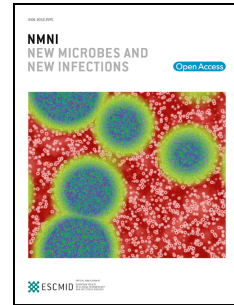


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COVID-19 infection recurrence presented with meningoencephalitis

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COVID-19 infection recurrence Presented with Meningoencephalitis

Abstract:

COVID-19 infection can involve many organs such as central nervous system and also would be relapse. In this article we presented a 64-year-old woman with microbiological confirmed COVID-19 induced respiratory distress that treated resulted by negative nasopharyngeal swab RT-PCR for COVID-19. But, after a few weeks; relapse occurred by symptoms of acute meningoencephalitis. Results for COVID-19 RT-PCR from her cerebrospinal fluid, nasopharyngeal and tracheal aspiration specimens became positive again whereas, negative COVID-19 serum antibodies. So, it should be mentioned that neurological involvement symptoms can be one of COVID-19 first or relapse presentation. So, regular evaluation of patients during the convalescence seems necessary.

Keywords: COVID-19, Encephalitis, Meningitis, Recurrence, Nervous system

Introduction:

Since early December 2019, coronavirus disease 2019(COVID-19) emerged in China and rapidly spread all over the world. The pathogen has been identified as a novel beta coronavirus that currently been named severe acute respiratory syndrome coronavirus 2 (SARS-COV-2)(1). The infected patients` symptoms ranged from asymptomatic to severe. Fever, cough and dyspnea are the most common complaints of patients, but involvement of other organs, including gastrointestinal, cardiac, kidney and nervous system involvement have been reported too (2, 3). Some patients present early with neurologic symptoms like anosmia, ageusia, seizure, stroke and myopathy along with mild respiratory symptoms, so new-onset neurological manifestations can be owing to COVID-19 (4).In this report, we describe one definite case of COVID-19 with pulmonary presentation that relapsed after a partial recovery with CNS manifestation.

Case Presentation:

A 64-year-old male referred to emergency room (Madaen Hospital,Tehran,Iran) on February 16 with acute progressive dyspnea and generalized weakness. At presentation, temperature was 37.2 C, oxygen saturation 94%, respiratory rate 22 breaths per minute, heart rate 110 beat per minute and blood pressure 110/80 mmHg. Primary laboratory test results indicated a leukocytosis (WBC:13400, Polymorph nuclear: 9648, Lymphocyte 2948 cell per microliter),ESR:11, quantitative CRP:4+, D-dimer >1000 u/ml and normal other routine lab tests.Past medical history revealed hypertension, ischemic heart disease and metastatic colorectal cancer from 15 months ago who had been treated with FOLFIRI regimen and the last

time of chemotherapy was 2 months ago. In order to acute dyspnea and high D-dimer, pulmonary thromboembolism suspected and Lung CT was performed, that showed pleural effusion in lower field of both lungs with collapse consolidation of basal segments and patchy ground glass opacities and there was no evidence of PTE on angiographic images (Figure 1-C) and normal pulmonary artery pressure on echocardiography.

Respiratory specimen by nasopharyngeal swab was tested for COVID-19 using qualitative real-time PCR (QiaSymphony system, QIAGEN, Hilden, Germany) was positive. Then patient was treated with intravenous ceftriaxone and clindamycin. In addition, she received Tab hydroxychloroquine (200 mg gavage twice daily) and Tab lopinavir/ritonavir (400/100 mg gavage twice daily). She regularly swabbed every week and aligned with partial recovery, the result of third nasopharyngeal swab RT-PCR for COVID-19 became negative, but she was still hospitalized. After 21 days suddenly her consciousness decreased and involved in respiratory distress again. She was empirically started on intravenous meropenem, vancomycin, ampicillin, acyclovir and steroids. In neurological evaluations there was no evidence of focal neurological deficit and meningismus, mild cortical atrophy on axial brain CT (Figure 1-A). Lumbar puncture was done and the cerebrospinal fluid (CSF) analysis showed 1920 cell count with 90% polymorphs, marked hypoglycorrhachia (glucose :10 with simultaneous blood glucose=162), elevated protein (pro=94/8). There was no bacterial growth after 48 hours of incubation and PCR result for herpesviridea was negative. Second Chest CT scan revealed diffuse alveolar infiltration in both lungs with bilateral pleural effusion (Figure 1-B) and tracheal aspiration culture led to growth of klebsiella pneumonia that was extremely drug resistant. The patient continued treatment for bacterial meningitis and ventilator associated pneumonia and colistin (IV), was added. Eventually, nasopharynx, tracheal aspiration and CSF specimens tested again for COVID-19 and incredibly all results were positive (Table 1). At that time, COVID-19 antibodies (IgM & IgG) were negative (Tested by Recombinant Immuno Blot Assay technique). These positive PCR results were obtained on April 9, about 21 days after the negative result of nasopharyngeal RT-PCR which in combination with antibody results, consistent with definite respiratory infection relapse and simultaneously, central nervous system involvement with COVID-19.

