

The 2019 novel coronavirus disease with secondary ischemic stroke: two cases report

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Case report

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Abstract

Background: The 2019 novel coronavirus disease is an outbreak of respiratory illness first detected in Wuhan, China in the end of Dec, 2019. The older patients complicated with underlying diseases are reported more likely to have clinical symptoms. But its secondary lesion is rarely reported.

Case presentation: We reported two cases of coronavirus infected pneumonia with acute ischemic stroke in patients at their middle-age. In both 2019 coronavirus diseases cases, neurological physical examination are normal before infection. Lymphocytopenia and high expression of cytokines and D-dimer were found from serum clinical laboratory test at admission. The dysarthria and limb muscle weakness are initial manifestations in one week after [2019 novel coronavirus](#) infection. The head CT and head/neck arterial CTA showed small-vessel occlusion. The patients were diagnosed with coronavirus diseases with secondary acute ischemic stroke. They were treated with tirofiban and followed up with daily aspirin and atorvastatin.

Conclusion: The present cases suggested that secondary ischemic stroke, which mainly manifested as small-vessel occlusion, should be considered for coronavirus disease patients with prompt diagnosis and treatment.

Background

On 31 December 2019, a novel type of coronavirus disease (COVID-19) has broken out from Wuhan, China. So far, the global number of confirmed reported cases of COVID-19 has surpassed 150000 in 143 countries over the world^[1]. The main clinical manifestations of this disease are lung symptoms such as fever, cough and wheezing ^[2,3]. Those patients with many concomitant diseases tend to develop into severe critically ill and likely to die of acute respiratory distress. Ling et al found 36% of the hospitalized patient had neurological manifestation such as headache and dizziness ^[4]. A large-scale [epidemiologic study](#) shown 1.5% of the COVID-19 patient has a history of cerebrovascular disease ^[2]. But the secondary lesion is rare reported. Here is a case report of two confirmed patients of COVID-19 with acute ischemic stroke at their middle age. These two patients got intensive care in the isolation ward and have been discharged from hospital recently.

Case Presentation

Case 1

A 45-year-old male was admitted for fever over one week on 5 Jan, 2020. The vital signs from a general physical examination were 38.3 degree for body temperature, 110 times/min for pulse, 24 times/min for breathing rate and 125/72 mmHg for blood pressure. The patient reported no history of hypertension, diabetes, hyperlipidemia, heart disease and no history of smoking and drinking. His neurological examination on admission was normal. The clinical serum laboratory examination showed an increased

serum amyloid protein (SAA) of 288.42 mg/L (normal range 0-10mg/L), C reactive protein (CRP) of 25.17 mg/L (normal range 0-10 mg/L), D-dimer of 15.21 mg/L (normal range 0-0.5 mg/L) and fibrinogen (FIB) of 4.87 G/L (normal range 2-4 G/L). The levels of serum cytokines are also increased extremely, including IL-8 of 438.20 pg/ml (normal range 0-62 pg/ml), IL-10 of 836.50 pg/ml (normal range 0-9.1 pg/ml) and IL-6 of 962.70 pg/ml (normal range 0-7 pg/ml). The white blood cell was normal together with lymphocytopenia (0.64 G/L, normal range 0.8-4 G/L). The levels of glucose, lipid and homocysteine are normal. The chest computed tomography (CT) scans showed typical bilateral patchy shadowing (Figure 1). The real-time RT-PCR assay for 2019-nCoV test is positive.

