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Reversible Neurological Syndrome with COVID-19: An Experience from Tertiary Hospital of Central India

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Abstract:-
Corona virus disease 2019 (COVID-19), primarily a disease of respiratory system, has been proven to involve both peripheral and central nervous system. Although pathogenesis of nervous system involvement is still elusive yet direct invasion of virus or autoimmunity is plausible explanation. Involvement of nervous system due to Severe Acute Respiratory Syndrome Corona Virus -2(SARS CoV-2) is associated with higher morbidity and mortality, therefore it is desirable to recognize them at its earliest for favourable outcome in these patients. We herein report 8 cases of different neurological syndrome involving peripheral and central nervous system. All of them recovered almost completely with appropriate management.
***Key words**:- COVID-19, SARS CoV-2, Neurological manifestation.*

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I. Introduction

Outbreak of Corona virus disease 2019 (COVID 19), caused by Severe Acute Respiratory Syndrome Coronavirus-2(SARS CoV-2) was first reported from Wuhan, Hubei province, China in December 2019. Due to its rapid pace of spread , It is declared as pandemic by WHO in march 11, 2020(1) . Till now more than 104 million confirmed cases with more than 2.26 million deaths has been reported worldwide. India currently has highest number of confirmed cases in Asia with more than 10.3 million reported cases and 154000 deaths till now (2). Corona virus is enveloped positive stranded RNA virus that predominately affects vertebrates. They are broadly distributed in different animal species including bats, cats, dogs, camels and mice. In humans corona virus infection is primarily associated with upper respiratory tract and gastrointestinal tract infection (3). Severe Acute Respiratory Syndrome Corona Virus (SARS CoV) in 2002-2003 and Middle East Respiratory Syndrome Corona Virus (MERS CoV) in 2012-2013 were other corona virus outbreak in last two decades. Neurological involvement had already been described in both SARS CoV and MERS CoV and were resulted in high mortality of 10% and 35% respectively(3) . Recent outbreak of COVID -19 is primarily characterized as respiratory system disease but there are growing evidences of neurological involvement in these patients(4). Little is known about pathophysiology, management and outcome of neurological involvement due to SARS CoV-2. We herein reporting series of 8 cases of different neurological syndromes in patients with COVID-19, admitted in COVID-19 hospital of tertiary referral centre of central India. All of them recovered completely with appropriate treatment. To the best of our knowledge no case of COVID 19 with neurological involvement is reported from this part of country.

II. Material And Method

Eight RT-PCR proven COVID 19 patients (Table -1) with simultaneous or sequential involvement of different neurological syndromes, admitted at COVID- 19 hospital of Maharani Laxmi Bai Medical college, Jhansi , Uttar Pradesh, India were included in this study. Clinical data of these patients were obtained from in patient medical case records. Mean age of patients were 51.8 years. Male to female ratio were 5:3. All of them presented with fever cough and dyspnoea of different clinical severity. Apart from detailed history and clinical examination all patients underwent complete blood count, Liver and renal function test, serum electrolyte, bleeding and coagulation profile, ABG analysis,12 lead electrocardiogram, procalcitonin and blood culture if total leucocyte count is high . Markers of inflammation including C-Reactive Protein, serum ferritin, d-dimer, Lactic Dehydrogenase and IL6 level were done. X-ray and High Resolution Computed Tomography (HRCT) of chest were done in all patients. Neuroimaging including CT scan head, MRI brain and other neuroelectrophysiological evaluations were done as and when required. All patients received standard treatment as per protocol lied bt ministry of health and family walfere ,Government of India for treatment of COVID 19 infection (5). Additional treatment for clinical neurological syndrome were administered as required.

Table 1 – Details of cases of COVID 19 with Neurological involvement

S. N	Age/sex	Clinical category	neurological symptoms	Co-morbidities	Clinical diagnosis	Relevant investigation	Treatment givin	outcome
1	58/M	Moderate	Acute onset ascending sensory motor weakness involving both upper and lower limbs 2 weeks after COVID 19 positivity	Diabetes mellitus, hypertension	Acute sensory motor poly neuropathy (AIDP)	Cyto-albuminic dissociation in CSF examination, NCV – demyelinating polyneuropathy with conduction blocks.	IVIG	Discharged in recovery phase after 2 weeks of admission
2	38/M	Severe	Headache, Irritability, abnormal behaviour,, hallucinations , recurrent seizure, , altered sensorium. After 1 week of COVID 19 positivity	Diabetis mellitus,	meningoencephalitis	MRI brain – T2 hyperintensity in bilateral thalamic and left temporo parietal area. CSF examination- raised protein , normal suger, lymphocytic pleocytosis.	Antiepileptics, steroids, antioedema measures and antibiotics.	Discharged with improving cognitive and motor functions
3	26/M		generalized bodyache and proximal weakness in all 4 limbs during 1st week of COVID 19 positivity	None	Acute Myositis	Raised serum CPK NAC	Steroids, analgesics, antiinflammatory medications	Recovered completely within next 10 days
4	68/M	mild	Acute onset right sided hemiparesis with right UMN facial palsy	Diabetes mellitus, hypertension , obesity	Cerebrovaascular accident	Left MCA infarct	Antiplatlets and ststins	Discharged on 14th day in recovery phase
5	72/M	Moderate	Acute onset altered behaviour, slurring of speech, right hemiparesis	none	Cerebrovascular accident	Acute subdural hematoma	Craniotomy and removal of hematoma	Discharged on 10th post operative day with good functional recovery
6	57/F	mild	Acute onset left facial palsy	none	LMN facial palsy	LMN facial palsy	steroid	Starts recovering in next 2 weeks
7	61/F	mild	Acute onset diplopia unable to abduct right eye	Diabetis mellitus	Right abduscence palsy	Right 6th nerve palsy	steroid	Recovered in next 3 weeks
8	38/M	mild	Fever cough sour throat , anosmia	none	decreased smell sensation	Olfactory nerve palsy	supportive	Recover in 3 weeks

