ABSTRACT

A 50 years old woman was referred to hospital with complaints of bluish black discoloration of skin or multiple ecchymosis since 6 days and skin rashes, pink changes or petechiae changes since 1 week, dark color stools since 3 days. She had a history of COVID-19 positive on past “3 months” back and she received the corticosteroids, antiviral drugs, broad spectrum antibiotics, anticoagulants, and vitamin B and C supplements. Now patient is admitted and investigated for further management. Her bone marrow examination reveals marrow cytological features are compatible with immune thrombocytopenic Purpura and peripheral examination reveals red cells are microcytic hypochromic with elongation forms, platelets are markedly reduced and elevation of CRP, reduction of the Hb, PCV, MCH, MCV, MCHC, APTT, Serum vitamin B12, Lymphocytes and
her HRCT-Chest shows CORADS 5, Rapid antigen test shows positive. A review on introduction of the disease, etiology, pathogenesis, pathophysiology, mechanism of thrombocytopenia in COVID-19 patients and grading is explained in literature review.

Keywords: Idiopathic thrombocytopenia; petechiae; ecchymosis; purpura, corona virus disease; antiviral drugs.

1. INTRODUCTION

Wuhan is the capital city of Hubei province in China. In December 2019, a cluster of unknown acute respiratory illness occurred to many patients. This virus subsequently spread to other states in China and patients have been identified in other countries also [1,2,3]. The disease is known as corona virus disease (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). It can be declared a pandemic by the World Health Organization on 11 March 2020 [1]. There are six types of corona viruses that can infect to humans have been identified those are HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, SARS-CoV and MERS-CoV. The first four viruses mainly cause the common cold, where as the SARS-CoV and MERS-CoV viruses cause Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). COVID-19is known to cause serious respiratory symptoms and complications but, available data suggest that the symptoms of the disease can also result from involvement of other body systems such as hematopoietic, neurological and immune system [4,5]. The most common symptoms of the disease is febrile illness, fatigue associated with respiratory symptoms such as dry cough, dyspnea and anorexia but other atypical manifestations of the infection have been observed [6] and human to human transmission of COVID-19has been conformed [7].

The term Idiopathic Thrombocytopenic Purpura refers to an Unknown origin or Thrombocytopenic state characterized by decreased numbers of circulating platelets, normal or increased numbers of megakaryocytic in the bone marrow [8,9]. It is divided into 2 forms those are Acute and Chronic. The Acute form most commonly occurs in 2-7years of age although it is also present in adults but it has no preference for gender and it resolves within 6 months. Chronic form occurs more often in females between 20-40years of age with females to male ratio of 3:1. It is more persistent disease, lasting for more than 6 months, has an insidious onset and incidence is unknown [10].

2. ETIOLOGY

1.30% Idiopathic
2.30% of Drugs related
3.30% of underlying disease

- Connective tissue disorder,
- Lymphoma,
- Chronic Lymphocytic Leukemia.

4.10% Viral Infection
- HIV, Rubella, Rubeola etc.

5. Genetics: SLE
6. Immune factors

- Autoantibody mediated destruction of Platelets.
- Predisposing conditions and exposures

3. PATHOGENESIS

ITP appears to be immunologically mediated. An ant platelet IgG antibody reacts with host Platelets, causing rapid destruction by the Reticuloendothelial system (Fig.1).

They are two main reasons. Those are

A) The demonstration of increased level of Platelet associated IgG antibodies in more than 90% of patient with ITP.

B) Some studies show normal individuals Developed thrombocytopenia when injected with plasma from patients with ITP.

4. PATHOPHYSIOLOGY

Lymphocytes produce anti platelet antibodies directed at platelet surface glycoproteins.

A) Platelets are taken up and internally degraded by antigen presenting cells (APCs)
B) APCs present platelet antigen in association with major histocompatibility complex (MHC) class II to T helper cells, which become activated
and secrete the Th1 cytokines interleukin-2 and IFN-g.
C) Th1 cytokines activate and drive auto reactive B cells to differentiate into autoantibody producing cells.

The IgG coated platelets are cleared by splenic macrophages, which results in thrombocytopenia.

The course of ITP is affected by pregnancy (relapse during pregnancy after remission worse if active).

Placental transfer of the IgG platelet antibodies can result in fetal or neonatal thrombocytopenia.

