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Article type : Case Study

Prolonged Confusional state as first manifestation of COVID-19

Delirium in COVID-19

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Abstract:

A 77 year old gentleman, normally fit and well, was admitted with acute confusion. On admission GCS was 14/15, vital signs were within the normal limits and bilateral crepitation at the lung base. Head CT scan normal. CXR showed some air space opacification. Investigations revealed hyponatraemia, raised CRP and positive for COVID-19. Treated with antibiotics and intravenous saline, sodium returned to normal. Delirium remained unchanged four weeks post incidence. Neurological manifestations were documented in patients with COVID-19, however no report has shown delirium as a primary manifestation. This case illustrates acute confusion may be the only presenting symptom of COVID-19 without overt lung disease.

Main Text:

A 77 year old caucasian gentleman, who was normally fit and well, was admitted on the 29th of March 2020 with acute confusion after a fall on the stairs. Six days prior to his admission he generally felt unwell, lethargic with unusual behaviour wondering around at night. He has had no seizure, cough, temperature or shortness of breath. He is known to have hypertension and was taking enalapril, indapamide, atorvastatin, aspirin and lansoprazole.

On examination, the patient was awake but inattentive, disoriented to place and time with GCS of 14/15. He was not in any form of cardiorespiratory distress and no evidence of injury to his head. The patient's vital signs were all within the normal limits including oxygen saturation. His neurological examinations were unremarkable except confusion and examination of his chest revealed bilateral mid zone and basal crepitation. Computed tomography scan of his head was normal with no evidence of intra or extra-axial haemorrhage (Figure 1). There was mild chronic small vessel ischemic changes. No cerebral atrophy and the basal ganglia, thalami, brainstem, CSF drainage pathway and posterior fossa structures were within normal limits. The chest x-ray showed air space opacification in the right lower zone and left peripheral mid and upper zone (Figure 2). Biochemical investigations revealed low sodium at 123 mmol/l, raised C-reactive protein at 44 mg/L, plasma and urine osmolality were 252 and 291, respectively. The rest of his biochemical and haematological investigations including lactate and troponin were all within the normal limits. An oropharyngeal swab test using RT-PCR was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2/COVID-19).

Patient was treated with antibiotics, levofloxacin 500mg for 5 days post admission, and intravenous 0.9% normal saline and his sodium over few days has gradually returned to normal. Up to 12% of patients with COVID-19 were noted to have hyponatremia[1] and in this case no other cause for low sodium or confusion was identified. An EEG during the course of his hospital stay was performed which showed no definite focal or generalised epileptiform activity. However, his prolonged confusion remained unchanged four weeks post the incidence and died on the 18th April 2020 due to a hospital acquired infection. No post mortem exam was performed due to service pressures because of the pandemic. Our patient has been receiving angiotensin-converting enzyme (ACE) inhibitor, enalapril. The interaction between the SARS-

CoV2 and ACE2 has been suggested as a potential virulence factor and there are concerns about the use of ACE inhibitors. The existing evidence is too limited to support or refute these concerns and yet we withheld his enalapril treatment[2].

We think our patient has a primary central nervous system (CNS) disease related to COVID-19 that led to delirium. Interestingly, he has never developed the respiratory symptoms of COVID -19 .

The cardinal feature of patients with COVID-19 is respiratory symptoms[3]. However, other organs involvement such as heart, gastrointestinal tract and nervous system has been documented[4]. Mao et al report of 214 COVID-19 patients, 36.4% were found to have neurologic manifestations at presentation, including headache, nausea, vomiting, confusion, ataxia, acute cerebrovascular disease, and seizures[5]. In addition, a report of 99 COVID-19 patients, 9% of patients presented with confusion on admission likely to be related to hypoxia or multiorgan damage instead of being a primary manifestation[6].

We have described a case of COVID-19 where acute confusion was the primary presentation without overt lung disease. Our case shed light that COVID-19 infections may involve central nervous system in susceptible individuals and may contribute to overall morbidity and mortality. There is increasing evidence that coronavirus infections such as SARS-CoV and now COVID 19 may directly involve the CNS [7]. The exact mechanism by which SARS-CoV enters the CNS remains unknown, but may involve entry via the olfactory bulb with retrograde trans-synaptic spread [8].

As the global pandemic continues to unfold, COVID-19 should be considered as a differential diagnosis in a patient with acute confusion without overt respiratory symptoms.

