade, leading to the formation of a stable blood clot [5].

Vasodilation: Platelets have been found to release substances that cause vasodilation or the widening of blood vessels. This can help to increase blood flow and deliver more oxygen and nutrients to tissues [6].

Immunomodulation: Platelets can modulate the immune response by releasing various cytokines and chemokines. They can also interact with immune cells, playing a role in the body's defense against infections [7].

Angiogenesis: Platelets can stimulate the growth of new blood vessels, a process known as angiogenesis. This can be beneficial in healing wounds and regenerating tissues [8].

Thromboxane A2 Synthesis: Platelets are the primary site of thromboxane A2 synthesis.

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Thromboxane A2 is a potent vasoconstrictor and platelet activator that plays a role in platelet aggregation and the formation of blood clots [9].

Fibrinolysis: While platelets play a role in clot formation, they also participate in the process of fibrinolysis, or the breakdown of blood clots. This is a delicate balance to prevent excessive bleeding and clot formation [10].

Bone Remodeling: Platelets are involved in bone remodeling, a process that involves the removal of old bone and the formation of new bone. This can be crucial in healing fractures and maintaining bone health [11].

Drugs Induced Immune Thrombocytopenia:

Numerous recent studies have helped identify various drugs linked to the development of Drug-Induced Thrombocytopenia Purpura (DITP). Dr. James N. George has contributed significantly to this field by gathering patient reports of immune-mediated thrombocytopenia. He currently documents over 300 drugs that have been associated with at least one confirmed or suspected case of DITP. Quinine was the first drug identified over a century ago as causing immune-mediated thrombocytopenia, but it's a rare cause of DITP, with only 26 cases per million patients treated. Heparin-induced thrombocytopenia (HIT) is a more common occurrence, impacting more than 1% of treated patients in certain clinical scenarios. HIT is distinguished from other DITP cases due to its association with thrombotic complications in nearly half of all instances and rarely severe bleeding [12,13].

Drugs Induced Non-Immune Thrombocytopenia:

The creation of platelets relies on the proper functioning of the marrow and a sufficient number of megakaryocytes, which are large cells that produce platelets. Certain cancer-fighting drugs can suppress the marrow, affecting all blood-forming cells, or just the megakaryocytes that produce platelets. This often leads to a decrease in the number of platelets in circulation.

The most common drugs causing this effect are chemotherapy medications like alkylating agents, antimetabolites, and cytotoxic drugs. However, some antiviral drugs, tolbutamide, and thiazide diuretics can also have this effect.

The impact of these drugs on the marrow and platelet production is usually seen over several weeks, reflecting the time needed to reduce the megakaryocyte population. As a result of these drugs, it's common to see a drop in platelet count, a condition known as thrombocytopenia. This is usually expected when treating with these types of drugs, so it's not a surprising finding for healthcare providers [14-18].

Some examples for drugs induced immune and non-immune thrombocytopenia

Abciximab, Carbamazepine, Ceftriaxone, Eptifibatide, Heparin, Ibuprofen, Mirtazapine, Oxaliplatin, Penicillin, Quinidine, Quinine, Ranitidine, Rifampin, Sulfasalazine, Suramin, Tirofiban, Vancomycin.

III. ETIOLOGY:

Primary Immune Thrombocytopenia (PIT): This is an autoimmune disorder where the body mistakenly produces antibodies against platelets, leading to their destruction.

Drug-Induced Immune Thrombocytopenia: This condition is triggered by certain drugs and includes the following:

- Heparin-induced thrombocytopenia (HIT): This is a condition where anti-platelet antibodies, activated by heparin, cause thrombosis in both arterial and venous systems.
- Quinine
- Sulfonamides, ampicillin, vancomycin, piperacillin
- Acetaminophen, ibuprofen, naproxen
- Cimetidine
- Glycoprotein IIb/IIIa inhibitors
- Over-the-counter remedies, supplements, foods like African beans, sesame seeds, walnuts, and beverages (herbal teas and cranberry juice)

Drug-Induced Non-Immune Thrombocytopenia:

- This condition occurs due to certain drugs like valproic acid, daptomycin, and linezolid, which suppress platelet production in a dose-dependent manner [19-22].

