

Pancytopenia Secondary to SARS-CoV 2 Infection-A Case Reprt

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Abstract

Pancytopenia is a condition when person has low count of all three types of blood cells causing a triage of anemia, leukopenia and thrombocytopenia. It should not be considered as a disease in itself but rather the sign of a disease that needs to be further evaluated. Among the various causes, viral infections like Human Immunodeficiency Virus, Cytomegalovirus, Epstein-Barr virus and Parvovirus B19 have been implicated. Pancytopenia is a rare complication and not commonly seen in patients with COVID 19 disease. Here, we report a case of pancytopenia in previously immunocompetent elderly male patient with SARS-CoV2 infection.

Introduction

The most common haematological and immunological findings of coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) are elevated inflammatory markers, hypercoagulable state and lymphopenia. Pancytopenia is a rare complication and not commonly seen in immunocompetent patients with COVID 19 disease. The common causes of pancytopenia in clinical practice are megaloblastic anemia, hypersplenism, drug induced bone marrow toxicity, leukaemia, radiation therapy, chemotherapy, immunosuppressive medications, connective tissue diseases and infections¹. Pancytopenia as a result of direct bone marrow suppression has been previously reported in viral infections like Human Immunodeficiency Virus, Cytomegalovirus, Epstein-Barr virus and Parvovirus B19. Here, we report a case of pancytopenia in previously immunocompetent elderly male patient with SARS-CoV2 infection.

Case Presentation

A 69-year-old male presented to the hospital emergency department with complaints of fever, dry cough, fatigue and progressive breathlessness for 15 days. He gave history of hypertension but was not on any regular treatment and follow up. On examination he had high blood pressure recording (150/90mm Hg right arm supine) with tachycardia, tachypnoea and was not maintaining oxygen saturation at room air (SpO₂ 80% on room air). He was febrile (101-degree fahrenheit) and had pallor. Initial laboratory workup on admission showed pancytopenia and deranged serum creatinine of 2.4 mg/dl (findings are summarized in Table 1). It showed total white blood cell count (WBC) 2,100/ μ L, haemoglobin 2.2gm/dl, platelet count 65,000/ μ L, urea 46mg/dl, creatinine 2.4mg/dl, total bilirubin 0.8mg/dl, lactate dehydrogenases (LDH) 353IU/L, aspartate aminotransferase (AST) 32U/L and alanine aminotransferase (ALT) 84U/L. His nasopharyngeal swab test for COVID-19 RT-PCR was positive. The chest radiograph showed non homogenous opacities involving left mid and lower zones (Fig. 1). He was diagnosed as a case of severe COVID 19 disease with pancytopenia and was transferred to COVID intensive care unit. He was managed with oxygen therapy, parenteral broad-spectrum antibiotics, packed red blood cell transfusion, injection dexamethasone (6mg IV once a day), antihypertensives, anticoagulant therapy (renal modified dose of injection low molecular weight heparin) and other supportive measures. His inflammatory markers were raised (C-reaction protein 20.5mg/L, D-dimer 0.80 μ g/L, ferritin 900 ng/mL,

lactate dehydrogenase 353 IU/L). His iron studies, serum folate and vitamin B12 were within normal range. His coagulation profile was normal. He was evaluated for the possible causes of pancytopenia which included leukaemia, myelodysplastic syndrome, malignancy, bone marrow failure, infections, drug induced bone marrow toxicity, connective tissue diseases and immunosuppressive medications. His serum antinuclear antibody test was negative. Ultrasound of abdomen showed features of bilateral medical renal disease with no organomegaly. Peripheral blood microscopic examination showed pancytopenia and normocytic normochromic anaemia with moderate anisocytosis. No evidence of haemolysis, sepsis or atypia seen (Fig. 2). Bone marrow aspiration and biopsy was done to determine the cause of pancytopenia which showed hypocellular marrow with cellularity less than 20% and increase in fat spaces (Fig. 3). There were focal areas of marrow elements showing trilineage haematopoiesis with markedly diminished myeloid, erythroid and megakaryocytic series. There was no evidence of any leukaemia, myelodysplastic syndrome (MDS), infections or metastatic deposits. Peripheral blood smear and bone marrow microscopic examination was suggestive of pancytopenia with hypocellular bone marrow (Figs. 2 and 3). During the hospital course, three units of packed red blood cells were transfused to the patient. The patient's clinical condition and haematology parameters improved with therapy (Fig. 4). He was discharged on Day 15 with WBC 7,200/ μ L, haemoglobin 7gm/dl and platelet count of 1,42,000/ μ L. His throat swab for COVID 19 PCR was negative at the time of discharge.

