



## A Case Report On Abnormal Uterine Bleeding with Multi-System Disorders

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**Abstract:** Autoimmune disease is a condition that attacks the immune system and leads to multi-system disorders like systemic lupus erythematosus and rheumatoid disorders, which initiates self-directed immune responses that result in clinical diseases, mainly in obstetrics conditions like recurrent pregnancy loss, pre-eclampsia are common. The study aimed to identify the relationship between connective tissue disorders and abnormal uterine bleeding patterns. A rare case of abnormal uterine bleeding with a past history of recurrent pregnancy loss was presented in the casualty with excessive menstrual bleeding in a state of hypovolemic shock. The patient complained of generalised malaise, giddiness, breathlessness, and palpitations for the past 2 months. She suffered recurrent epistaxis for the past 2 months and experienced symptoms like loss of appetite, recurrent vomiting for the past 15 – 20 days, and rashes over the face and cheeks for 6 months. Her haemoglobin was 2.4g/dL, and the platelets were less than 10,000 with bicytopenia at the time of admission She was shifted to ICU and haemodynamically stabilized by packed red blood cells, fresh frozen plasma, and platelets. Following this, she was treated with antifibrinolytics, and severe anaemia was corrected with multiple PRBC transfusions. Multiple single-donor platelet transfusions were also done. After recovery, the patient was discharged with an advice to continue hydroxychloroquine. Immune dysregulation and inflammation together contribute to the development of menstrual disorders among women with Rheumatoid Disorders which can be well managed with systematic therapeutic plans at the initial stage.

**Key Words:** Mixed connective tissue disease, auto-immune disorder, systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, auto-antibodies, antigen-antibody complex, antinuclear antibodies

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## I. INTRODUCTION

Anaemia is the most common complication in premenopausal women due to heavy menstrual bleeding. Menstrual abnormalities contribute to 5 -10% of iron deficiency anaemia presented by women.<sup>1-3</sup> In autoimmune diseases, patients present with anaemia due to heavy menstrual bleeding which is due to haemolysis.<sup>4-6</sup> Heavy menstrual bleeding is seen in 49% of pre-menopausal women with systemic lupus erythematosus (SLE), which present with anemia<sup>7-9</sup> About 78% of autoimmune diseases are seen among women. This massive disparity is mainly due to genetic causes, stress, and hormones.<sup>10- 13</sup>Hormones are signaling chemicals that our body used to control and regulate cells throughout the body<sup>14-16</sup>. Glucocorticoids are steroid hormones often used in the treatment of lupus, taking advantage of the body's natural regulation system as corticosteroids. Women with lupus have high prolactin and oestrogen levels and low testosterone levels. Thus women with lupus or any autoimmune disease tend to bleeding episodes not only due to alteration in coagulation but also due to the hormonal imbalance.<sup>17,18</sup> Mixed connective tissue disease (MCTD) is a rare systemic autoimmune disease with an overlapping feature of at least two connective tissue diseases (CTD), including systemic lupus erythematosus (SLE), systemic sclerosis (SSC), polymyositis (PM), dermatomyositis (DM) and rheumatoid arthritis (RA) along with the presence of a specific antibody, anti-UI- ribonucleoprotein (RNP) previously known as an antibody to extractable nuclear antigen (ENA). MCTD has no unique clinical features, and there is a considerable inter-individual variation in clinical manifestations.<sup>13</sup> Mixed connective tissue disorders affect significantly more women than men, and gynaecological disorders may have an additional negative impact on women's health. Among patients with RDs, the disturbance of gynaecological health would be caused by several factors, such as chronic inflammation, hormonal imbalance, and drug effects, including psychological and cultural issues.<sup>14,15</sup> As the menstrual cycle is controlled by the hypothalamus-pituitary ovarian axis; estrogen increases with the follicular stimulating hormone to form the uterus lining during the follicular phase. FSH causes the growth of the ovarian follicles. Pulsatile gonadotropin-releasing hormone initiates the secretion of follicular stimulating hormone and luteinising hormone. Follicle-stimulating hormone released by the anterior pituitary stimulates the growth of primordial follicles into graffian follicles. One dominant graffian follicle develops, which matures, ripens, and ovulates. Progesterone is secreted from the corpus luteum, and menstruation occurs as the endometrium sheds down. When the hypothalamopituitary ovarian axis fails to function or due to the autoimmune diseases which causes alteration of the coagulation cascade, both may lead to heavy menstrual bleeding.<sup>11,12</sup> A number of evidence have been published on pregnancy outcomes and recommendations on preconception care. However, limited data are available on menstruation- related disorders in MCTDs<sup>16</sup>. A rare case with abnormal uterine bleeding and a history of recurrent pregnancy loss was presented in the casualty with excessive menstrual bleeding in a state of hypovolemic shock. The patient was later diagnosed with MCTD. Thus, the study