Infections:

- Viral Infections: HIV, hepatitis C, Ebstein-Barr virus, parvovirus, mumps, varicella, rubella, Zika virus
- Sepsis: This condition causes bone marrow suppression.
- Helicobacter pylori
- Leptospirosis, brucellosis, anaplasmosis, and other tick-borne infections
- Malaria, babesiosis: These intracellular parasite infections are associated with thrombocytopenia and hemolytic anemia.

Apart from the above, the following conditions can also cause thrombocytopenia:

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- Hypersplenism due to chronic liver disease
- Chronic alcohol abuse
- Nutrient deficiencies (folate, vitamin B12, copper)
- Autoimmune disorders like systemic lupus erythematosus, rheumatoid arthritis
- Pregnancy: Gestational thrombocytopenia is a mild form, while moderate-severe thrombocytopenia can occur in preeclampsia and HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome.

Other Causes:

- Myelodysplasia
- Malignancy: This includes cancer with chronic DIC, cancer with marrow suppression (leukemia, lymphoma, solid tumors)
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Thrombotic microangiopathy (TMA)
- Thrombotic thrombocytopenic purpura (TTP): This condition is characterized by fever, renal failure, thrombocytopenia, and microangiopathic hemolytic anemia with or without neurologic manifestations.
- Hemolytic uremic syndrome (HUS): This is caused by Shiga toxin-producing organisms (E. coli and Shigella), typically seen in children.
- Drug-induced TMA: This includes quinine, specific chemotherapy agents
- Antiphospholipid antibody syndrome
- Aplastic anemia
- Inherited thrombocytopenia: This is often seen in children, and rare in adults.
- Von Willebrand disease type 2
- Alport syndrome
- Wiskott-Aldrich syndrome
- Fanconi syndrome
- Thrombocytopenia-absent radius syndrome
- Bernard–Soulier syndrome
- May-Hegglin anomaly [23].

IV. EPIDEMIOLOGY:

Ages, genders, and ethnicities all have varied normal platelet count ranges. The platelet counts of women, adolescents, and non-Hispanic Blacks are somewhat greater [24].

V. CLINICAL CONDITION:

5.1 Increased platelet destruction

• Non-immune causes:

- Septicemia or inflammation
- Disseminated intravascular coagulation (DIC)
- Thrombotic thrombocytopenic purpura (TTP)

• Immune causes:

- Autoimmune: either idiopathic or secondary immune thrombocytopenia
- Alloimmune: following a blood transfusion
- Drug-induced: including heparin, quinine, quinidine, gold, sulfa antibiotics, rifampicin, vancomycin, NSAIDs, and others

5.2 Reduced platelet production

- Alcohol, cytotoxic drugs
- Aplastic anemia
- Leukemia, myelodysplasia
- Metastatic invasion of marrow
- Certain infection

5.3 Hypersplenism

-The spleen houses approximately 30% of the total platelet mass. When there's increased platelet pooling in the spleen, it leads to thrombocytopenia in patients with hypersplenism. In such cases, up to 90% of the total platelet mass could be present in the spleen.

5.4. Hemodilution

- Involves the infusion of blood products, colloids, or crystalloids [25,26].

VI. MECHANISMS OF THROMBOCYTOPENIA:

6.1 Pseudo thrombocytopenia
6.2 Decreased platelet production
6.3 Increased platelet destruction
6.4 Dilutional thrombocytopenia
6.5 Distributional thrombocytopenia

6.1 Pseudo Thrombocytopenia

Pseudo thrombocytopenia is a condition where platelets clump together due to an autoantibody that is triggered by the EDTA anticoagulant used in routine blood tests. This leads to a falsely low platelet count because the clumped platelets are not counted by the analyzer. The platelet count in blood anticoagulated with citrate is usually normal as citrate's chelation of calcium prevents the alteration of the GP IIb/IIIa molecule. Pseudo-thrombocytopenia can also occur due to platelet adherence to leukocytes. This condition is identified by examining the peripheral blood film. It affects about 1 in 1000 people and is not clinically significant.