III. Discussion

More and more literature on neurological manifestation of COVID 19 disease is emerging across the globe. A systemic study from Wuhan china, reported neurological finding in 214 patients hospitalized with COVID 19(6). Neurological symptoms were noticed in 49 out of 58 patients of COVID 19 in study conducted in France(7). The most common neurological symptoms of COVID 19 are headache , anosmia, aguesia, stroke, encephalitis, cranial nerve palsies , peripheral neuropathy, myositis and rhabdomyolysis(8). Mechanism of neurological injury was unclear but Involvement of nervous system is thought to related to either direct viral invasion or immune complex mediated neuronal injury. Direct neuroinvasion could plausibly achieved by

several routes including trans synaptic transfer across infected neurons, entry via olfactory neuron, infection of vascular endothelium and leucocyte migration across the blood brain barrier(3). Spike protein on viral surface of SARS CoV 2 bind to the Angiotensin Converting Enzyme 2 (ACE 2) receptor on mammalian host cells with help of transmembrane protease serene 2 (TMPRSS 2) enzyme. TMPRSS 2 is needed to activate spike protein(9). The presence of ACE 2 receptor on human cell determines viral cellular trophism in various body organs. ACE 2 receptors are expressed in airway epithelia, kidney cells , lung parenchyma, small intestine, vascular endothelium and widely in nervous tissue including astrocyte and oligodendrocytes. of substentia nigra, medial temporal lobe and olfactory bulb(3). Systemic inflammatory response syndrome, sepsis, multi organ failure, acidosis are additional threat to neurological insult(3).

Headache is most common neurological symptom along with fever vomiting and breathlessness. it is found in more than one third of patients of COVID 19(8,10). Neuroinflammatory mechanisms has been invoked as cause of headache and evidences have found that cytokines and chemokies triggers nociceptive sensory neurone resulting in headache. Anosmia and agusia, once considered most specific symptom of COVID 19 and reported in 88.5 and 88.0 in Germany. However, patients hospitalized in Wuhan , it was reported in 5.6% and 5.1 % respectively(11).

Impairment of consciousness was reported in 37% of patients hospitalized at Wuhan(6). Possible mechanism of altered sensorium in these patients include direct infection and damage of brain parenchyma, toxic –metabolic encephalopathy, seizures and demyelinating diseases(3). Direct invesion of SARS CoV2 was considered as possible mechanism of encephalitis and T2 weighted hyper intensities in bilateral thalamus and temporoparietal area was reported in these patients,. Cerebrospinal fluid (CSF) examination revealed raised protein , normal sugar and normal cells but SARS CoV2 could not be detected in CSF of these patients. Failure to detect SARS COVID 2 in these patients strengthen the hypothesis of immune complex mediated neurological insult as cause of encephalitis. Similar findings was also reported by Poliadgi et al(12).

Five percent of patients hospitalized in Wuhan had acute stroke(6). Acute ischemic stroke is most commonly reported vascular complication of COVID 19 but cerebral venous thrombosis, intracerebral hemorrhage and sub dural hematoma has also been reported. Old age, severe covid 19 disease manifestation, more cerebrovascular risk factors, higher levels of inflammatory markers were more prone to develop stroke(3). Patho physiology behind cerebrovascular disease in patients of COVID 19 includes hypercoagulable state, vascular endothelial damage and systemic inflammation leading to thrombosis and vasculitis(13).

Gullain barre syndtome or acute inflammatory demyelinating polyneuropathy is reported in COVID 19 either as para infectious or post infectious neurological syndrome(14). Molecular mimicry is possible mechanism for neuronal insult in which infecting virus likely share epitopes similar to component of peripheral nerve which stimulate autoreactive T and B cells. Apart from AIDP, acute motor axonal neuropathy (AMAN) has also been reported in COVID 19 infections(15).

Ocular motility disorder including Miller Fischer syndrome and abducent nerve palsy have been reported in patients of COVID 19. Enhancement of optic nerve sheath and Tenon's capsule suggest direct viral leptomeningial invasion in these patients(15,16). Persistent fatigue, myelgia, weakness, depression ,is reported in chronic post covid syndrome. peripheral and autonomic nervous system dysfunction may be plausible cause of post covid syndrome. Autonomic dysfunction is also reported with a case of AMAN(17).

IV. Conclusion

Recent pandemic of COVID 19 caused by SARS CoV2 involve each and every organ of human body, therefore presents as myriad and protean manifestations. Involvement of nervous system by COVID 19 fetched attentions of researchers owing to high degree of morbidity and mortality. In this study we attempt to highlight potentially fatal but treatable neurological complications along with most recent evidences of mechanism of neuronal insult of COVID 19. Direct or indirect association of these neurological syndrome with COVID-19 infection can not be ascertained in present case series due to obvious reasons therefore large scale descriptive analytical studies are require to determine exact incidence, pathophysiology and spectrum of neurological involvement in COVID 19.

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