aimed to identify the relationship between connective tissue disorders and abnormal uterine bleeding patterns.

## 2. CASE REPORT

A 38yrs old female patient reported to a casualty with hypovolemic shock with a history of abnormal menstrual bleeding for 60 days that was not responding to any medication. The patient complained of generalised malaise, giddiness, breathlessness, and palpitations for 2 months. She suffered recurrent epistaxis for the past 2months and experienced symptoms like loss of appetite, recurrent vomiting for 15 – 20 days, and rashes over the face and cheeks for 6 months.

### 2.1. Past History

The patient was a known case of rheumatoid arthritis since 8 years and was under regular medication (Tab. HCQ 200 mg twice a day, Tab. Methotrexate 10 mg, and Tab. Prednisone 10 mg once a day). There was no history of drug allergy or any surgery.

### 2.2. Marital History

The Patient was married for the past 22 years and was a non-consanguineous marriage.

### 2.3. Obstetric History

The patient had a history of 3 recurrent abortions 7 years back. She had been evaluated for the same and has not taken any infertility treatment.

### 2.4. Management

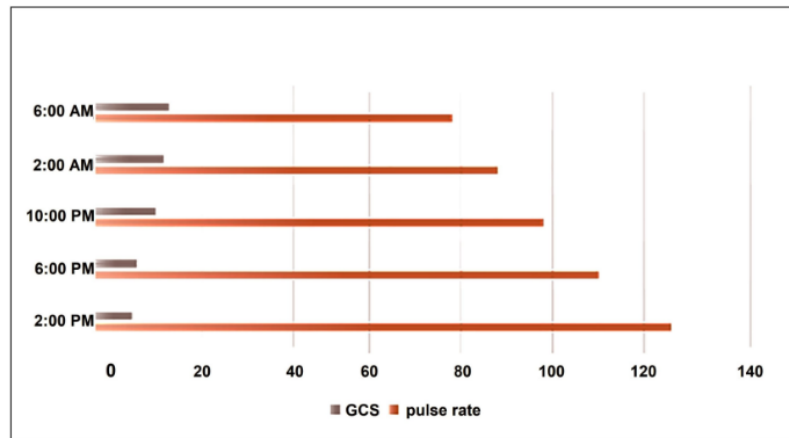
The patient was admitted with hypovolemic shock. Her haemoglobin count was 2.4g/dL, and the platelets were less than 10,000 with bicytopenia. She was shifted to ICU and haemodynamically stabilized by packed redblood cells, fresh frozen plasma, and platelets. Following this, she was treated with antifibrinolytics, and severe anaemia was corrected with multiple PRBC transfusions. Multiple single-donor platelet transfusions were also done.

### 2.5. Time Line

Even though the timeline of the disease diagnosis was around 8 years, the autoimmune disease flare-up occurred within the past 60 days, following which the patient presented with the complaints. The patient was under treatment since admission, and the acute flare-up of the autoimmune disease was resolved in a week.

### 2.6. Diagnostic Assessment

Fig-1 shows the vital signs of the patient during the observation period. Initially, the patient was assessed based on her signs and symptoms, and treatment was started upon to stabilize the patient. Further, hemodynamic investigations were done to confirm the disease and treated for the same.