6.2 Decreased Platelet Production

Reduced platelet production can occur due to bone marrow failure in conditions like aplastic anemia and PNH. Bone marrow suppression can be caused by exposure to certain drugs such as valproic acid, daptomycin, chemotherapy agents,

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and irradiation. Chronic alcohol abuse, inherited thrombocytopenia, viral infections, and systemic conditions like nutrient deficiencies, sepsis, and myelodysplastic syndrome can also lead to reduced platelet production. These conditions result in thrombocytopenia.

6.3 Increased Platelet Destruction

Normal platelet lifespan is 8 to 10 days, and they are removed by monocytes/macrophages of the reticuloendothelial system. In immune-mediated thrombocytopenia, anti-platelet autoantibodies bind to platelets and megakaryocytes, leading to increased platelet destruction and decreased production. These autoantibodies are present in conditions like primary ITP, drug-induced ITP, lymphoproliferative disorders, autoimmune conditions like SLE, and chronic infections like HEP C, HIV, and Helicobacter pylori. Non-immune mediated increased platelet destruction can occur in conditions like mechanical valve replacement, preeclampsia/HELLP syndrome, DIC, and thrombotic microangiopathy. In conditions like DIC and thrombotic microangiopathy, increased platelet consumption within thrombi takes place [27].

6.4Dilutional Thrombocytopenia

Large amounts of packed red blood cell transfusion can lead to dilutional thrombocytopenia due to the absence of viable platelets in these cells. Patients receiving more than 20 units of packed red blood cells in 24 hours should be given platelet concentrates to prevent this.

6.5 Distributional Thrombocytopenia

This condition is also known as 'apparent thrombocytopenia', as the overall platelet count is normal. Normally, one-third of platelets are stored in the spleen. In cases of splenomegaly or hypersplenism, which can be caused by portal hypertension or other factors, this sequestration can increase to as much as 90%. This condition may also be accompanied by leucopenia and anemia. Despite a decrease in circulating platelet count, the total platelet mass and their overall survival remain unaffected. Therefore, while patients may exhibit significant 'apparent' thrombocytopenia, they rarely experience clinical bleeding, as their total platelet mass remains normal [28].

VII. MECHANISMS OF DRUGS INDUCED THROMBOCYTOPENIA:

7.1 Hapten-dependent antibody:

Molecules with a molecular weight of less than 2–5 kDa, such as drugs, organic compounds, peptides, and oligosaccharides, generally cannot trigger an immune response. These smaller molecules, known as Haptens, can induce an immune response when they are bonded to a carrier protein. Penicillin and its derivatives are a prime example of this group. Penicillin is part of an extensive family of compounds whose primary structural element is a beta-lactam ring paired with a thiazolidine ring. When the beta-lactam ring opens due to the presence of free amino groups on proteins, the penicillin group forms a covalent bond with the epsilon-amino groups of lysine residues in proteins. This covalent attachment can disrupt the protein's antigen processing in various ways, leading to an immune response.

Penicillin-induced immune hemolytic anemia is a known side effect of penicillin therapy. However, thrombocytopenia caused by the "Hapten" mechanism is a relatively uncommon occurrence.

7.2 Drug-dependent antibody (Quinine–type antibody or compound or conformational–dependent antibody):

In simple terms, the root cause of the issue at hand is the binding of antibodies to platelets. These antibodies are diverse and they target different specific regions on key platelet membrane proteins, often targeting proteins like GPIb/IX, GPV, and GPIIb/IIIa as well as PECAM-1, but only when a certain drug is present in a solvable form. Antibodies in a single patient are usually extremely specific, only targeting a single protein.

Certain drugs like quinine and quinidine are most commonly associated with this issue, but also several other medications including sulfonamide antibiotics and drug metabolites play a role in this process. These antibodies seem to target a composite region made up of the drug attached noncovalently to one or several sites of the platelet proteins, or a structural change somewhere else on the protein molecule that comes into existence when the implicated drug is present in soluble form.

