COVID-19-associated papilledema secondary to cerebral venous thrombosis in a young patient

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The severity of coronavirus disease 2019 (COVID-19) has been frequently associated with acute respiratory distress syndrome. In this case report, an atypical presentation of COVID-19 in young with a thromboembolic event is reported. The patient initially presented with fever of unknown origin not responding to therapy. On examination, visual acuity was 20/20 in both eyes with bilateral disc oedema and disc haemorrhage in the right eye. Erythrocyte sedimentation rate, C-reactive protein and D-Dimer were elevated. Magnetic resonance venography (MRV) revealed features suggestive of cerebral venous thrombosis. Timely diagnosis and intervention have prevented a fatal outcome.

Key words: Cerebral venous thrombosis, coronavirus, papilledema

The severity of coronavirus disease 2019 (COVID-19) has been frequently associated with acute respiratory distress syndrome. This case report highlights an atypical thromboembolic event manifestation of COVID-19 irrespective of pulmonary or respiratory symptoms at presentation.[1-3]

Case Report

A 22-year-old female patient without co-morbidities presented with fever, headache, diplopia, and recurrent episodes of transient loss of vision which lasted for a few seconds in both eyes since two days. On examination, best-corrected visual acuity was 20/20 in both eyes with false localising sign. The anterior segments were normal with bilateral disc oedema and disc haemorrhage in the right eye [Fig. 1]. The patient was lucid and oriented, without focal neurological deficits. Real-time reverse-transcription polymerase chain reaction testing of a nasopharyngeal swab was advised and it confirmed SARS-CoV-2 infection. Magnetic resonance imaging (MRI) revealed prominent subarachnoid space around the optic nerve and flattening of the posterior sclera noted on both sides with the diagnosis of papilledema [Fig. 2]. Lumbar puncture was done, revealing elevated intracranial pressure with the cerebrospinal fluid analysis being normal and negative for pathogens. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and D-dimer were elevated [Table 1]. Magnetic resonance venography (MRV) revealed bilateral transverse sinus thrombosis [Fig. 3]. Prompt anticoagulation therapy with subcutaneous heparin, intravenous methylprednisolone and antibiotics were started. Immediately the progression of cerebral venous thrombosis (CVT) decreased as observed by the improvement of clinically resolving papilledema [Fig. 4] and decreasing D-Dimer, CRP and ESR values. The patient was also symptomatically better with full and free extra-ocular movements.

Discussion

Though COVID-19 has been associated with acute respiratory distress syndrome, this report highlights an atypical thromboembolic event manifestation.[10] The possible pathophysiology is as follows: the virus is reported to promote dysfunction of endothelial cells, leading to excess thrombin generation and inhibition of fibrinolysis as in this case showing raised prothrombin levels.[16] Moreover, hypoxemia is associated with an elevation of blood viscosity and activation of hypoxia-related genes that mediate coagulation and fibrinolysis, favouring thrombotic events.[5]

During the process of plasma coagulation, as soluble fibrins are generated, D-Dimers are released as characteristic degeneration products of cross-linked fibrin. Low D-Dimer concentrations are often used to exclude venous thrombotic events (VTE) like deep vein thrombosis of the leg (DVT) and pulmonary embolism (PE). On the other hand, increased D-Dimer levels indicate the activation of coagulation and following fibrinolytic processes demanding for further diagnostic and therapeutic approaches.

In this scenario, we report an unusual presentation in a previously healthy patient infected with SARS-CoV-2 characterised by catastrophic cerebral venous thrombosis.
in young. Though fever with dehydration could also be a precipitating factor, COVID-19 was another potential risk factor. CVT is a rare cause of stroke, accounting for approximately 0.5% of all stroke cases, and associated with a reported mortality of 4%. The superior sagittal sinus is more frequently reported cerebral venous structure involved; however, in our case, the transverse sinus was involved [Fig. 3].

Hyper-coagulable State in other scenarios versus in COVID-19

The annual incidence of venous thromboembolic events is approximately one in 1000 adults. In addition to inherited risk factors for venous thromboembolism, numerous acquired risk factors for venous thromboembolism exist, such as infections and inflammatory diseases. Even before the outbreak of the coronavirus pandemic, increased D-Dimer levels were reported in influenza-like infections owing to the activation of coagulation by respiratory viruses.[7]

The recently published International Federation of Clinical Chemistry Guidelines on COVID-19 strongly suggest D-Dimer testing in patients with COVID-19, since studies on SARS-CoV-2 revealed a high correlation between severity and outcome of COVID-19 in patients with increased D-Dimer levels.[6] D-dimer, fibrin/fibrinogen-degradation products, and fibrinogen are significantly higher among patients with COVID-19. Indeed, D-dimer levels were >500 ng/mL in this patient too at the time of reporting the diagnosis, being >1,000 ng/mL as seen in Table 1.

Despite the activated coagulation mechanism in COVID-19, even disseminated intravascular coagulation (DIC) can develop in severe cases.[9] Increased D-dimer levels can serve as a predictor of developing acute respiratory distress in COVID-19, mentioning the probability of micro pulmonary embolism especially in severe forms of COVID-19.[10] More studies are needed to clarify the direct relationship of the SARS-CoV-2 and thromboembolic disease.

Early identification of CVT utilising MRV and D-Dimer is critical as depicted in this situation because prompt administration of anticoagulant therapy (heparin), and steroids (methylprednisolone) will decrease the progression of cerebral oedema, intracranial pressure, and haemorrhage rates, improving outcomes as seen in Fig. 4. The doses of steroids were tapered and heparin was stopped once the patient got symptomatically better with the reduction of the D-dimer levels, ESR and CRP.

Conclusion

An unusual presentation with catastrophic cerebral venous thrombosis in previously healthy young patients infected with SARS-CoV-2 was demonstrated. Ophthalmologist being the first responder, in this case, needs to keep in mind this possibility. No conclusions can be drawn other than the fact that it provides hints, as to the accumulating evidence that COVID-19 is a serious contributor to hyper-coagulation, increasing the fatality of the disease. Heightened awareness of this atypical but potentially treatable complication of the COVID-19 disease spectrum is encouraged.
Figure 3: (a) Magnetic resonance venogram (MRV) revealing bilateral transverse sinus thrombosis (red arrows). (b) Sagittal view of MRV showing the same (red arrows)

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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Figure 4: (a, c and e) showing resolving papilledema and disc haemorrhage in right eye. (b, d and f) showing resolving papilledema in left eye