Discussion

The novel SARS-CoV 2 virus is the etiological agent for COVID 19 disease and the respiratory system is involved in majority of patients. The clinical presentation of the disease is variable, including asymptomatic infection, mild upper respiratory infection and severe pneumonia with respiratory failure². The involvement of haematological system in COVID-19 disease has been reported in an increasing number of patients. The most common and well reported haematological complications in patients of severe COVID-19 disease are hyperinflammatory state, coagulopathic complications and lymphopenia³. Though platelets and haemoglobin levels are normal infrequently thrombocytopenia is also observed⁴. Pancytopenia is rarely reported in immunocompetent patients with severe COVID 19 disease.

Pancytopenia is a condition when person has low count of all three types of blood cells causing a triage of anemia, leukopenia and thrombocytopenia. It should not be considered as a disease in itself but rather the sign of a disease that needs to be further evaluated. The possible causes are nutritional deficiencies, megaloblastic anemia, hypersplenism, malignancies, radiation therapy, chemotherapy drug induced bone marrow toxicity, connective tissue diseases and immunosuppressive medications¹. All these conditions were ruled out in our patient during hospital stay. Pancytopenia as a result of bone marrow suppression has been reported in viral infections and commonly implicated viruses are Human Immunodeficiency Virus, Parvovirus B19 Epstein-Barr virus and Cytomegalovirus⁵. The decreased myeloid, erythroid and megakaryocytic series was observed in bone marrow biopsy of our patient indicating bone marrow suppression. There was no evidence of lymphoma, fibrosis and myelodysplasia in bone marrow biopsy. There are very few case reports on SARS-CoV2 induced pancytopenia⁶. Issa N et al reported the first case

of persistent pancytopenia associated with SARS-CoV2 bone marrow infiltration in an immunocompromised patient⁷. However, our patient was immunocompetent. He was found to have chronic kidney disease during evaluation which alone could not explain the severe anemia and associated pancytopenia. Ufuk F et al reported a case of COVID-19 associated pancytopenia which was complicated by neutropenic enterocolitis⁸. Our patient responded well to the supportive care and there were no complications during hospital stay. Once the patient's infection resolved, his blood counts improved and at the time of hospital discharge his leucocyte and platelet count had normalized and only anemia remained. Hersby DS et al also reported a similar self-limiting clinical course of patient with COVID 19 induced pancytopenia⁹.

The possible pathophysiology of pancytopenia secondary to SARS CoV2 infection could be linked to the angiotensin converting enzyme 2 receptor(ACE 2 receptor), which is present in bone marrow in lower levels¹⁰. It is possible that direct infection of myelocytes by SARS CoV-2 virus could lead to bone marrow suppression as seen in other viral infections like HIV, Parvovirus B19, Epstein-Barr virus and Cytomegalovirus. Other possibility is that after viral infection an antigenic epitope on myelocytes could be exposed which can lead to the production of autoantibody and destruction of blood cells. Also, hyperinflammatory state is a key feature of severe COVID-19 disease and It is well known that certain cytokines, such as the interferons and tumor-necrosis factor- α can affect hematopoietic stem cells and thus impair hematopoiesis¹¹. Lung is a site for platelet biogenesis and a reservoir for hematopoietic progenitors and with SARS-CoV 2 infection leading to lung injury, it is possible that the destruction of lung hematopoietic progenitors could also contribute to the pancytopenia¹².

Conclusion

SARS CoV 2 infection leading to pancytopenia is rare. We reported a case of pancytopenia associated with COVID-19 disease likely caused by bone marrow suppression.