5. CASE REPORT
A 50 years old woman was referred to hospital with complaints of bluish black discoloration of skin or multiple ecchymosis since 6 days and skin rashes, pink changes or petechiae changes since 1 week, dark color stools since 3 days. She had a history of COVID-19 positive on past “3 months” back in treatment.

6. PAST MEDICAL AND MEDICATION HISTORY
Chief Complaints: Cough, Shortness of breath since 4 days.

Diagnosis: COVID - 19 Positive, viral Pneumonia

7. PERIPHERAL BLOOD SMEAR
- Red cells are micro cystic hypochromic with elongated forms
- Platelets are markedly reduced

Table 1. Physical examinations

| Vitals                      |       |
|-----------------------------|-------|
| Pulse rate                  | 84    |
| Respiratory rate            | 20    |
| Blood pressure              | 130/80|
| Temperature                 | 98.6  |

Table 2. Systemic examinations

| CVS          | S1S2+  |
|--------------|--------|
| CNS          | E4V5M6 |
| RS           | BAE+, Clear |
| P/A          | Normal |
| SPO2         | 100%   |

8. BONE MARROW
- Marrow cytological features are compatible with immune thrombocytopenic Purpura (Fig. 2).

Blood Group: AB Positive (blood transfusion was done)

![Fig 1. Mechanism of thrombocytopenia in COVID-19 patients [11,12,13]](image-url)
Table 3. Lab tests

| Parameters          | Abnormal values | Normal values      |
|---------------------|-----------------|--------------------|
| Haemoglobin         | 9.1 g/dl        | 14-16 g/dl        |
| PCV                 | 30.6%           | 37-47%             |
| MCV                 | 61.5fl          | 80-95 fl           |
| MCH                 | 18.2pg          | 27-33 pg           |
| MCHC                | 29.6g/dl        | 31-36 g/dl        |
| RDW                 | 19.0%           | 12.2-16.1%        |
| PCV                 | 15000Cells/cu.mm| 1,50,000-4,00,000 Cells/cu.mm |
| PT                  | 11.9 seconds    | 11-13.5 seconds   |
| APTT                | 24.6 seconds    | 30-40 seconds     |
| Serum vitamin B12   | 139.6 pg/mL     | 200-900 pg/m      |
| Serum folic acid    | 4.9 ng/ml       | 2.7-17.0 ng/ml    |
| Fibrinogen levels   | 326.7 mg/dL     | 200-400 mg/Dl     |
| Direct anti-globulin test | Negative         |                    |
| Indirect anti-globulin test | Negative       |                    |

Table 4. Drug chart

| Drugs                | Doses   | Frequency |
|----------------------|---------|-----------|
| Inj. Pan             | 40mg    | OD        |
| Inj. Vitamin B12     | 1000mcg | OD        |
| Tab. Fovite          | 5mg     | OD        |
| Cap. Orofer-XT       | 1capsule| OD        |
| Inj. Methylprednisolone | 1gm   | OD        |
| Tab. Primolut-N      | 4mg     | TID       |
| Tab. Zolpidolom      | 5mg     | HS        |

Table 5. Lab investigations

| Tests                          | Result          |
|--------------------------------|-----------------|
| HRCT-Chest                     | CORADS 5        |
| Rapid antigen test             | Positive        |
| C-Reactive protein             | 250mg/L         |
| Serum ferritin                 | 48ng/ml         |
| Blood group                    | AB Positive     |

Table 6. Hematology

| Parameters     | Abnormal values | Normal Values |
|----------------|-----------------|---------------|
| Hb             | 7.5 g/dl        | 11-14g/dl     |
| PCV            | 26%             | 35-47%        |
| Lymphocytes    | 15%             | 26-46%        |
| Polymorphs     | 77%             | 40-65%        |
| ESR            | 50mm/hr         | 0-30mm/hr     |

