International Journal of Life Science Research Archive

ISSN: 0799-6640 (Online)

Journal homepage: https://sciresjournals.com/ijlsra/

(CASE REPORT)

Check for updates

Immune thrombocytopaenia as initial presentation of systemic lupus erythematosus: A case report and literature review

Ewere Marie Ogbimi [1, 2, *], John Raphael [3], Onoriedeode Thompson Ologbo [4, 5] and Ebiringa Blaise Anyanwu [6, 7]

[1] *Department of Medicine, Faculty of Clinical Medicine, College of Health Sciences, Delta State University Abraka, Delta State, Nigeria.*
[2] *Department of Internal Medicine, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria.*
[3] *Rheumatology Unit, Department of Internal Medicine, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria.*
[4] *Department of Pathology, Faculty of Clinical Medicine, College of Health Sciences, Delta State University Abraka, Delta State, Nigeria.*
[5] *Heamatology unit, Department of Pathology, Delta State University Teaching Hospital, Delta State, Nigeria.*
[6] *Department of Family Medicine, Faculty of Clinical Medicine, College of Health Sciences, Delta State University Abraka, Delta State, Nigeria.*
[7] *Department of Family medicine, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria.*

International Journal of Life Science Research Archive, 2024, 06(02), 045–051

Publication history: Received on 15 March 2024; revised on 04 May 2024; accepted on 07 May 2024

Article DOI: https://doi.org/10.53771/ijlsra.2024.6.2.0048

Abstract

Immune Thrombocytopenic Purpura (ITP) may be the initial presentation of Systemic Lupus Erythematosus (SLE). We present a case report of a 22year old female who was a known patient with ITP diagnosed 6years previously at the Haematology unit when she had initially presented on account of petechial skin rashes and spontaneously bleeding gums worsened by brushing her teeth. She was then found to have a platelet count of zero with anemia and had been on intermittent steroid therapy till she developed recurrent joint pain necessitating referral to Rheumatology unit to evaluate for lupus. Further investigations revealed elevated autoantibodies suggestive of SLE. She was then commenced on Mycophenolate mofetil and Hydroxychloroquine.

Keywords: Immune Thrombocytopenic Purpura; Systemic Lupus Erythematosus; Platelet Count; Mycophenolate Mofetil; Hydroxychloroquine

1. Introduction

Immune Thrombocytopenia Purpura (ITP), previously known as Immune Idiopathic Thrombocytopenic Purpura, is an acquired disease of young adults and children which is immune mediated and characterised by a transient or persistent decrease of platelet counts. In ITP, splenic sequestration and phagocytosis results from platelets being coated with autoantibodies to platelet membrane antigens [1]. ITP may also be defined as isolated thrombocytopenia with no other cause of thrombocytopaenia or clinically apparent associated conditions [2-4].

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with a remitting or relapsing course and usually involves multiple systems. It is characterised by the production of various autoantibodies and by several clinical manifestations, some of which are haematological [5,6].

* Corresponding author: Ewere Marie Ogbimi

2. Case report

We present a case of a 22year old female, who was referred to the Rheumatology clinic from the Haematology unit with complaints of recurrent joint pain in the previous 1 year. Joint pain was of insidious onset, involving the shoulders, elbows, and knees predominantly and occasionally the small joints of the hands. Recent episode was noticed a week prior to presentation and involved the shoulders and elbows with swelling of the right shoulder joint. Joint affectation was of inflammatory pattern and symptoms temporarily relieved by Prednisolone and non- steroidal anti- inflammatory drugs. She had no history of skin rash, oral ulcers, hair loss, headaches, seizures or psychosis, chest pain, cough nor difficulty in breathing. There were no associated renal symptoms, dryness of the eyes or mouth, no redness of the eyes, nor impaired vision. She did not report a preceding fever or diarrhea.