The specific regions recognized by antibodies in patients with quinine- and sulfonamide-induced low platelet count have been identified for some target molecules. However, the exact location has only been pinpointed for a few

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quinine-dependent antibodies, which are shown to bind to a specific 70 amino acid domain of GPIIIa, and further narrowed down to a 17-amino acid sequence. The binding site of a quinine-dependent antibody that specifically targets GPIb has been traced to an 11 amino acid sequence of the protein. It was also found that certain positions in GPIX protein play a crucial role in the formation of the quinine-dependent anti-GPIX antibody binding site. There is also evidence that within GPIX, there exists a site that is favored not only by quinine but also by antibodies induced by other drugs such as rifampicin and ranitidine. Antibodies that react to platelets induced by sulfonamide antibiotics were reported to interact primarily with regions displayed only on the intact GPIIb-IIIa complex [29].

7.3 Drug–specific antibody:

One common way that drugs work is by creating specific antibodies. Let's take the example of Abciximab, which is a type of antibody made from human and mouse genes. This drug has been linked to causing a certain type of blood disorder. It works as an anti-clotting agent, by sticking to certain sites on blood platelets and blocking the connection of another protein, fibrinogen. This stops the platelets from sticking together and forming blood clots.

However, there can be some serious side effects. For example, 1-2% of people taking Abciximab for the first time, and 10-12% of those taking it again, already have antibodies in their blood that target the drug-bound platelets, leading to a rapid drop in platelet count. In other cases, this drop in platelets may not happen until 6-8 days after taking the drug because the body needs time to produce new antibodies in response to the drug.

7.4 Fibrinogen receptor antagonist-dependent antibody:

Platelet inhibitors, also known as fibans, that mimic arginine-glycine-aspartic acid are utilized to avert restenosis following a coronary angioplasty procedure. The drugs in this category, such as tirofiban and eptifibatide, attach to GPIIb/IIIa, leading to a structural alteration that obstructs the interaction between platelets and fibrinogen. As a result, the creation of platelet thrombi is suppressed. The development of thrombocytopenia due to these agents is predominantly attributed to the presence of naturally occurring antibodies that identify the freshly constituted drug-platelet complex when fibers are present. Consequently, thrombocytopenia may manifest within hours of commencing the drug. While the mechanism of DITP is akin to the drug-specific antibodies that bind to abciximab, the reported occurrence of DITP with fibans is relatively less, ranging from 0.1% to 2%.

7.5 Autoantibody generation:

In approximately 1% of patients administered with gold salts and a smaller fraction of patients given other drugs like procainamide and levodopa, thrombocytopenia bears a striking resemblance to autoimmune idiopathic thrombocytopenia. The precise mechanism remains elusive. However, studies indicate that these medications may evoke the production of autoantibodies specific to platelets. A prevailing hypothesis is that the drug interferes with platelet surface glycoproteins, leading to the creation of unidentified peptides that trigger an immune response. Despite the existence of significant unknown aspects of this phenomenon, it has been observed to occur in 1.0% of patients treated with gold salts and is exceedingly rare with procainamide and other drugs [30].

7.6 IMMUNE COMPLEX PROCESSES:

The initial proposition was that the antibodies responsible for Drug-Induced Immune Thrombocytopenia (DITP) identify and bind to the circulating drug, creating immune complexes that inadvertently interact with platelets, leading to their elimination. Yet, such theoretical immune complexes have not been empirically verified. Subsequent findings revealed that Drug-Dependent Antibodies (DDAbs) adhere to platelets through their Fab receptors, not their Fc receptors.

A unique immune complex process is to blame for thrombocytopenia, a condition characterized by low platelet count, in cases of Heparin-Induced Thrombocytopenia (HIT). HIT diverges from most other forms of drug-induced immune thrombocytopenia because the culpable antibodies latch onto complexes formed by a non-covalent reaction between a platelet alpha granules release, the CXC chemokine platelet factor 4 (PF4; CXCL4), and heparin. This reaction yields immune complexes that interact with the Fc gamma RIIA receptor on platelets, provoking platelet activation, rather than merely encouraging their destruction within the reticuloendothelial system.

