Unusual Observations of Neurological Cases in Patients with Simultaneous Corona Infection - (A Hospital-Based Study)

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Abstract

Among the several cases of Coronavirus, presenting with mainly respiratory symptoms, in our isolation ward, it was observed that there were cases which presented with neurological symptoms. Such cases apparently appeared initially as normal neurological varied presentations. However, due to strong suspicion related to certain unusual aspects, both clinical and investigation based and also due to failure of treatment, as done in such cases, we surmised that they could be related to Corona. This article describes 6 such cases, which were initially in suspected area awaiting SAARS CoV2 report and later seen either in Corona ward if positive or in ward or intensive ward when they became twice negative. Initially they were treated on routine neurological lines but later on confirmation of SAARS CoV2, treatment patterns were changed due to non responsiveness to conventional treatment and variation in the progress were observed.

Introduction

The 2020-novel coronavirus (SAARS CoV2) has been declared a world pandemic by WHO. Initially named novel coronavirus, is a single-stranded RNA virus with a spike studded envelope, mimicking a crown, from where the name has been derived. In addition to the respiratory system involvement, recent evidence has shown that SARS-CoV-2 can affect other organ systems including nervous, vascular, digestive, urinary, haematological and so on. Here in this article, we have described such cases which presented as routine neurological cases. However, their behaviour was different, especially, in response to standard treatment regimens.

Methodology

In this article, we discussed neurological cases, who presented atypically like no high fever, cough etc but were proved to be positive for SAARS-CoV2.

Whenever there was a suspicion from either history or associated complains, they were admitted in separately without contact with normal cases. Once found positive, they were shifted to Isolation ward and if negative, and stable to ward/Intensive care units. These neurological cases are described including their presentation and management.

Results

Case 1

A cardiothoracic surgeon, who had previous history of diabetes, hypertension and CAD, was already on dual antiplatelets and statins. He presented with sudden onset gait disturbance and a transient period of detachment from surroundings for few minutes. It was found that he had diarrhoea 2 weeks back which was better. Neurological examination showed only a mildly ataxic gait. MRI showed a mildly ataxic gait. MRI however showed an acute lesion in parieto-occipital area along with multiple scattered small old infarcts in b/l MCA and ACA territories.

Conservative treatment continued with increasing the dose of antiplatelets and statins. However in his routine blood tests, his counts revealed both leukocytopenia and thrombocytopenia on 3 consecutive days and his gait deteriorated further. Chest CT, initially showed ground glass appearance, later, improved. He was then prescribed HCQS along with his other medications. Gradually his gait improved, with physiotherapy and repeat MRI was same, although by this time his counts became normal. Idea is to keep in mind haematological changes in stroke in a patient of corona.

Case 2

A young 19-year female with a history of travel to Delhi, without any known history of epilepsy, presented with 3 episodes of generalised tonic clonic seizures at home. After the last attack she did not regain consciousness and was brought to hospital ER. Since there was a history of travel, she was kept in isolation instead of routine ICU.

At bedside there was no apparent neurodeficit. Although she was arousable but very drowsy. She continued to have 2 further attacks and then became completely unconscious, with GCS 4. Her blood gases showed acidosis and she was intubated & fully ventilated. She was initially loaded with Fosphenytoin and kept at 150 mg thrice daily. The convulsions stopped. Pupils were small and non-reacting.

A bedside EEG, showed evidence of continuous spike and wave discharges, and assuming she was in non-convulsive status, she was started on Midazolam infusion up to 0.4mg/kg/hr. In the meantime, her routine blood examination showed a leukocyte count of 3500/L, Haemoglobin 9 gm/l and platelets 70000. CXR was normal. MRI showed patchy hyperintensities b/l in paraventricular areas. Corona test was positive.

She was added Lopinavir with Ritonavir combination and HCQS. Next day repeat EEG showed intermittent spikes, but no status.