She is a patient of the Haematology unit and was on management for immune thrombocytopenia diagnosed 6 years ago when she had initially presented on account of petechial skin rashes and spontaneously bleeding gums worsened by brushing her teeth. She was then found to have a platelet count of zero with anaemia and has been on intermittent steroid therapy till she developed recurrent joint pain necessitating referral to Rheumatology unit to evaluate for lupus. There is no family history of similar symptoms, SLE or other autoimmune disorders.

Physical examination findings were essentially normal except for pallor and tenderness over the elbows and shoulders with swelling over the right shoulder joint.

2.1 Investigation Results from 6 years ago at point of diagnosis of ITP

- ***Full Blood Count (FBC) and Erythrocyte Sedimentation Rate (ESR):*** The ESR was 56 mm/hr, while the Haemoglobin concentration was 8.9 g/dl (12.0-16.0). The Packed Cell Volume (PCV) was 23.9 % (36- 48) while the White Blood Cell (WBC) count was 4.73 x 10^9 /L (4.0-11.0). The Lymphocytes constituted 24.2 % of the WBC with a count of 1.67 x 10^9 /L (1.00-4.00). The Neutrophils made up 66.2 % of the WBC with a count of 4.56 x 10^9 /L (2.00-7.50). The initial platelet count of our patient was 0 x 10^9 /L (150-450).
- ***Peripheral blood film:*** Dimorphic red blood cells (RBCs) with normocytic normochromic cells and microcytic hypochromic cells, no schistocytes were seen. The Lymphocytes appeared adequate in number on blood film, neutrophils were mostly mature with about 3 segments. The Platelets appeared reduced in number with megakaryocytes, no platelet clumps visualized.
- ***Bone Marrow Aspirate:*** Erythroid hyperplasia with increased megakaryopoiesis.
  Viral serologies were all negative. Serum electrolytes, urea and creatinine(E/U/Cr), and Urinalysis were within normal.

The impression for this patient was ITP with other considerations being Evan's syndrome and a Myeloproliferative disease.

2.2 Investigation results after review in Rheumatology clinic

- ***FBC and ESR:*** The ESR was 105 mm/hr with a haemoglobin concentration of 10.6 g/dl. The WBC count was 4.9 x 10^9 /L. The Lymphocytes made up 44 % of the WBC with a count of 2.1 x 10^9 /L while the Neutrophils constituted 52 % of the WBC. The platelet count was 266 x 10^9 /L.
- ***Urinalysis:*** This revealed one plus protein, uPCR 76.2 mg/day (<150 normal or mild proteinuria).
- ***SEUCR, LFT, SERUM URIC ACID:*** SEUCR, LFT and serum uric acid were all normal.
- ***ENA PANEL:*** An ENA panel revealed ANA of 1:2560, Anti- ds DNA +++, Anti-RIB ++, and Anti- Nucleosome ++. A diagnosis of SLE was made.

The ITP diagnosed 6 years ago was managed with serial pulse doses of Methylprednisolone and she had marked improvement with occasional flares. Last flare was 3 years prior to presentation to the Rheumatology clinic. Based on the above, she was placed on the following in the Rheumatology clinic; Tab Prednisolone 10 mg daily, Tab Hydroxychloroquine (HCQ) 200 mg daily (after being assessed for maculopathy), Tab Calcium vit D 1 daily, Tab Mycophenolate Mofetil (MMF) 500 mg bd, Tab Rosuvastatin 10 mg nocte, Sunscreen SPF30 2 hourly.

3. Discussion

Immune Thrombocytopenia Purpura (ITP), previously known as Immune Idiopathic Thrombocytopenic Purpura, is an acquired disease of young adults and children which is immune mediated and characterised by a transient or persistent decrease of platelet counts. In ITP, splenic sequestration and phagocytosis results from platelets being coated with

autoantibodies to platelet membrane antigens.[1] ITP may also be defined as isolated thrombocytopenia with no other cause of thrombocytopaenia or clinically apparent associated conditions [2-4].