The patient was treated with oxygen therapy, ribavirin (0.5g, i.v. drip, Q12h), and venous rehydration solution. At 9 a.m. on Jan 6th, the patient found to have stroke symptoms, such as speak unclearly, weakness of left limb (4/5 muscle strength throughout), shallow of left nasolabial groove and tongue toward to left. The muscle strength declined to 1/5 of upper limb and 2/5 of lower limbs at 5 p.m in the afternoon. The NIHSS score was 9 points. The laboratory examination displayed increased levels of D-dimer (32mg/L) and decreased level of FIB (1.06 G/L), together with longer prothrombin time (PT, 14.7s, normal range 11-14s) and thrombin time (TT, 22.7s, normal range 9-20s). But the head CT (Figure 2A) and neck arterial CTA (Figure 2C, 2D) didn't show any obvious abnormalities at that time. The patient was treated with atorvastatin (20mg, p.o., q.d.), tirofiban (0.1ug/kg.min, continuous intravenous pumping for 48 hours), following by daily aspirin (100mg, p.o.) and clopidogrel (75mg, p.o.). On 8 Jan, neurological function defects about dysarthria and left limb weakness of the patient got recovery gradually. Repeat head CT re-examination 2 days later showed right corona radiata infarction (Figure 2B). The patient didn't have fever in the later of hospitalization and his lung symptoms was significantly improved. The patient discharged from hospital on 3 Feb with mild dysarthria. His left limb muscle strength score gets to 5. The NIHSS score declined to 2 points from 9 and MRS score was 1 point on the discharge day.

Case 2

A 50-year-old male was admitted for fever over 9 days with sudden left limb weakness for 28 hours on 10 Feb. The patient reported smoking history for 20 years, without other histories of hypertension, diabetes, hyperlipidemia and heart disease. The patient has left thyroid cancer removal surgery on 19 Jan in our hospital and discharged after recovery. The routine surgical evaluation on 17 Jan didn't found any other abnormalities from colour-doppler ultrasound test and CT angiography examination except for basilar artery fenestration (Figure 3A). The general physical examination at admission on 10 Feb were 37.8 degree for body temperature, 78 times/min for pulse, 18 times/min for breathing rate and 132/76 mmHg for blood pressure. The neurological examinations showed shallow of left nasolabial groove, tongue toward to left and dysarthria, with left upper limb muscle strength score 3 and positive reflex of Babinski's sign. The NIHSS score was 7 points. The laboratory examination displayed increased levels of SAA (>300mg/L), CRP (93.15 mg/L), D-dimer (19.86 mg/L), longer PT (15.4 s) and lymphocytopenia (0.39 G/L). The levels of serum cytokines, such as IL-8 of 84.90 pg/ml (normal range 0-62 pg/ml), IL-1b of 36.60 pg/ml (normal range 0-5 pg/ml) and IL-10 of 26.70 pg/ml (normal range 0-9.1 pg/ml) are increased. The levels of glucose, lipid and homocysteine are normal. The COVID-19 were diagnosed with

typical bilateral patchy shadowing from chest CT (Figure 4) and positive RT-PCR assay test. The head CT on 10 Feb presented right basal ganglia infarction (Figure 3B). The patient was treated with oxygen therapy, ribavirin (0.5g, i.v. drip, Q12h), and venous rehydration solution, following by daily aspirin (100mg, p.o.), clopidogrel (75mg, p.o.) and atorvastatin (20mg, p.o.). During hospitalization, the patient didn't have a fever again and the lung symptoms get relieved obviously. But the neurological function defects get recovery gradually. The patient discharged on 1 Mar with mild dysarthria. The left limb muscle strength score is 4, NIHSS score is 5 and MRS score was 3.

Discussion And Conclusions

We report 2 cases of COVID-19 in patients with acute ischemic stroke. Previous studies have paid a lot of attention to multiple organs except for lung were also involved in COVID-19 [5]. Recently Hu et al found neurological symptoms existed in one third of hospitalized patients [4]. The other studies on coronavirus induced diseases (such as SARS [6], MERS [7]) also shown cases of central nervous system damage.

From the history of these two patients, their neurological physical examination showed normal before 2019-nCoV infection. The initial speculation is the acute ischemic stroke is a secondary lesion after COVID-19 in one week. The possible mechanism might because of coronavirus attacks the human body through the angiotensin-converting enzyme-2 (ACE2) [8] that distributed on blood vessel and multiple organs [9]. Then the virus trigger cytokine cascade that could aggravate ischemic brain damage and increase the risk of intracerebral hemorrhage [10] and blood coagulation disturbances. This hypothesis supported by highly expression of cytokines and D-dimer from these two patients to a certain degree. Notably, these two patients were at middle-age and should had a lower risk of stroke. They didn't show any symptoms of [deep venous thrombosis](#) or large vessel occlusion with endoluminal thrombosis in spite of high levels of D-dimer, either. We suspected that the small-vessel occlusion was secondary lesion following coagulopathy during 2019-nCoV infection. Unfortunately, we could not have more exhaustive neurological examinations during this hospitalization because of the special infectious circumstances. So there are still some concerns need to clarify between coagulopathy induced increased D-dimer and the virus-induced ischemic stroke from the view of clinical application.