Gradually Midazolam was tapered over 72 hrs and she could be extubated on 5th day by which time she regained
and on ventilator. At that point he was gradually recovering, and his chest symptoms, signs and ventilator requirements were coming down. Gradually he was weaned, conscious throughout, and shifted to medical ICU, after SAARS CoV2 was negative with tracheostomy. It was very difficult to bring him to t-piece and hence tracheostomy had to be kept for airway protection. He then complained of bodyaches with mild weakness of all 4 limbs. A CPK was sent and it was found to be over 2000. However, bromocriptine was not started as this was not thought to be due to NMS but rather due his still mildly raised INR, and Liver enzymes, lumbar puncture was not ventured, and so we could not prove therefore any albumin-cytological dissociation.

In this case we found motor neuropathy, although we cannot conclude whether his neuropathy was related to Coronavirus or prolonged ventilation. But he definitely had myopathy, which is reported in Coronavirus and his high initial CPK was contributory too.

Case 5

A thirtyfive year old lady, with corona having mild sore throat and low-grade fever had been recovering and except a little patchy opacity in left base in initial Chest X-ray, was otherwise asymptomatic. While she was in ward, after becoming SAARS CoV2 negative she complained of severe headache. She has been a known episodic migraneur since several years. She was extremely anxious from admission and required regular counselling.

On the 10th day she started complaining of increasing intensity of headache and she started incessant vomiting. She was put on i/v fluids, Ondanasser and Pantoprazole and paracetamol thrice but showed no improvement. Her lab electrolytes showed Sodium 121meq and Potassium 3.2. She was given necessary supplementation and dexamethasone (steroid) 4mg thrice was added.

She was sedated. 2 days later her headache reduced and by 4th day, her i/v medicines and fluids were stopped. However, steroids were tapered off in 5 days. She was put on Amtriptiline 25mg at bedtime and Zolmitriptan nasal spray SOS. She became fit by day 17. We concluded that this status migranosus could be related to sudden changes in inflammatory markers in brain as a consequence of Corona. However, existing literature was not sufficient to verify this hypothesis.

Case 6

75-year-old diabetic, hypertensive, Covid patient, although well controlled, presented with fever, cough and typical ground glass CT chest appearance. He was treated conservatively with antibiotics, steroids and HCQS. He was recovering as far as his respiratory symptoms and signs were concerned. Suddenly on the seventh day he started complaining of uncoordinated movement of left upper limb with difficulty in vision. On examination it was found he had a right homonymous hemianopia and left sided cerebellar signs. MRI brain showed that he had a left cerebellar and left occipital infarcts and MR angio of neck showed complete occlusion of left vertebral artery. He was immediately started on dual antiplatelets and statins. His blood counts were normal, but D-Dimer was highly raised, around 900. He was shifted to medical ICU for better monitoring and also to detect any intermittent arrhythmia as the nature of the CVA was also thought to be an embolic episode.

Echo and Holter were normal. His symptoms persisted, but after 5 days of Heparin infusion, his D-Dimer reduced and repeat MRI and angio were same. A CT angio of lungs (done to rule out pulmonary embolism) was normal. His stay was quite prolonged, physiotherapy continued, and he was discharged on 21st day with normal D-Dimer and residual neurodeficit.

Discussion

From the above cases, it is clear that Coronavirus can cause a spectrum of neurological disorders. However, the presentations were not causative but necessarily observations only.

Different modes of both Anterior and posterior circulation CVA, Epilepsy...
Fig. 2: Corona and the Central Nervous System. Mechanisms of Tropism and Presentations

Table 1: Summary of Case Studies. Shows symptoms at commencement, medications administered and any features of interest. HT = Hypertension, DM = Diabetes mellitus