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease involving multiple systems, with a chronic remitting or relapsing course. It is characterised by several clinical manifestations with production of various autoantibodies which may be haematological [5,6]. Thrombocytopenia ($<100\times10^9$/L) attributable to an autoimmune mechanism similar to that of immune thrombocytopenia (ITP) has been reported in 20% to 40% of patients with SLE [5,7,8]. ITP may play a role in early-stage SLE, however, the incidence of SLE in patients with ITP and the potential relationship between them is still unclear [9].

Zhu et al in a retrospective cohort study that used nation-wide population-based data to assess the risk of SLE in patients with ITP, demonstrated that the patients with ITP had a 26- time higher risk of new-onset SLE compared with the control population. Furthermore, the study demonstrated consistent findings of significant higher risk of SLE in patients with ITP across four different regression models, with men having a decreased risk of SLE compared with the women [6]. Our patient is female with SLE developing 6years from a diagnosis of ITP.

ITP is classified as primary or secondary according to the presence or absence of an underlying etiology. ITP can occur at any stage of SLE, but it has been observed to occur as an initial manifestation in some patients. This can pose a diagnostic challenge, as the symptoms of ITP may be the only presenting feature of SLE, and other clinical features of the disease may not become apparent until later stages. Thrombocytopenia in SLE is associated with a worse prognosis and higher mortality from the disease. It has been linked with severe disease course including neuropsychiatric disorders, renal involvement, hemolytic anemia and anti- phospholipid syndrome [6].

Pamuk et al. in a systematic meta-analysis revealed that almost 2 % with primary ITP went on to develop SLE, of which 17.5 % had positive ANA titers. This indicated that a positive ANA titer is a significant risk factor for development of SLE in patients with primary ITP [10]. Furthermore, the risk of future development of SLE in primary ITP patients was found to be higher compared with the general population with female ITP patients being particularly at higher risk. ITP patients with positive ANA titers represent a distinct high-risk group requiring a close follow-up. The risk of developing SLE in ITP patients seems to increase with time [10,11]. These were all demonstrated in our patient being female, with high ANA titers and SLE developing 6years from initial diagnosis of ITP.

3.1 Epidemiology

ITP is a condition that predominantly affects young women. Some studies have corroborated a female predominance in younger adults with a female to male ratio of 3:1, others have not. Most studies show a similar incidence of ITP in males and females over the age of 60 years. SLE has a female to male ratio of 9-12:1. Thrombocytopenia ($<100\times10^9$ /L) has been reported in 20 % to 40 % of patients with SLE and is usually attributed to an autoimmune mechanism similar to that of idiopathic immune thrombocytopenia (ITP) [5].

Acute ITP presenting in childhood affects both sexes equally, and most have a benign course.

The chronic form affects individuals between 20-50 years. In a study in Greece, thrombocytopenia was found to be present at diagnosis in 12 % and cumulatively in 16 % [12].

It has been estimated that 3 to 15 percent of patients with apparently isolated ITP go on to develop SLE. It may be the first manifestation of lupus in up to 16% of patients, presenting months or as early as 10 years before diagnosis [5,12].

In Nigeria, a study in the South- South, done to show the laboratory and clinical profile of SLE patients identified thrombocytopenia in 34.6 % of the subjects [13]. A Retrospective study done in ABUTH Zaria, over a 10year period identified 9 cases of ITP, 6 females, 3 males, aged 6-20 years. The commonest manifestation was epistaxis (88.9 %) and one of the subjects had ICH. All the patients had megakaryocytic hyperplasia [2]. A similar study in OAUTH over an 11year period had 11 cases of ITP, 7 females and 4 males, aged 10-55 years. Two of the females were positive for SLE test [14].