**Fig 1: Vital signs of the patient during the observation period**

## 2.7. Therapeutic Intervention

The patient was initially stabilised with intravenous fluids followed by packed red blood cells, FFP, and platelets. Simultaneously, an anti-fibrinolytic was administered to the patient to control the bleeding, and anaemia was also corrected. No change in therapeutic intervention was made.

## 2.8. Nursing Perspectives

Routine patient care was given along with intravenous fluids, and was observed for any other flare-up reaction or allergic reaction.

## 3. DISCUSSION

The study was conducted on a female subject diagnosed with mixed connective tissue disorder and a known case of rheumatoid arthritis and systemic lupus erythematosus with regular treatment. The case had abnormal uterine bleeding with severe anaemia and pancytopenia in shock and a past history of recurrent pregnancy loss in the early trimester. This is a rare scenario presented with gynaecological complications. Autoimmune disorders are self-directed immune responses that result in the circulating endogenous antibodies interacting with self-antigens to form immune complexes. These are deposited in a tissue, causing tissue damage with resultant clinical disease<sup>3</sup>. The pathophysiology of SLE shows the overproduction of autoantibodies directed against various nuclear components and cell-surface antigens. So, when the disease is active, an inflammatory reaction is generated by the antigen-antibody complexes found along the basement membranes of affected organs and is mediated by cytokines, complement activation, and prostaglandin production.<sup>1</sup> Antinuclear antibodies (ANAs) are detected in almost 99% of patients with SLE. Mixed connective tissue disease (MCTD) is under rheumatic "overlap syndromes," which is used to describe when a patient has features of more than one classic inflammatory rheumatic disease that includes systemic lupus erythematosus, polymyositis, scleroderma, and rheumatoid arthritis.<sup>5</sup> Women are more affected by rheumatic diseases than men. The pathogenesis involves abnormal uterine bleeding mainly due to the interrelationship between sex hormones, and immunity<sup>8</sup> Estrogen and progesterone are signalling modulators of the immune system, playing a role in lymphocyte maturation, activation, and synthesis of antibodies and cytokines<sup>1</sup>. On the other hand, gynaecological diseases such as endometriosis

and adenomyosis have a strong immune background<sup>2</sup>. Thus, immune dysregulation and inflammation may contribute to the development of menstruation-related disorders among women with Rheumatoid Disorders. The management of rheumatoid disease in women is a challenge for clinicians. It should be evaluated accurately in the gynaecological aspects (menstruation, fertility, maternity, and sexuality), and they should be managed as an interdisciplinary teamwork approach by the rheumatologist and gynaecologists.

## 3.1. Therapeutic Outcomes

The patient presented with severe anaemia (Hb - 2.5mg/dL) and a platelet count less than 10,000. The condition was first treated with 5 units PRBCs and 8 units of random donor platelets. Further improvement was made to stop the bleeding with a thrombopoietin receptor agonist (Tab.Revolade) and methylprednisolone. After recovery, the patient was continued with a discharge plan and hydroxychloroquine.

## 4. CONCLUSION

The case observations show that the acute flare-up of the autoimmune disease was managed symptomatically with antifibrinolytic after stabilizing the patient with multiple red blood cell transfusions and platelets. Correlating the pathogenesis of the disease, the rheumatic disease affects the woman of reproductive age, evolving as abnormal uterine bleeding due to the inter-relationship between the sex hormones and immunity. Thus, it may be concluded that immune dysregulation and inflammation together may contribute to the development of menstruation-related disorders among women with Rheumatoid Disorders which can be well managed with systematic therapeutic plans at the initial stage.

## 5. ACKNOWLEDGEMENT

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## 6. INFORMED CONSENT

Written informed consent was obtained from the patient in her language according to the standard protocols, explaining the purpose of the study. The study was conducted maintaining confidentiality about the patient.

## 7. AUTHORS CONTRIBUTION STATEMENT

Dr. Niranjani conceptualized, curated the data, designed the study, and prepared the original draft. Dr. T. G. Revathy and Dr. Varshini analysed and completed the data, and necessary inputs were given for designing the manuscript. All authors

discussed the methodology and results and contributed to the final manuscript.

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## 8. CONFLICT OF INTEREST

Conflict of interest declared none.