<table>
<thead>
<tr>
<th>Case ID</th>
<th>Sex</th>
<th>Age</th>
<th>History of Initial Presentation</th>
<th>Treatment Regimen</th>
<th>Unusual Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1)</td>
<td>M</td>
<td>75</td>
<td>Yes Gait Disturbance, Mild temperature and cough</td>
<td>Antiplatelets, statins, HCQS</td>
<td>Coagulopathy in Covid can cause extensive CVA(ischaemic)</td>
</tr>
<tr>
<td>2)</td>
<td>F</td>
<td>19</td>
<td>No Generalized tonic clonic seizures, Loss of consciousness</td>
<td>Phosphenytoin, Midazolam infusion, Lopinavir, Ritonavir and HCQS</td>
<td>Simple management of status is not enough in a Cvid setting, Protease inhibitors and HCQS may be necessary</td>
</tr>
<tr>
<td>3)</td>
<td>M</td>
<td>57</td>
<td>Yes Chest symptoms</td>
<td>GTN Infusion, Prazosin</td>
<td>ARB or ACE should be avoided as antihypertensives in Hypertensive CVA in a Covid setting and platelets should be monitored</td>
</tr>
<tr>
<td>4)</td>
<td>M</td>
<td>47</td>
<td>No Gradual ongoing recovery from COVID (Isolation Ward)</td>
<td>Monitoring CPK may help identify Myopathy in Covid.</td>
<td>Prolonged ventilation or Covid per se may cause critical care neuropathy. Myopathy is already reported</td>
</tr>
<tr>
<td>5)</td>
<td>F</td>
<td>35</td>
<td>No Mild temperature and sore throat</td>
<td>Ondansetron, Pantoprazole, Dexamethasone, Amitrerpine</td>
<td>Steroids may be helpful in controlling Severe migraine in Covid setting</td>
</tr>
<tr>
<td>6)</td>
<td>M</td>
<td>75</td>
<td>Yes Fever, cough, ground glass CT chest appearance</td>
<td>Dual antiplatelets and statins, physiotherapy</td>
<td>Covid can give extensive occlusion of large arteries causing large infarcts</td>
</tr>
</tbody>
</table>

including status, myopathy, doubtful critical illness neuropathy, headaches – even amounting to status migranosus, were new to us in a background of Coronavirus due to different presentations and response to different forms of therapy.

The above Pie chart depicts the different types of cases of Neurology seen in patients of corona cited in Figure 1. (Legend and citation given in figure - A Summary of the Clinical Presentations in the case studies as seen in concert with COVID positive results in 6 admitted patients.).

Deaths from COVID-19 are chiefly due to a major immune inflammatory response and diffuse alveolar damage. The body responds to the infection by recognizing the viral RNA when it is replicating within the host cell using intracellular receptors.

This in turn, leads to several downstream signalling cascades with the end result of producing an army of defence cytokines to curb the viral spread. The pro-inflammatory cytokine up regulation (interleukin (IL)-1, IL-6, TNF, and interferon γ) in this disease is a valid target for anti-TNF therapy. Blockade of TNF alone is clinically effective in many diseases, despite the presence of other pro-inflammatory cytokines and mediators.

This severe immune storm which takes place in the entire Neural-axis as well as the whole body has been figuratively described in the above picture, titled Corona and the central nervous system, mechanisms of tropisms and presentation in the above picture cited in Figure 2. (Legend and citation in figure given - Corona and the Central Nervous System. Mechanisms of Tropism and Presentations.) It not only emphasises the immune storm in the brain and entire neural axis but the whole body in general.

Finally the 6 cases has been summarised in a table, given below and named as Table 1 (Cited as summary of case studies).

Conclusion

SAARS CoV2 is a highly contagious disease that has become a pandemic. Patients infected may show neurological symptoms at the commencement. These cases are intriguing and important, and one has to consider these above observations as having possible association to Corona in their pathogenesis. Neurologists should scrutinise these symptoms closely and have a high index of suspicion when evaluating patients in an endemic area. Early recognition may help initiate treatment and isolation so as to prevent clinical worsening and spreading of the virus. Since the pathogenesis of the novel Coronavirus still remains to be explained accurately, vaccine development is a monumental task. Until these efforts are fruitful, strict monitoring of patients and carefully selected treatment routines, particularly for those with unusual neurological features are essential.

Acknowledgement


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Anupam Prakash 4*

Introduction

Ramesh Aggarwal 1, Aparna Agrawal 2, Anil Gurtoo 3, Vivek Suman 1, Shivraj Meena 1, Retrospective Analysis during Peak of 2020 Pandemic in India

the Hallmark of COVID-19 in Diabetes: Observations from a