To take consider of the possibility of small-vessel occlusion developed into progressive stroke, we use tirofiban instead of aspirin and clopidogrel with the informed consent in case 1 according to Chinese experts consensus on clinical application of tirofiban in atherosclerotic cerebrovascular diseases [11]. The patient's neurological function got recovery rapidly in 2 days. Such platelet glycoprotein II.b/III.a receptor antagonists could act on the final common channel of thrombosis. Their efficacy was found no significant difference in the incidence of symptomatic intracranial hemorrhage compared with aspirin [12, 13].

It's worth mention that these are the only two cases of COVID-19 with secondary acute ischemic stroke out of 764 hospitalized patients in Hubei Provincial Hospital of Integrated Chinese and Western Medicine

till 9 Mar, 2020. We suggest early diagnosis and treatment should be consider for COVID-19 patients with secondary ischemic stroke, which mainly manifested as small-vessel occlusion.

Abbreviations

COVID-19: Coronavirus disease; 2019-nCoV: 2019 novel coronavirus; CT: computed tomography; CTA: computerized tomography angiography; RT-PCR: reverse transcription-polymerase chain reaction; SAA: serum amyloid protein; FIB: fibrinogen; CRP: C reactive protein; PT: prothrombin time; TT: thrombin time; NIHSS: National Institutes of Health Stroke Scale; MRS: Modified Rankin Score

Declarations

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Authors' contributions

B.F. collected data and wrote the manuscript. B.F, Y.C, P.L. were responsible for the clinical management of the patient. All authors revised the manuscript and approved the final version.

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Availability of data and materials

No datasets were analyzed during current study.

Ethics approval and consent to participate

Not applicable.

Consent for publication

The patients gave informed consent for the publication of this case reports. Copy of the written consent is available for review by the editor of this journal.

Competing interests

The authors state that they have no conflicts of interest.

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Figures

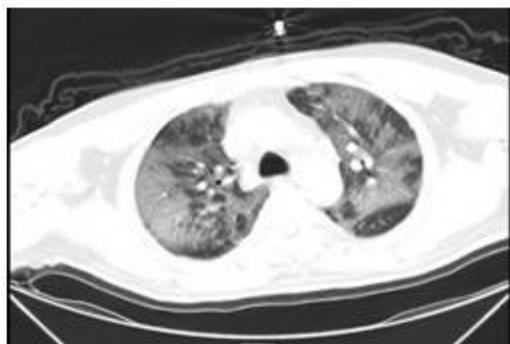


Figure 1

CT imaging of case 1 infected with 2019-nCoV on 5 Jan, 2020, illness day 7.