3.2 Pathogenesis of Thrombocytopaenia in SLE

There exact cause of reduced platelet count in SLE remains largely unknown, however the prognostic value of thrombocytopenia and its correlation with disease activity in SLE are recognized [15]. The major factors contributing to SLE-associated thrombocytopenia include excessive platelet destruction and/or reduced production from megakaryocytes [16]. Though SLE patients with thrombocytopenia often have elevated levels of antiplatelet antibodies

and/or APS antibodies, many SLE patients without thrombocytopenia may also have these autoantibodies [15-17]. SLE patients without thrombocytopenia have been demonstrated to have an association between SLE disease activity and antiplatelet antibodies [18]. The exact antigens involved in SLE-associated thrombocytopenia are less well defined compared with ITP where platelet glycoproteins are specific antigenic targets for antiplatelet antibodies [17].

In SLE thrombocytopenia, the implicated antigens are antigenic glycoproteins on platelet membranes [5]. Other autoantibodies include the antiphospholipid antibodies, anti- thrombopoietin (TPO), anti TPO receptor. Just like ITP, the most frequent antibodies in SLE thrombocytopenia are the anti IIb/IIIa antibodies. Other identified antibodies include; anti CD40 ligand molecule, antibodies against glycoprotein (Gp)Ia/IIA, HLA I, GpIb/Ix complex, though uncommon [5,19, 20].

3.3 Evaluation of Thrombocytopenia in the Setting of SLE

Patients who are not acutely ill but have isolated, mild thrombocytopenia, the evaluation includes a thorough history for medications and other illnesses that may affect the platelet count, as well as review of the FBC. Additional testing may be done sequentially or simultaneously for vitamin B12 and folate deficiencies, liver disease, and coagulation abnormalities, especially antiphospholipid antibodies, as appropriate, based on the history and preliminary laboratory results [9].

For patients who are acutely ill or have new onset of thrombocytopenia plus other cytopenias (such as neutropenia, anaemia), haematology consultation is recommended. The patient should have a thorough history and physical examination; review of medications; review of the blood smear for schistocytes or other abnormal cells, coagulation testing, and testing of renal and hepatic function. Disorders to be considered include ITP, thrombotic microangiopathies, severe infections and severe drug reactions [9].