Approximately 10% of HIT patients also face a considerable risk of thrombosis. The rate of thrombosis is 3-6% among patients treated with

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unfractionated heparin for a week, while it is infrequent with low-molecular-weight heparin.

TYPE	*MECHANISM*	*DRUGS*
Hapten-induced Antibody	drug binds to platelet membrane and stimulates the production of antibodies	Cephalosporins and penicillin
"Quinine – type" Antibody	The drug binds to membrane glycoprotein and antibody Fab, increasing antibody affinity and binding to platelet GP.	Quinine, quinidine, linezolid, vancomycin,
Drug-specific antibody	The monoclonal antibody attached to its target is recognized by the antibody.	Abciximab
Fibrinogen receptor antagonist-dependent antibody	Antibodies identify drugs that bind to GP IIb/IIIa and cause conformational alterations.	Tirofiban,
Autoantibody induction	The medication causes the production of an autoantibody that only attaches to platelet GP.	Procainamide, gold salts, L-dopa
Immune complexes	Drugs attach to antibodies that induce PF4, which then activates platelets through FcγRIIa receptors.	Heparin

Table 1: Mechanism of Drugs induced thrombocytopenia

VIII. DIAGNOSIS:

8.1 When diagnosing a patient, inquire about the kind and length of symptoms like bruising, bleeding, or tiny red spots on the skin. Take into account recent health issues such as diarrhea, neurological symptoms, and sore throat. Also, keep track of associated symptoms like fever, limping, and pain in the limbs. Be aware of any medicines the patient is taking. Check their family's history for any bleeding problems. Evaluate the risk of the patient having HIV or other immunity-related disorders.

8.2 During the physical examination, check for fever and assess the severity of the illness. Children who appear severely ill and have low platelet counts need immediate examination. Look for signs of bleeding. Other symptoms like short height, small head size, bone disorders, dark skin patches, underdeveloped sexual organs, chronic skin inflammation, and frequent infections in a boy could indicate a congenital low platelet count. An enlarged spleen or swollen lymph nodes could suggest serious conditions like leukemia, cancer, HIV infection, or a storage disease. Children with a condition called ITP do not have yellowing of the skin or an enlarged liver or spleen. Joint inflammation, mouth sores, or a specific type of rash might indicate an autoimmune disease [31].

8.3 Order a full blood count test with a detailed breakdown and platelet count. If there's anemia or a low neutrophil count (<1500/mm3) along with a low platelet count, it can help guide the next steps. While a low neutrophil count can occur with

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infection, if it's also accompanied by a significant low platelet count, it may indicate bone marrow failure. Anemia could indicate bone marrow failure, blood cell destruction within blood vessels, an autoimmune disease, HIV infection, or blood loss due to bleeding from low platelet count.

8.4 Review the blood smear. If there are fragments of red blood cells, it suggests blood cell destruction within blood vessels. Certain types of red blood cells can provide important clues. Look at the size and shape of the platelets and their uniformity. Boys with a condition called Wiskott–Aldrich syndrome have very small platelets. Large platelets can suggest fast platelet replacement, as seen in ITP, or a congenital low platelet count, such as Bernard–Soulier syndrome, or a MYH9-related disease, such as May–Hegglin anomaly. A condition called Type 2b von Willebrand disease is linked with low platelet count [32].

8.5 Before carrying out a bone marrow test, it's crucial to seek advice from a hematologist. This ensures critical procedures like biopsy and chromosome and lymphoid markers studies are not overlooked. Just because there are no signs of lymphadenopathy, organ enlargement, or leukemic cells in a blood smear, doesn't mean leukemia can be ruled out.

8.6. ITP is typically the main reason for sudden low platelet count in a healthy child. In newborns who are generally healthy, alloimmune thrombocytopenia should also be taken into account. Nonetheless, other potential diagnoses for the low platelet count should always be considered. The presence of antinuclear antibody (ANA) or a positive Coombs test suggests the possible existence of an autoimmune disease like systemic lupus erythematosus (SLE). Whether to conduct a bone marrow test should be decided on a case-by-case basis. Children who aren't experiencing significant bleeding are monitored through repeated CBCs and platelet counts. Once the platelet count returns to normal, further counts aren't necessary. It's unusual for the condition to come back.

