Infantile Immune Thrombocytopenic Purpura Secondary to Perinatal Transfer of SARS-CoV-2 Antibody

Immune thrombocytopenia (ITP) has been described following several viral infections [1], and since the onset of the coronavirus disease (COVID-19) pandemic, several reports of acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection-associated ITP in adults have emerged [2]. In children, more than the acute infection, multi-system inflammatory syndrome (MIS-C) presenting with thrombocytopenia has been reported [3].

A 6-week-old girl, born full term with uneventful antenatal and postnatal period, was brought with multiple purplish skin lesions all over the body since one day, followed by a right sided focal seizure lasting for 40 minutes. She looked pale with multiple ecchymotic patches all over the body. She required multiple anti-epileptic drugs along with mechanical ventilation. Her computed tomography brain showed sub-arachnoid and intra-parenchymal hemorrhage in the left parieto-temporal region while laboratory investigations revealed severe thrombocytopenia (platelet count $<100\times10^9$/L) with anemia (hemoglobin, 6.7 g/dL). Coagulation profile, dengue serology, HIV serology, hepatitis B antigen, inflammatory markers (C-reactive protein, serum ferritin), liver and renal function tests were normal. Peripheral blood smear showed no evidence of hemolysis, with a negative direct Coomb test. Nasopharyngeal swab for COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) was negative.

A packed red blood cell transfusion was given for the anemia. She was also transfused random donor platelets but thrombocytopenia persisted. Further evaluation showed high immature platelet fraction and increased megakaryocytes in bone marrow suggesting peripheral destruction of platelet. Considering diagnosis of severe infantile ITP, she was given intravenous (IV) pulse methylprednisolone (MPS) at 30 mg/kg/day for 3 days followed by oral prednisolone. On probing the parents further, mother revealed having upper respiratory tract infection symptoms during the last trimester of pregnancy, with loss of smell and taste in father at the same time. Both mother and the infant tested positive for IgG antibody to the nucleocapsid spike protein of SARS-CoV-2. As thrombocytopenia was persistent ($<10\times10^9$/L), the infant was given 2 g/kg of intravenous immunoglobulin (IVIG), following which the platelet count increased to 44×10^9/L at 72 hours. Child was extubated on day 5 of stay. Post-extubation, she showed no neurological deficits while subsequent platelet counts normalized within one week. She was discharged after 10 days of stay on tapering dose of prednisolone. The serial platelet count on subsequent follow-ups showed a rising trend.

ITP is often a retrospective diagnosis based on exclusion of other causes of thrombocytopenia and assessment of the response to treatment. Diagnosing ITP secondary to SARS-CoV-2 remains a challenge considering the various coexistent conditions associated with COVID-19 including a systemic hyper-inflammatory state, a distinct coagulopathy and therapeutic anticoagulation using hepari. Mild thrombocytopenia has been detected in 58-95% of severe cases of COVID-19 with the mechanisms for the same likely being multifactorial [4]. The combination of viral infection and mechanical ventilation leads to endothelial damage triggering platelet activation, aggregation and thrombosis in the lung, causing vast platelet consumption. Direct infection of bone marrow by coronaviruses results in an auto-immune trigger against the blood cells with low grade disseminated intravascular coagulation [4]. The expression of ACE2 surface receptor, the receptor used by SARS-CoV-2 to invade host cells, in hematopoietic and lymphoid tissues and resultant autoimmune antibody production and CD34+ mediated specific cell death and thrombocytopenia has been suggested [5].

In our patient, the diagnosis of COVID-19 antibody associated ITP is supported by an isolated thrombocytopenia, a low post-transfusion platelet increment, the exclusion of other causes, good response to treatment with MPS plus IVIG and historical evidence of parents having COVID-19 like illness in final trimester of pregnancy with demonstration of SARS-CoV-2 IgG antibodies in both the infant and the mother. The above represents a newer perspective on possible presentation of infantile ITP post maternal COVID-19 infection. The mechanisms of thrombocytopenia in ITP have been attributed to the development of platelet autoantibodies directed toward the different platelet antigens including platelet surface glycoproteins [6]. Similar mechanisms secondary to SARS-CoV-2 IgG antibodies may be postulated. The emergency treatment of ITP with severe bleeding such as in our infant warrants the use of combination therapy with pulse MPS and IVIG [7]. Our infant received the combination therapy in a similar chronology and had an incremental rise in platelet count within a week. Recent data in neonates born to COVID-19 positive mothers have demonstrated the transfer of maternal SARS-CoV-2 IgG antibodies across the placenta after asymptomatic as well as symptomatic infection during pregnancy [8].

In the current epidemiological scenario, in neonates and young infants presenting with isolated thrombocytopenia, a possibility of SARS-CoV-2 antibody mediated immune thrombocytopenia should be kept in mind. It will help pediatricians to recognize early and provide prompt immunomodulation. Similar experience, if reported, would need to be taken into consideration before concluding on the possible pathophysiology involved and standard therapy.

JITENDRA OSWAL, BHAKTI SARANGI,*
KARTHIK BADARAYAN
Department of Pediatrics, Bharati Hospital and Research Centre, Pune-Satara Road, Katraj-Dhankawadi, Pune, Maharashtra.
**dr.bhaktisarangi@gmail.com*

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