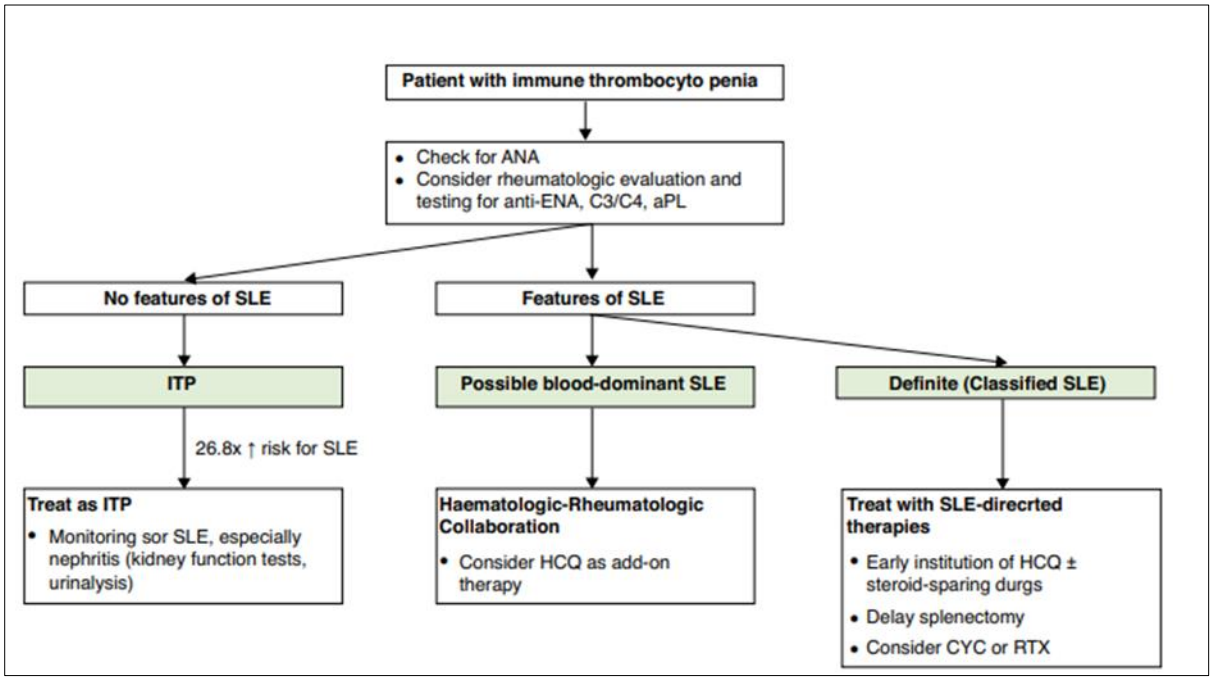

Figure 1 Approach to the patient who presents with immune thrombocytopenia [9]

Thrombocytopenia (<100 000/mm3) is present in ~10% of patients with SLE at diagnosis and in ~15-20% cumulatively over the course of the disease. ANA, antinuclear antibodies; anti-ENA, antibodies to extractable nuclear antigens; aPL, antiphospholipid antibodies; CYC, cyclophosphamide; HCQ, hydroxychloroquine; ITP, immune thrombocytopenic purpura; RTX, rituximab.

3.4 Treatment

ITP and immune mediated Thrombocytopenia in SLE bear many similarities in treatment because of the similarities in pathophysiology. Achieving a complete or partial platelet response in severe thrombocytopenia requires emergency therapy and this also eliminates haemorrhagic complications. There is need for maintenance treatment to prevent

relapse. Generally, patients without bleeding manifestations and with a platelet count > 50×109/l do not require treatment in the absence of coexistent haemostatic disorders, anticoagulation treatment, trauma or major surgery. The decision to treat when thrombocytopenia is the only disorder in SLE is based on the haemorrhagic manifestations and platelet count [5, 9].

The cornerstone for initial treatment is Corticosteroids. High dose oral prednisolone or pulse high dose methylprednisolone (MP) with or without intravenous immune globulin (IVIG) are used in the acute phase. Second line agents include hydroxychloroquine (HCQ), danazol, immunosuppressive drugs like azathioprine (AZA), mycophenolate mofetil (MMF), cyclosporine (CSA), mycophenolate mofetil (MMF), cyclophosphamide (CYC), and biological therapies such as rituximab [5, 9].

Romiplostim and Eltrombopag are thrombopoietin receptor agonists which have been widely used for the treatment of ITP in reported literature and also seem to have a role in SLE thrombocytopenia [5, 9]. For recurrent or resistant cases (Controversial in SLE because of the role of the kidneys in immune complex clearance), Splenectomy is an option. Treatment with hydroxychloroquine may be considered for patients with ANA positivity or have additional but not enough features to allow a confident diagnosis or classification of SLE (incomplete SLE) [5, 9]. Our patient received treatment with hydroxychloroquine.

4. Predictive features in ITP for development of SLE

Factors significantly related to the development of SLE within 1 year following ITP diagnosis include Young age (< 40 years), ANA positivity, and organ bleeding. Anaemia and lymphopenia developing during the course of management of ITP may also predict a future diagnosis of SLE. Hence, there is need for continued follow-up for the detection of SLE development in patients with ITP, particularly those with young age, ANA positivity, or organ bleeding [15-18]. Our patient was young, 16(years) when diagnosed with ITP. She developed SLE 6(six) years later.

Table 1 Differentiating ITP from TTP and DIC

LABORATORY TEST	TTP	ITP	DIC
PLATELETS	Low	Very low	Mildly low to low
MAHA	Yes	No	Yes
HAEMOGLOBIN	Reduced	Normal	Reduced
PERIPHERAL SMEAR	Schistocytes	Large platelets	Schistocytes
HAEMOLYSIS	Abnormal	Normal	Abnormal
CREATININE	Often normal or mildly elevated	Normal	Normal or elevated
PT/INR/PTT	Normal	Normal	Elevated
D-DIMER	Normal to increased	Normal	Increased
FIBRINOGEN	Normal	Normal	Decreased

DIC, disseminated intravascular coagulation; INR, international normalised ratio; ITP, immune thrombocytopenic purpura; MAHA, microangiopathic hemolytic anemia; PT, prothrombin time; PTT, partial thromboplastin time; TTP, thrombotic thrombocytopenic purpura [21].