Discussion

Covid-19 is betacoronavirus that bind to the angiotensin-converting enzyme 2(ACE2) to enter the cell. ACE2 is present in several multiple human organs, including nervous system, so SARS-COV-2 which causes upper respiratory tract disease, can infect neural cell and cause different neurologic appearance such as encephalitis (5, 6, 7, 8). Some of the patients had demonstrated re-fever and positive PCR test after discharge from hospital. It might be due to the biological characteristics of COVID-19 or even related to the re-infection. (9)

Moriguchi et al, reported a case of meningoencephalitis associated with SARS-COV-2 that the specific COVID-19 RNA was detected in a CSF sample but was not detected in the nasopharyngeal swab. Also brain MRI showed abnormal signal changing of temporal lobe

suggesting encephalitis. (10) Our case had meningitis/encephalitis with CSF pattern completely consist with bacterial meningitis but with negative culture for bacterial pathogens and positive CSF sample PCR for SARS-COV-2. In literature review CSF analysis of cases that reported with encephalitis/meningitis consisted with mild lymphocytic pleocytosis (11, 12, 13). In order to our patient was under antimicrobial treatment, the result of negative CSF culture for bacterial growth is not conclusive. As a limitation bacterial PCR exam for CSF was not done. So, we cannot exactly contribute the pattern of CSF analysis with COVID-19. Chen et al, reported a confirmed case of covid-19 whose oropharyngeal swab test for SARS-COV-2 became positive again after two sequentially negative results. The probability of false negative result may increase with an oropharyngeal or nasopharyngeal swab test alone or can be affected by the experience of the operator, the site of sampling and the viral load of the specimen. (14)

Our case had positive PCR result for SARS-COV-2, 21 days after negative result. This positive result was confirmed with three separate samples of nasopharynx, tracheal aspiration and CSF. To differentiate re-infection from recurrence of the disease, specific antibody testing was performed and both COVID-19 IgM and IgG were negative. These results suggest the possibility of recurrence but negative result of antibody test may be related to the past medical history of our patient and the immunosuppression due to malignancy and chemotherapy. Although there was no leukocytopenia or lymphopenia, Because the lack of accurate information about the patient's humoral status, we cannot make a correct judgment about her immune condition.

Conclusion:

To the best of our knowledge, it's the first study that reports relapse of COVID-19 with meningoencephalitis manifestation. So it should be mentioned that neurologic symptoms as well as respiratory symptoms, may be the first presentation of COVID-19 and in pandemic period, we should be kept this expectancy in our mind, to avoid delayed diagnosis or misdiagnosis. Also given the possibility of re-positive SARS-COV-2 RNA in patients who have improved and to prevent further transmission, regular evaluation of patients during the convalescence, seems necessary.

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Conflict of interests:

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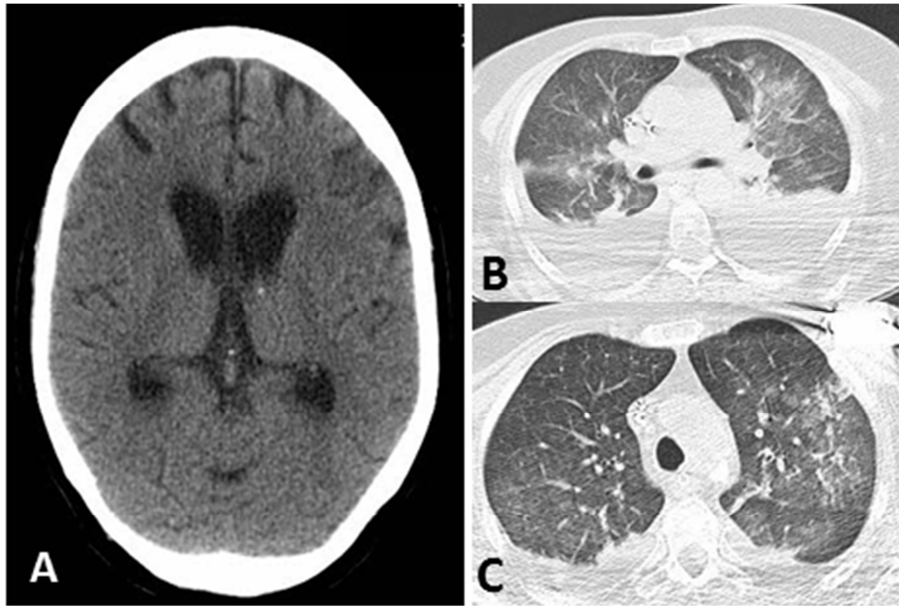


Figure 1: Brain CT Scan demonstrate mild senile cortical atrophy (A); First Lung CT Scan demonstrate bilateral pleural with collapse consolidation of basal segments and patchy ground glass opacities (C); Second Lung CT Scan demonstrate increase in pleural effusion amount and ground glass opacities(B).

Table 1- The result of patient COVID-19 RT-PCR timeline

Specimen	Date	PCR Result
Nasopharyngeal Swab	Feb 16,2020	Positive
Nasopharyngeal Swab	Feb 23,2020	Weakly Positive
Nasopharyngeal Swab	March 1,2020	Negative
Nasopharyngeal Swab	March 8,2020	Negative
Nasopharyngeal Swab	March 22,2020	Positive
Tracheal aspiration	March 22,2020	Positive
Cerebrospinal fluid	March 22,2020	Positive

Table 1- The result of patient COVID-19 RT-PCR timeline

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Figure 1- Axial brain CT Scan showed mild cortical atrophy (A), First lung CT scan revealed pleural effusion in lower field of both lungs with collapse consolidation of basal segments and patchy ground glass (C) and second lung CT showed diffuse alveolar infiltration in both lungs with bilateral pleural effusion (B) and

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