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A CASE OF CLINICAL ITP IN A PATIENT WITH COVID19

General Medicine

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ABSTRACT

Since December 2019, China has experienced an outbreak of SARS COV2 known as Coronavirus Disease or COVID19.Subsequently it led to pandemic all across the globe. SARS-COV-2 is known to present with a variety of manifestations ranging from a completely asymptomatic course or a mild URTI (Upper respiratory tract infection) to a full blown LRTI (Lower Respiratory Tract Infection) with ARDS (Acute Respiratory Disease Syndrome) like features, ALIs (Acute Lung Injury), Pulmonary or Pan-endothelitis, overwhelming rapidly escalating Cytokine Storm, Multi-Organ Dysfunction Syndrome (MODS), Stroke, Encephalitis, Myocarditis, Septicemia, Acute Kidney Injury, Septic shock and several other complications(2). Here we report a rare association of SARS-COV2 infection with Immune Thrombocytopenic Purpura.

KEYWORDS

INTRODUCTION:

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by persistent thrombocytopenia (peripheral blood platelet count < 150×10^{9}/l) due to autoantibody binding to platelet antigen(s) causing their premature destruction by the reticuloendothelial system, and in particular the spleen(6). There is also an inhibition of platelet release from the megakaryocyte. ITP is characterised by mucocutaneous bleeding and a low platelet count. Rarely life threatening bleeding may occur in the form of central nervous system bleeding(1). Several risk factors have been described for ITP including environmental, drugs, infection and genetic factors. Viral infections such as Human immunodeficiency virus (HIV), Hepatitis C virus (HCV), Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Parvovirus, Rubella, and measles(7). Secondary immune thrombocytopenias occur in patients with other underlying autoimmune disorders (e.g. systemic lupus erythematosus), or malignant disease (e.g. chronic lymphocytic leukaemia)(6). Thrombocytopenia in COVID19 can be as a result of Disseminated Intravascular Coagulation(DIC), Sepsis, Drug Induced(3). We report a single case of Immune Thrombocytopenic purpura seen in a case of COVID19.

CASE REPORT:

We report a case of a 48 year old female patient, a housewife, known case of Hypertension since 14 years(on treatment) and Type 2 Diabetes since 2 years(off treatment) presented to us in a fever clinic with chief complaints of fever associated with sore throat. Fever was high grade, intermittent in nature associated with bodyache. She had consulted for the same where nasopharyngeal and oropharyngeal RT-PCR was done which was positive for SARS COV2. Chest CT was done which was suggestive of CT severity index of 32/40. She was home isolated for 14 days and was prescribed with Tablet Favipiravir 200mg 4BD for 14 days, Tablet Azithromycin 250mg 1BD for 3 days, Tablet Doxycycline 100mg 1BD for 5 days, Tablet Ivermectin 12mg 1OD for of 5 days, Tablet Hydroxychloroquine 200mg 1BD for 7 days, Inj Methylene Blue 2ml intravenous and as nebulisation(single dose). But she was having persistent fever and had developed shortness of breath for which she was admitted to a hospital where she was treated with Injectable Steroids, Low molecular weight Heparin for 3 days. However she did not get better and presented to us with the same complaints (Day 21 of symptom onset). On arrival, Temperature was 98.4 degrees fahrenheit, Pulse rate was 80 per minute, Blood pressure was 130/80mm of Hg, Respiratory rate was 20 per minute and Saturation of oxygen was 99% on oxygen at 4L per minute. Respiratory system examination revealed bilateral infra-axillary and infra-scapular crepitation at mid to end inspiratory phases on auscultation. Other systemic examinations were unremarkable. She was admitted in the department of General Medicine in a dedicated COVID19 High Dependency Unit Hospital. Relevant investigations were done. She tested positive for SARS-CoV-2 by her Nasopharyngeal and Oropharyngeal Swabs by RTPCR. Arterial blood gases revealed respiratory alkalosis with no compensation. Blood investigations were suggestive of elevated COVID19 inflammatory markers like C-Reactive protein, Lactate Dehydrogenases and Ferritin, d-dimer, Vitamin B12 and D deficiencies, uncontrolled Type 2 Diabetes Mellitus. Radiological investigations revealed bilateral lower zone haziness in a Chest Radiograph. Patient was treated with Oxygen support and a standard institutional protocol with Injection Ceftriaxone, Injection Methylprednisolone and low molecular weight heparins, Injectable multivitamins and Insulin. Patient gradually improved in the initial few days and Oxygen support was gradually weaned off. Chest Radiograph showed improvement and blood investigations revealed decrease in levels of C-Reactive protein, LDH. But there were persistently high levels of D-dimer and Ferritin. Serial Blood Hemogram were suggestive of thrombocytopenia(Day 25 of symptom onset). Peripheral blood smear was suggestive of the same. In view of thrombocytopenia, low molecular weight heparin, Ceftriaxone were stopped. General examination was unremarkable except for a few petechiae over the soft palate. Further blood investigations were done which was suggestive of negative levels of Anti-Nuclear Antibody(by Indirect Immunofluorescence) and negative levels of Antibody against Platelet Factor 4 (to rule out heparin induced thrombocytopenia). Ultrasonography of the abdomen revealed splenic size of 9cm. In view of persistent fall in absolute platelet count as low as 4000 per cumm and presence of mucosal petechiae, four units of Platelet Rich Concentrate were transfused. On the following day, hemogram was suggestive of transient increase in the level of platelet count. After 3 days blood counts revealed further drop in platelet count(20000 per cumm) for which again two units of Platelet Rich Concentrate were transfused. An expert opinion from Hematologist was taken for the same and a provisional diagnosis of clinical Idiopathic Thrombocytopenic Purpura was kept and was prescribed with Oral Prednisolone according to weight. A single dose(250mcg) of Inj Romiplostim was also given. Hemogram showed increment in the level of absolute platelet count(90000 per cumm) in the next 48 hours. The patient was discharged in a hemodynamically stable condition with oral steroids and vitamin supplementation. Hemogram following one week revealed platelet count of 225000 per cumm. Patient is hemodynamically stable at present and continues to follow up.