5. Conclusion

ITP can be an initial presentation of SLE. SLE presents occasionally with non-specific symptoms and ITP can be one of the early manifestations. It is important to recognise the association between ITP and SLE, as early detection and management of SLE can improve patient outcome. The treatment of ITP in SLE patients would require a multidisciplinary approach, including haematologists, rheumatologists and immunologists. Proper evaluation for SLE should be carried out in patients with ITP especially children and women of reproductive age.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from the patient.

References

[1] Justiz Vaillant AA, Gupta N. ITP-Immune Thrombocytopenic Purpura. [Updated 2023 May 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537240.

[2] Hassan A, Adebayo A, Musa AU, Suleiman AM, Ibrahim IN, Kusfa IU, Aminu MS. Clinical feature and management of immune thrombocytopenic purpura in a tertiary hospital in Northwest Nigeria. Niger Med J. 2017 Mar-Apr;58(2):68-71. doi: 10.4103/0300-1652.219343. PMID: 29269984; PMCID: PMC5726176.

[3] Kühne T, Imbach P. Management of children and adolescents with primary immune thrombocytopenia: controversies and solutions. Vox Sang. 2013 Jan;104(1):55-66. doi: 10.1111/j.1423-0410.2012.01636.x. Epub 2012 Jul 17. PMID: 22804721.

[4] George JN, Kojouri K. Immune thrombocytopenic purpura. In: Kitchens CS, Alving BM, Kessler CM, editors. Consultative Hemostasis and Thrombosis. 2nd ed. Philadelphia: Saunders-Elsevier; 2007. p. 123-38. [Google Scholar].

[5] Galanopoulos N, Christoforidou A, Bezirgiannidou Z. Lupus thrombocytopenia: pathogenesis and therapeutic implications. Mediterr J Rheumatol. 2017 Mar 28;28(1):20-26. doi: 10.31138/mjr.28.1.20. PMID: 32185250; PMCID: PMC7045921.

[6] Zhu FX, Huang JY, Ye Z, Wen QQ, Wei JC. Risk of systemic lupus erythematosus in patients with idiopathic thrombocytopenic purpura: a population-based cohort study. Ann Rheum Dis. 2020 Jun;79(6):793-799. doi: 10.1136/annrheumdis-2020-217013. Epub 2020 Apr 2. PMID: 32241798.

[7] Rabinowitz Y, Dameshek W. Systemic Lupus Erythematosus after “idiopathic” thrombocytopenic purpura: a review. A study of systemic lupus erythematosus occurring after 78 splenectomies for «idiopathic» thrombocytopenic purpura, with a review of the pertinent literature*†. Ann Intern Med 1960;52:1–28. [PubMed] [Google Scholar].

[8] Mestanza-Peralta M, Ariza-Ariza R, Cardiel MH, Alcocer-Varela J. Thrombocytopenic purpura as initial manifestation of systemic lupus erythematosus. J Rheumatol. 1997 May;24(5):867-70. PMID: 9150074.

[9] Fanouriakis A, Bertsias G, Boumpas DT. Population-based studies in systemic lupus erythematosus: immune thrombocytopenic purpura or 'blood-dominant' lupus? Ann Rheum Dis. 2020 Jun;79(6):683-684. doi: 10.1136/annrheumdis-2020-217356. Epub 2020 Apr 20. PMID: 32312772.