Table 01

Test Name	Result
Haemoglobin	2.2 g/dl
Total leucocyte count	2,100/ μ L
Differential leucocyte count	N-68%,L-29%,M-2%,E-1%
Platelet count	65,000/ μ L
INR	1.2
Urea	46 mg/dL
Creatinine	2.4 mg/dL
Uric Acid	8.7 mg/dL
Albumin	2.1 gm/dl
Bilirubin Total	0.3 mg/dL
Protiens	6.0 gm/dL
SGOT/AST	32 U/L
SGPT/ALT	84 U/L
Albumin	2.6 g/dL
Globulin	3.4 g/dL
Sodium	134 meq/L
Potassium	5.1 meq/L
LDH	353 U/L
D-dimer	0.8
Ferritin	900 ng/ml
CRP	20.3mg/dL
Procalcitonin	< 0.5ng/ml

Declarations

Funding-Not applicable.

Conflicts of interest - The authors declare no competing interests.

Ethics approval- Not applicable

Consent to participate-Not applicable

Consent for publication-Taken from patient

Availability of data and material-Not applicable

Code availability-Not applicable

Authors contribution- All the authors have been involved in the review of the case report.

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Figures

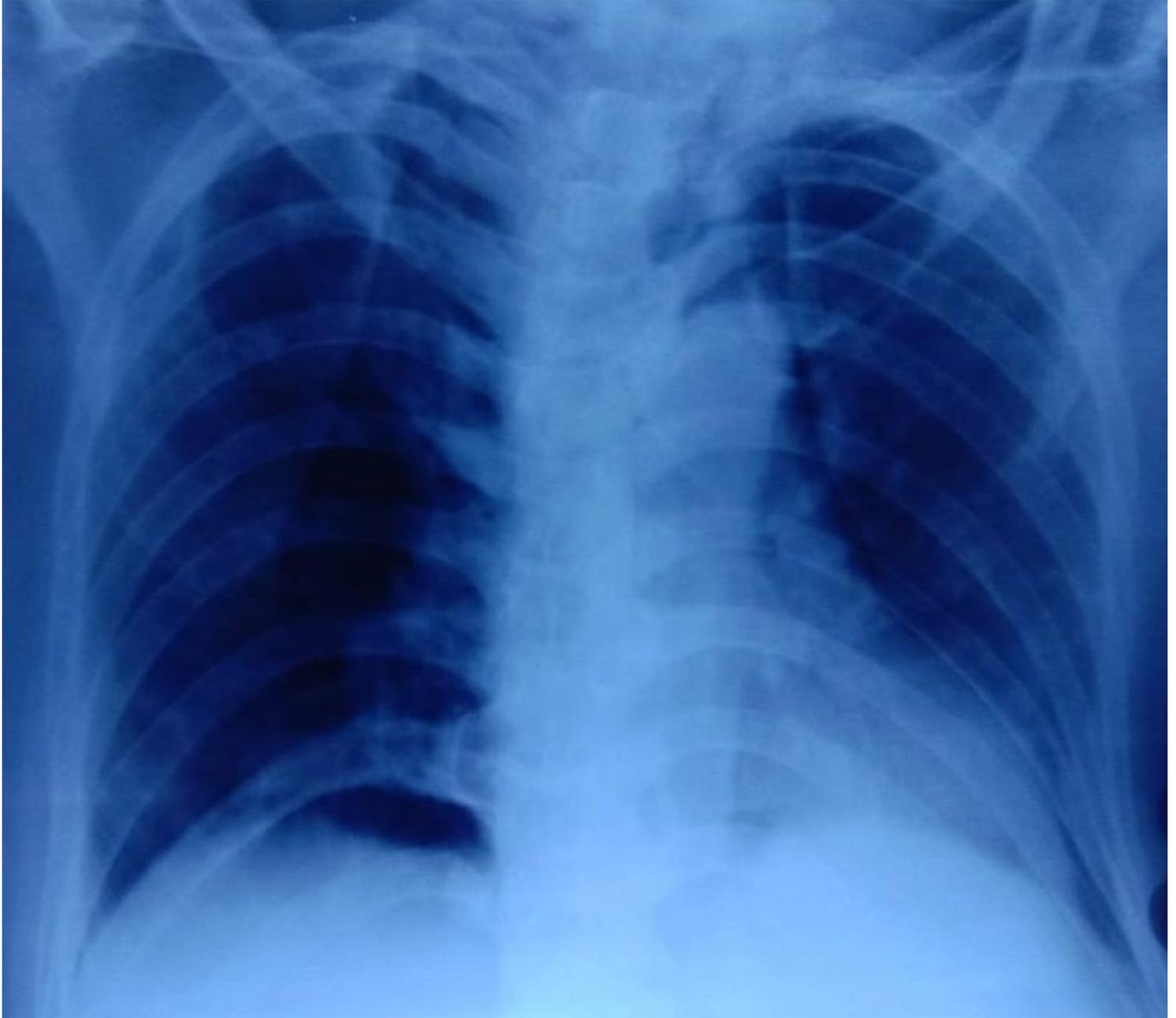


Figure 1

It showed total white blood cell count (WBC) 2,100/ μ L, haemoglobin 2.2gm/dl, platelet count 65,000/ μ L, urea 46mg/dl, creatinine 2.4mg/dl, total bilirubin 0.8mg/dl, lactate dehydrogenases (LDH) 353IU/L, aspartate aminotransferase (AST) 32U/L and alanine aminotransferase (ALT) 84U/L. His nasopharyngeal swab test for COVID-19 RT-PCR was positive. The chest radiograph showed non homogenous opacities involving left mid and lower zones