8.7. Since spleen and lymph node enlargement are uncommon in children with ITP if a child with significantly low platelet count shows these symptoms (and there's no obvious alternative reason like chronic spleen enlargement due to portal hypertension implying hypersplenism or test results pointing to HIV infection), it's recommended to perform a bone marrow test as soon as possible [33].

IX. TREATMENTS:

9.1 If you're on several medications, stop any new ones you've started in the last two weeks, particularly antibiotics. Switch to different medications if needed.

9.2 Transferring platelets isn't usually effective while the problematic drug or its byproduct is still in your bloodstream.

9.3 In cases of immune system issues, corticosteroids like dexamethasone or prednisone are usually recommended to increase platelet levels. These are taken daily as a pill or tablet. Within two weeks, especially with high-dose dexamethasone, your platelet count should start to normalize. Your doctor will then likely reduce your dose gradually over 4 to 8 weeks. Repeat treatments may be needed, but once your platelet count is normal, no further treatment is required. Be aware that prednisone can have side effects like sleep issues, weight gain, frequent urination, reduced bone density, and acne. Also, your platelet count might decrease once you stop the treatment [34].

9.4 For severe cases of low platelet count and bleeding, or high risk of bleeding, high doses of IV immunoglobulin may be administered. If prednisone isn't effective or you can't tolerate steroids, or if your count drops post-treatment, your doctor may recommend IVIG. This is administered via IV, typically several hours a day for 1 to 5 days. IVIG can rapidly increase your platelet count, but the effect is temporary. It's suitable for those who need a quick boost in levels or can't take steroids. Possible side effects include nausea, vomiting, headaches, and fever [35].

9.5 If other treatments fail, surgical removal of your spleen (Splenectomy) might be suggested. The spleen destroys platelets, so removing it can help increase your platelet count, but it's not always successful. Note that removing your spleen can increase your risk of infections, especially in the first 3 months post-surgery [36].

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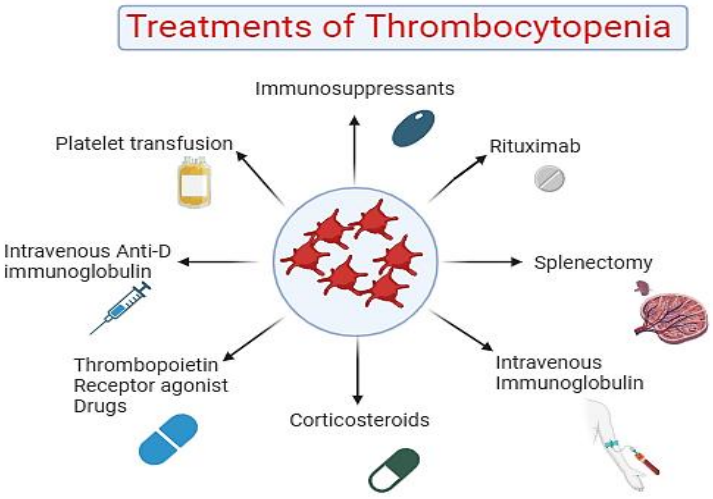

Fig 2: Treatments of Thrombocytopenia

X. CONCLUSIONS:

Thrombocytopenia, a condition where the blood has an unusually low number of platelets, can sometimes be caused by certain medications. This can be hard to identify, especially when it's triggered by an immune response. The main way we figure out if a drug is causing thrombocytopenia is by ruling out other possible causes and seeing if the timing of the issue lines up with when the suspect drug was given. Nowadays, we have more and more tests that can identify if a drug is causing the problem by looking for specific antibodies that target platelets. However, these test results may not always come back quickly enough to help with the initial diagnosis and treatment plan. Therefore, a thorough review of all the medical and lab data is crucial in making an accurate diagnosis and providing the best care for the patient.

Compliance with ethical standards

Disclosure of conflict of interest

There was no conflict of interest among the authors

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