[10] Pamuk ON, Ali SM, Hasni S. Development of systemic lupus erythematosus in patients with immune thrombocytopenic purpura: A systematic meta-analysis. Autoimmun Rev. 2023 Apr;22(4):103297. doi: 10.1016/j.autrev.2023.103297. Epub 2023 Feb 11. PMID: 36781038; PMCID: PMC10078978.

[11] Pamuk ON. Thrombocytopenia in Patients with Systemic Lupus Erythematosus. Eur J Rheumatol. 2023 Oct;10(4):159-162. doi: 10.5152/eurjrheum.2023.23069. PMID: 37885267; PMCID: PMC10765209.

[12] Nikolopoulos D, Kostopoulou M, Pieta A, Karageorgas T, Tseronis D, Chavatza K, Flouda S, Rapsomaniki P, Banos A, Kremasmenou E, Tzavara V, Katsimbri P, Fanouriakis A, Boumpas DT. Evolving phenotype of systemic lupus erythematosus in Caucasians: low incidence of lupus nephritis, high burden of neuropsychiatric disease and increased rates of late-onset lupus in the 'Attikon' cohort. Lupus. 2020 Apr;29(5):514-522. doi: 10.1177/0961203320908932. Epub 2020 Feb 27. PMID: 32106788; PMCID: PMC7168806.

[13] Emorinken A, Dic-Ijiewere MO, Erameh CO, Ugheoke AJ, Agbadaola OR, Agbebaku FO. Clinical and laboratory profile of systemic lupus erythematosus patients at a rural tertiary centre in South-South Nigeria: experience from a new rheumatology clinic. Reumatologia. 2021;59(6):402-410.

[14] Salawu L, Durosinmi MA. Immune thrombocytopaenic purpura: 11-year experience in Ile-Ife, Nigeria. Afr J Med Med Sci. 2001 Mar-Jun;30(1-2):99-103. PMID: 14510161.

[15] Jiang Y, Cheng Y, Ma S, Li T, Chen Z, Zuo X, et al. Systemic lupus erythematosus-complicating immune thrombocytopenia: From pathogenesis to treatment. J Autoimmun. 2022 Oct;132: 102887. doi: 10.1016/j.jaut.2022.102887. Epub 2022 Aug 25. PMID: 36030136. Accessed February 10, 2024.

[16] Linge P, Fortin PR, Lood C, Bengtsson AA, Boilard E. The non-haemostatic role of platelets in systemic lupus erythematosus. Nat Rev Rheumatol. 2018;14(4):195 213. (10.1038/nrrheum.2018.38) [PubMed] [CrossRef] [Google Scholar].

[17] Scherlinger M, Richez C, Tsokos GC, Boilard E, Blanco P. The role of platelets in immune-mediated inflammatory diseases. Nat Rev Immunol. 2023;23(8):495 510. (10.1038/s41577-023-00834-4) [PMC free article] [PubMed] [CrossRef] [Google Scholar].

[18] Zufferey A, Kapur R, Semple JW. Pathogenesis and therapeutic mechanisms in immune thrombocytopenia (ITP). J Clin Med. 2017;6(2):16. (10.3390/jcm6020016) [PMC free article] [PubMed] [CrossRef] [Google Scholar].

[19] Nojima J, Kuratsune H, Suehisa E, Futsukaichi Y, Yamanishi H, Machii T, Iwatani Y, Kanakura Y. Association between the prevalence of antibodies to beta(2)-glycoprotein I, prothrombin, protein C, protein S, and annexin V in patients with systemic lupus erythematosus and thrombotic and thrombocytopenic complications. Clin Chem. 2001 Jun;47(6):1008-15. PMID: 11375285.

[20] Muñoz-Rodríguez FJ, Reverter JC, Font J, Tàssies D, Cervera R, Espinosa G, Carmona F, Balasch J, Ordinas A, Ingelmo M. Prevalence and clinical significance of antiprothrombin antibodies in patients with systemic lupus erythematosus or with primary antiphospholipid syndrome. Haematologica. 2000 Jun;85(6):632-7. PMID: 10870121.