INVESTIGATIONS:

Blood Investigations	REFERENCE RANGE	Day 0	Day 2	Day 5	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13
Hemoglobin(g/dl)	12-18	13.1	13.8	13.3	14.1	13.2	14	11	12.8	11.2
Total counts(cumm)	5200-12400	10300	9810	6880	9180	8610	10560	11500	12410	9670
Absolute Platelet Count(cumm)	130-400	262000	207000	101000	35000	18000	4000	30000	30000	20000
Blood Urea(mg/dl)	15-45	11.3	29.4	38.7						12.5
Serum Creatinine(mg/dl)	0.7-1.3	0.4	0.36	0.44						0.39
Serum Alanine Aminotransferase(U/L)	10-49	37	33	40	53		49			37
Serum Alkaline Phosphatase(U/L)	45-129	48	56	53						73
S.Bilirubin Total(mg/dl)	0.3-1.3	0.33	0.33	0.28						0.44
S.Bilirubin Direct (mg/dl)	0.0-0.3	0.11	0.11	0.11						0.12
Total Proteins(g/dl)	5.7-8.2	5.8	5.9	5.7						6.1
S.Albumin(g/dl)	3.2/4.8	3.9	3.8	3.7						4.1
C-Reactive Protein(mg/L)	>5	57.89	57.73	8.18	1.31		1.29			
S.LDH(U/L)	100-250	314	428	358	330		293			246
S.Ferritin(ng/ml)	10-282	740	794	1381	971		931			535
INR	0.8-1.2	1.17	1.07	0.99						0.99
Activated Partial Thromboplastin Time		29.4	26.3	25.7						24.5
d DIMER(mcg/ml)	0.0-0.5	0.75	0.42	0.44			1.4			1.19
Procalcitonin(ng/ml)	<0.01	0.06	0.02	0.02						
Erythrocyte Sedimentation Rate(mm/hr)	0-20	73								
HBA1C	5.7-6.4	12.7								
HIV(ELISA)		Negative								
HBSAG(ELISA)		Negative								
HCV(ELISA)		Negative								
Vitamin D(ng/ml)	30-100	7.46								
Vitamin B12(pg/ml)	211-911	197								
TSH(microIU/ml)	0.35-5.5	2.31								

DISCUSSION:

In a case of three patients published by Gienke Bomhof et al. it showed auto-antibodies to platelets in only one patient whereas in other two patients a clinical diagnosis was kept.(3). In a case series of 14 patients in a study published by Matthieu Mahevas et al. showed thrombocytopenia in all patients after ruling out Disseminated Intravascular Coagulation and sepsis. Hemorrhagic manifestations were heterogeneous. Four patients had severe bleeding. An immune mechanism was suspected after the first week of infection. Among the suspected mechanisms, antibodies directed against virus glycoproteins may cross react with platelet surface integrins like glycoprotein GPIIb/IIIa. The short time between COVID‒19 first symptoms and ITP onset in some patients of present series suggests the presence of extrafollicular B‒cell generating cross‒reactive antibodies against platelets. In contrast, delayed ITP and ITP relapses evoke a germinal centre response resulting in persistent pathogenic antibodies secretion(4). In a study published by Sukrita Bhattacharjee et al. a total of 45 newly diagnosed patients of ITP with COVID19 were taken. Moderate to severe COVID19 illness were seen in 75% of patients. 30% of patients had no signs of bleeding. Majority (29%) of the patients were treated with intravenous immunoglobulin (IVIG) only. Glucocorticoids were used alone in 22% cases and in combination with IVIG in 24.5% cases.Rest patients were given thrombopoietin receptor agonists (TP-RA) were used in 9 patients, either with IVIG or both IVIG and glucocorticoids.(5)

Our patient did not have any past history of autoimmune disease, malignancy or environmental exposure. A negative autoimmune profile and peripheral smear ruled out systemic autoimmune disease as a cause for the same. She presented to us at Day 21 of symptom onset and had a moderate COVID19 pneumonitis. However, the patient did receive a short course of Beta lactam antibiotics during hospital stay. Antibiotics, heparin were stopped in view of thrombocytopenia. Still platelet count continued to fall. DIC, sepsis, heparin and drug induced thrombocytopenia were ruled out. She had a hemorrhage in the form of petechiae on soft palate. We transfused six units of Platelet rich concentrate as a prophylaxis. However only a transient improvement in platelet count was observed and serial hemogram suggested fall in platelet level.Study published by Sukrita Bhattacharjee et al. showed treatment with IVIG, thrombopoietin receptor agonists and oral glucocorticoids. However, we managed our patient with low dose oral glucocorticoids and a single dose of thrombopoietin receptor agonist and she showed a good response to it.

CONCLUSION:

To conclude, we report a case of Idiopathic thrombocytopenic purpura developing in a patient after the febrile state of COVID19 Pneumonitis(at third week of symptom onset). It was associated with severe thrombocytopenia and mucosal petechiae. It was diagnosed clinically and a favourable outcome was obtained by a single dose of thrombopoietin receptor agonist and oral steroids.

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