Conflict of Interest:

There is no conflict of interest

REFERENCES

1. Zhou F, Yu T, Du R et al, Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395: 1054–62

2. Sommerstein R, Gräni C. Preventing a COVID-19 pandemic: ACE inhibitors as a potential risk factor for fatal COVID-19. BMJ 2020;368:m810-m810 (https://www.bmj.com/content/368/bmj.m810/rr-2.)

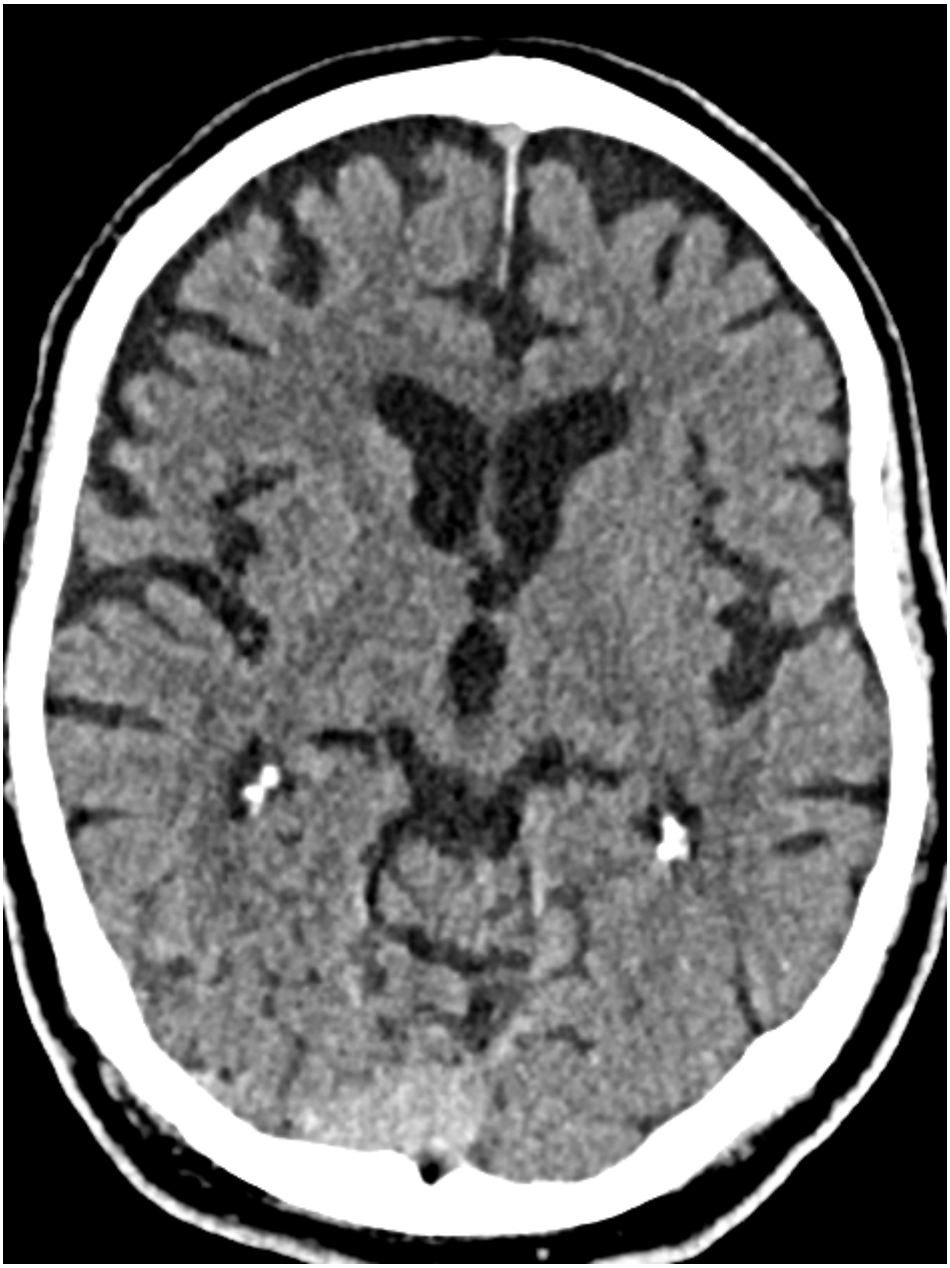
3. Wang D, Hu B, Hu C et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585