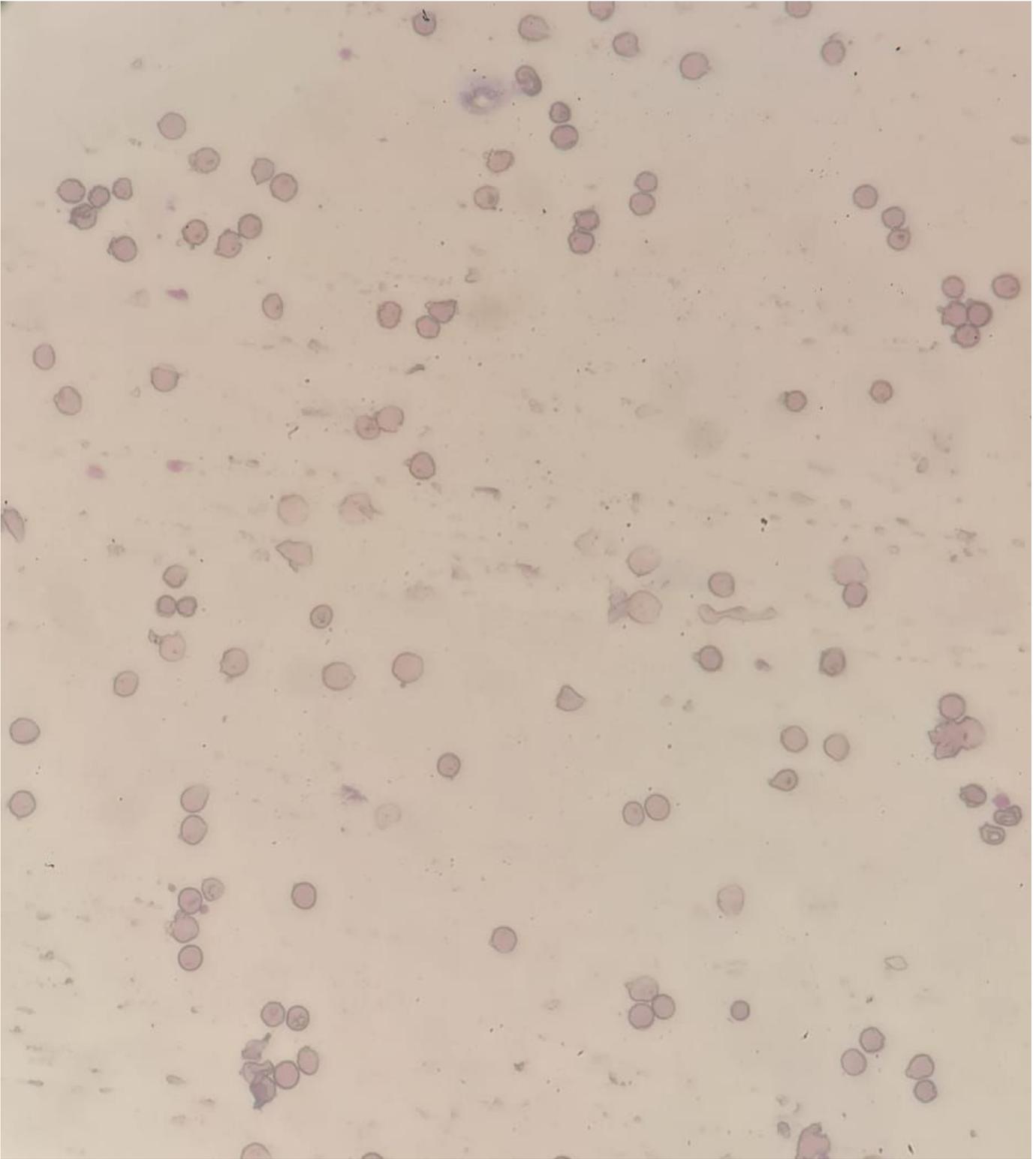


Figure 2

His serum antinuclear antibody test was negative. Ultrasound of abdomen showed features of bilateral medical renal disease with no organomegaly. Peripheral blood microscopic examination showed pancytopenia and normocytic normochromic anaemia with moderate anisocytosis. No evidence of haemolysis, sepsis or atypia seen