Table 7. HRCT-Chest severity

| CT-Severity      | % of involvement | Score |
|------------------|------------------|-------|
| Right upper lobe | 5-25%            | 2     |
| Right middle lobe| 5%               | 1     |
| Right lower lobe | 5-25%            | 2     |
| Left upper lobe  | 5-25%            | 2     |
| Left lower lobe  | 25-50%           | 3     |
| Total            |                  | 10    |
| Severity         |                  | Moderate |
Table 8. Hospital treatment

| Drugs                        | Doses |
|------------------------------|-------|
| Tab. Augmentin               | 6 doses|
| Tab. Pantocid-DSR            | 6 doses|
| Syp. Ascoril                 | 18 doses|
| Tab. Prednisolone            | 12 doses|
| Tab. Dexamethasone           | 6 doses|
| Inj. Cloxane                 | 12 doses|
| Tab. Limcee                  | 6 doses|
| Cap. Becosules               | 6 doses|
| Inj. Remdesiver              | 6 doses|

Table 9. Discharge medications

| Drugs            | Dose     | Frequency |
|------------------|----------|-----------|
| Tab. Pantocid-DSR| 40/30mg  | OD        |
| Tab. HCQ         | 200mg    | BD        |
| Tab. Limcee      | 500mg    | OD        |
| Tab. Omnacortil  | 20mg     | BD        |
| Tab. Dabiclot    | 110mg    | BD        |
| Cap. Becosules   | 1 capsule| HS        |

Fig. 2. This is the picture to the patient. The patient who is suffered with COVID-19 can developed the Idiopathic Thrombocytopenic Purpura

9. DISCUSSION

Idiopathic Thrombocytopenic Purpura is one of the rare diseases. The incidence of the disease is more in females when compared to males. The most common cause of the disease is unknown. The standard treatment given to the patient is corticosteroids, intravenous immunoglobulins (IVIG) and Anti-D immune globulin the patients who having the Rh-positive blood group. In this condition patient have the Marrow cytological features are compatible with immune thrombocytopenic Purpura, Red cells are micro cystic hypochromic with elongated forms, Platelets are markedly reduced and elevation of C-Reactive protein, reduction of the Hemoglobin, packed cell volume, mean corpuscular hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin concentration, APTT, Serum vitamin B12, Lymphocytes and her HRCT-Chest shows CORADS 5, Rapid antigen test shows positive.

We observed the decreasing level of platelets due to an immunologic reaction that can be seen in viral infections is the most common cause as it has been seen in dengue, influenza and HIV infections [14]. Like the SARS-CoV and MERS-CoV viruses [11], SARS-CoV may induce the thrombocytopenia and the mechanism involves the abnormal immune function, impairing bone marrow hemopoiesis directly [15,16] and lung damage [17]. Previous studies have reported thrombocytopenia in patients with COVID-19 during the infection [18,19,20]. This is commonly represented by significant lymphopenia [21].

Lymphocytes and their sub types play a vital role in maintenance of the immune system [22]. The
decreasing the lymphocytes and their subtypes, especially the CD4+ T cells, CD8+ T cells and NK (CD56+) cells was significantly indicates an impairment of the immune system caused by the SARS-CoV-2 infection, which might be trigger an autoimmune response [23]. CD4+ T cells help B cells to produce the virus specific antibodies and CD8+ T cells can kill the virus infected cells by using the cytotoxicity mechanism. Therefore the depletion and dysfunction of the lymphocytes and their subtypes induced the immune system become abnormal. This results the thrombocytopenia.

10. CONCLUSION

A 50 years old female patient was admitted in hospital with complaints of bluish black discoloration of skin or multiple ecchymosis since 6 days and skin rashes, pink changes or petechiae changes since 1 week, dark color stools since 3 days. She had a history of COVID-19positive on past “3 months” back in treatment. Her peripheral examination reveals Red cells are micro cystic hypochromic with elongated forms, Platelets are markedly reduced and bone marrow test reveals that Marrow cytological features are compatible with immune thrombocytopenic Purpura. Her lab tests reveal that elevation of C-reactive protein and reduction of the Hemoglobin, packed cell volume, mean corpuscular hemoglobin, mean corpuscular volume, and mean corpuscular hemoglobin concentration, APTT, Serum vitamin B12, Lymphocytes and her HRCT-Chest shows CORADS 5, Rapid antigen test shows positive. The novel corona virus can also cause the systemic involvement those are Respiratory and Hematopoietic complications.

SUPPLEMENTARY MATERIAL

Supplementary material available in this following link:
https://www.journaljpri.com/index.php/JPRI/libraryFiles/downloadPublic/17

CONSENT

As per international standard or university standard, patient’s consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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