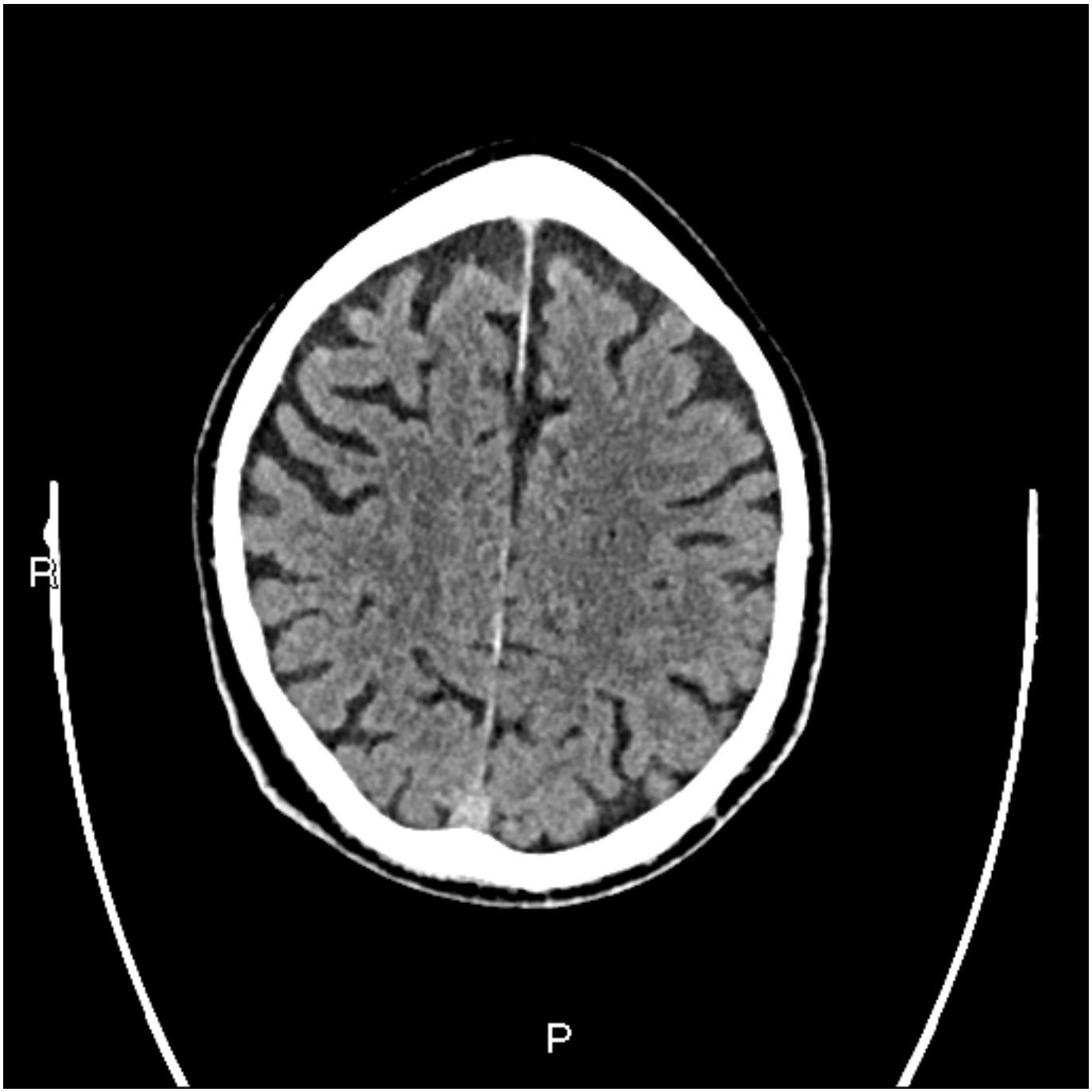
4. Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020. doi:10.1056/ NEJMoa2002032 https://www.nejm.org/doi/full/10.1056/NEJMoa2002032

5. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol. Published online April 10, 2020. doi:10.1001/jamaneurol.2020.1127
6. Chen N, Zhou M, Dong X. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lacent. Published January 30, 2020. doi.org/10.1016/S0140-6736(20)30211-7
7. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. ACS Chem Neurosci. 2020:0-3. doi:10.1021/acschemneuro.0c00122
8. Desforges M, Le Coupanec A, Dubeau P, et al. Human coronaviruses and other respiratory viruses: Underestimated opportunistic pathogens of the central nervous system? Viruses. 2019;12(1):14. doi:10.3390/v12010014

Figure 1: Plain CT head – There are mild chronic small vessel ischaemic changes seen. No cerebral atrophy. Basal ganglia, thalami and brainstem structures are within normal limits. CSF drainage pathways are within normal limits. Brainstem and posterior fossa structures are within normal limits.