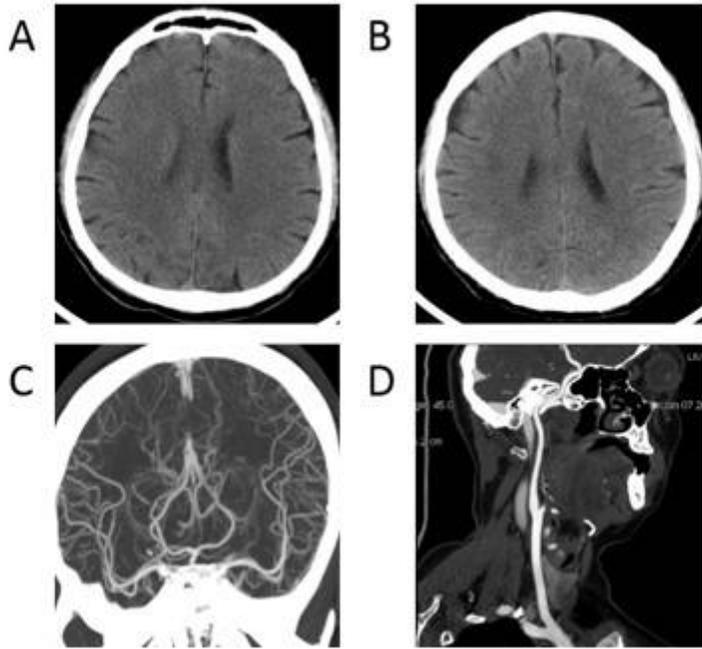


Figure 2

The head CT and head/neck arterial CTA of case 1 infected with 2019-nCoV. A: head CT on 6 Jan, 2020, illness day 8, B: Repeat head CT on 8 Jan, 2020, illness day 10; C: head arterial CTA on 6 Jan, 2020, illness day 8, D: neck arterial CTA on 6 Jan, 2020, illness day 8.

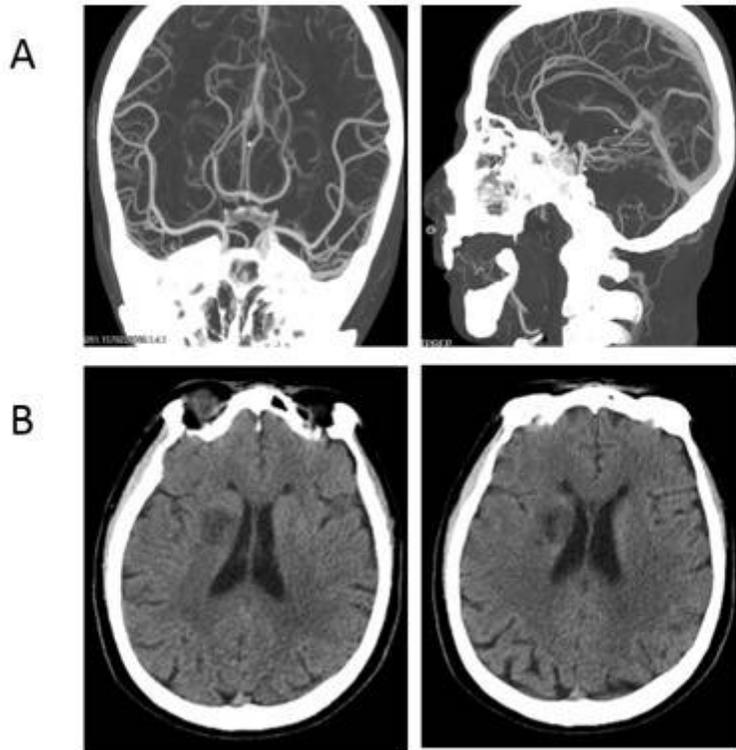


Figure 3

The head/neck atrial CTA and head CT of case 2 infected with 2019-nCoV. A: head CTA on 17 Jan, 2020, routine surgical evaluation before thyroid cancer removal surgery, B: head CT on 10 Feb, 2020, illness day 9.

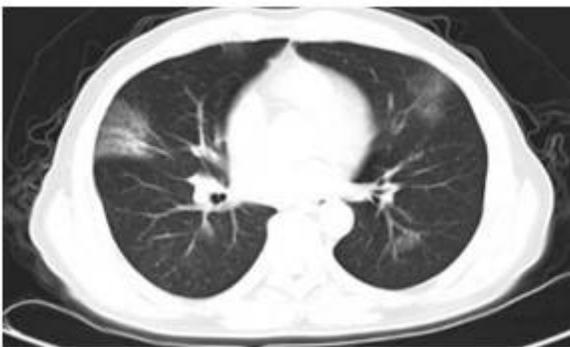


Figure 4

CT imaging of case 2 infected with 2019-nCoV on 10 Feb, 2020, illness day 9.

Supplementary Files

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- [CAREchecklistEnglish20131BFcovid19.pdf](#)