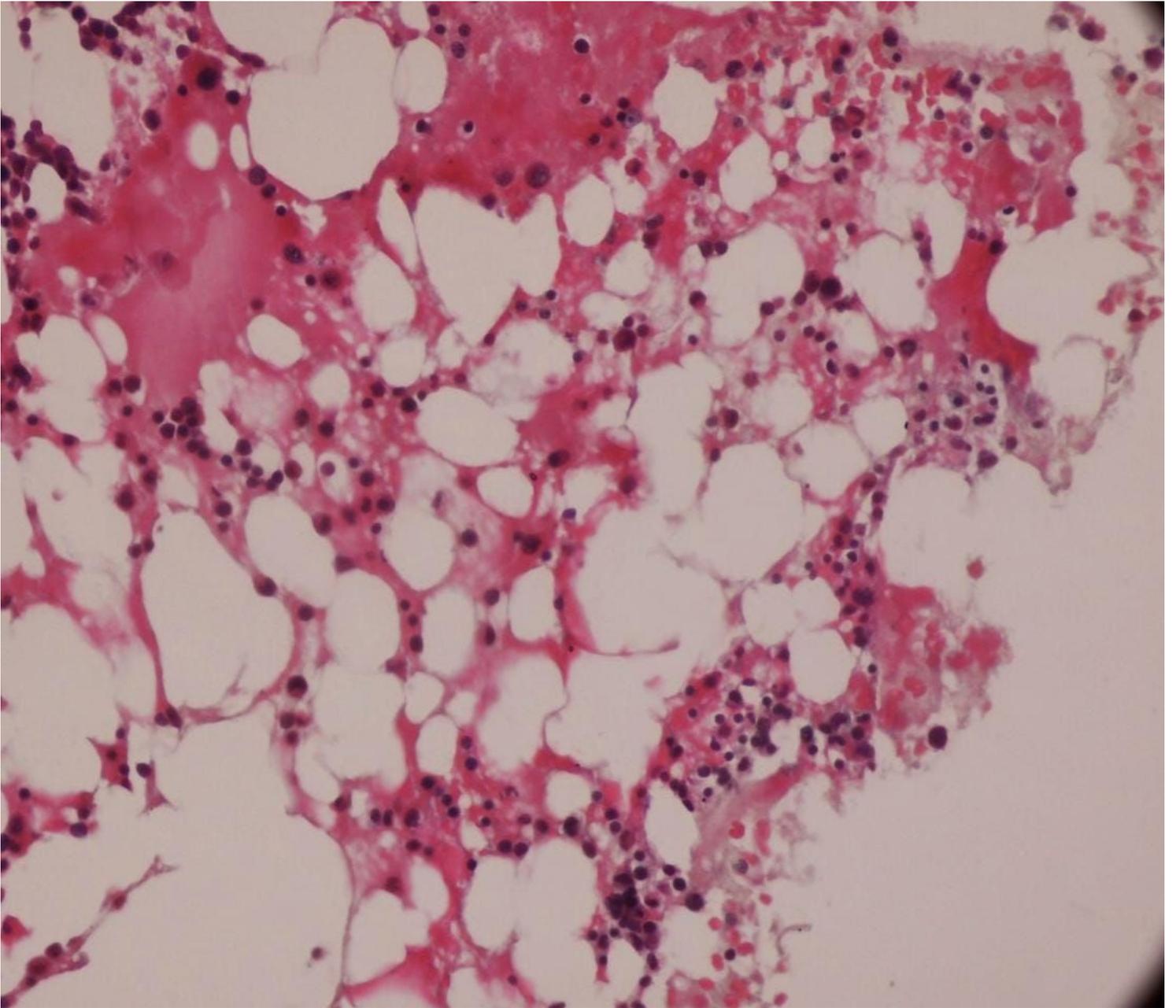


Figure 3

Bone marrow aspiration and biopsy was done to determine the cause of pancytopenia which showed hypocellular marrow with cellularity less than 20% and increase in fat spaces