Figure 2: Chest-X-ray - air space opacification in the right lower zone and left peripheral mid and upper zone

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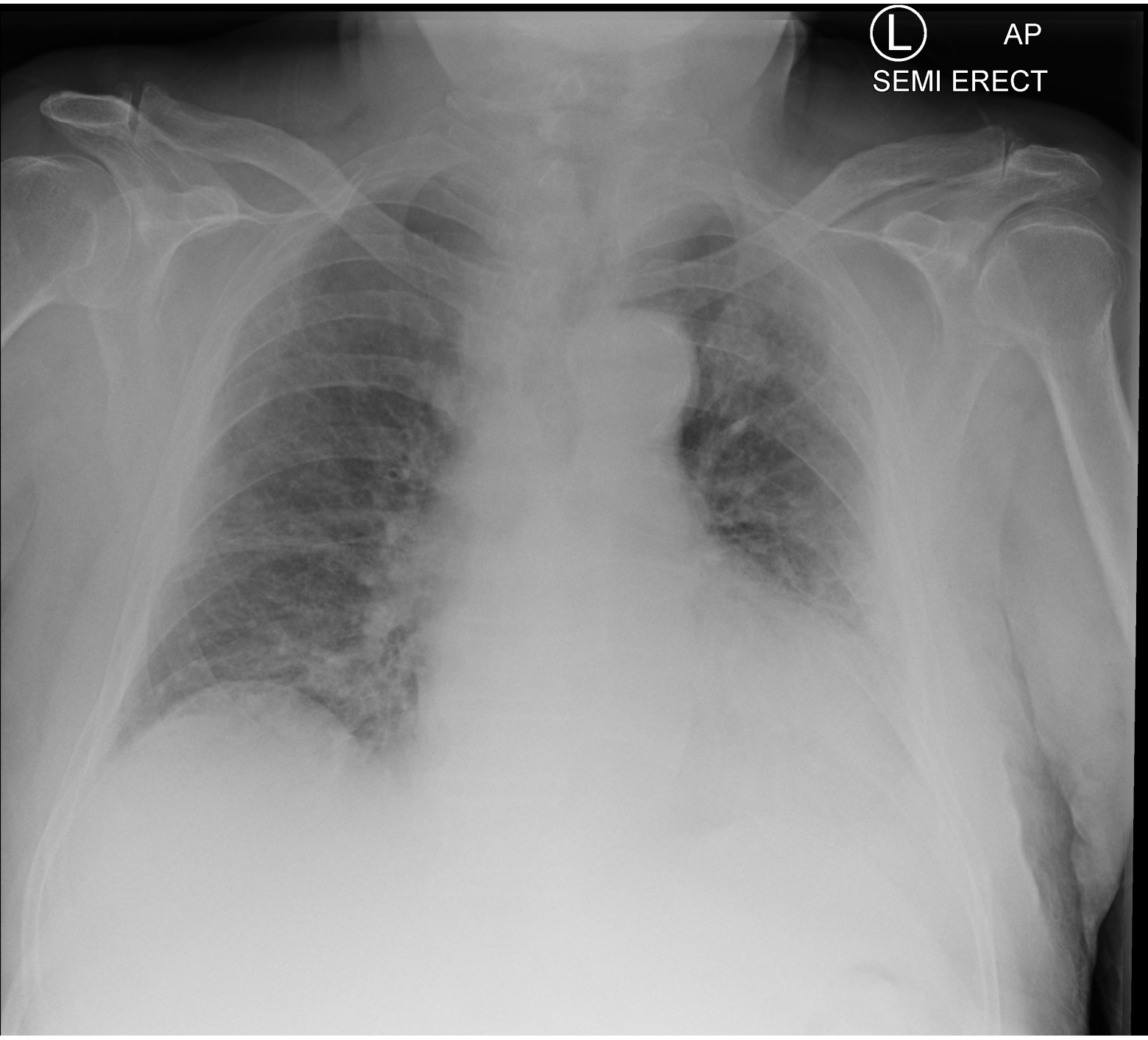
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