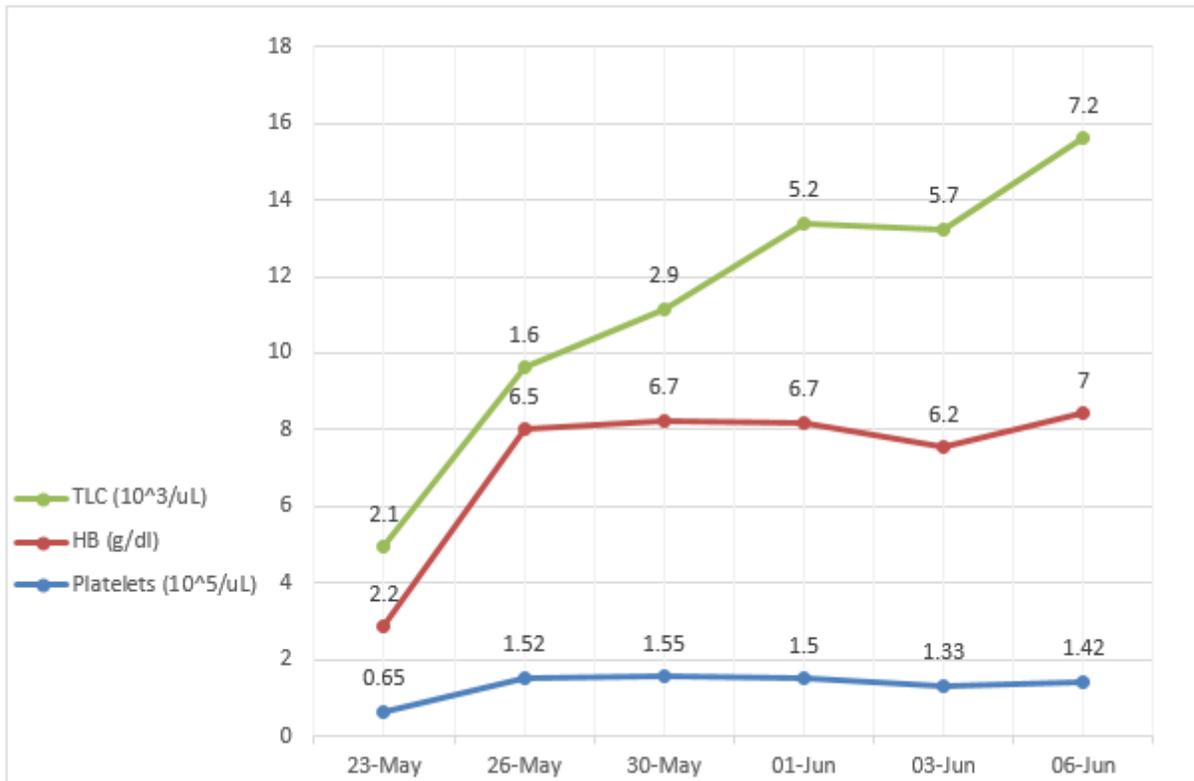


Figure 4

During the hospital course, three units of packed red blood cells were transfused to the patient. The patient's clinical condition and haematology parameters improved with therapy