

## Central Disequilibrium Could be an Early Sign and Symptom of Rapidly Progressive SARS-CoV-2 related Respiratory Failure

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**ABSTRACT:** We describe a 90-year-old male presenting with disequilibrium, loss of balance and difficulty walking for three days prior to initial presentation. Interestingly, he denied cough, fever or dyspnea prior to arrival. Over the course of 48 hours, the patient developed acute respiratory distress syndrome (ARDS) requiring intubation, diagnosed with COVID-19 infection and was treated in the intensive care unit where he died. Since the initial cases in Wuhan China in Dec 2019, the medical and epidemiological communities have learned much about the presenting features, symptomatology, epidemiology, transmission and common physical, laboratory and radiological findings of this disease. Although common symptoms are already established, it is very important to learn and record atypical symptoms or presentations of this highly contagious disease. By doing so, we will be able to recognize earlier atypical symptoms and prevent the environmental exposure to Health care workers and future patients as well. We report that Central disequilibrium may be such as initial presenting sign and symptom of impending respiratory failure from SARS-CoV-2 virus. These atypical findings such as presyncope may precede common respiratory complications of SARS-CoV-2.

**Keywords:** Central Disequilibrium; CNS; covid-19 coronavirus; SARS-CoV-2

**INTRODUCTION:** The SARS-CoV-2, also known as the novel 2019 Coronavirus, has become an accelerating pandemic since first identified in 2019 in Wuhan, China. It has spread globally, showing alarming rates of mortality with over 600,000 cases and over 27,000 deaths. With an R0 around 2.5-2.9 (R0>1 indicates the disease will spread between people and may be lead to epidemic), it remains a very contagious virus and it warrants deeper understanding of presenting features for early screening and isolation interventions. Although we have gained some substantial information regarding its transmission, more common symptoms (Fever-77%, Cough-80%, Headache, Diarrhea, Fatigue)<sup>i</sup>, and CT chest findings similar to the SARS pattern<sup>ii</sup>,

there is much more to know regarding rare and atypical symptoms that made be a prelude to the development of more severe symptoms requiring higher levels of care. Except for some late reports on anosmia, neurological symptoms have not yet been reported in SARS-CoV-2 induced COVID-19. Human CoV, SARS-CoV-1 and MERS COV has been extensively reported to cause neuroinvasion and neurological symptoms.

### **CASE REPORT:**

We describe a 90-year-old male with past medical history of gastroesophageal reflux, benign prostatic hyperplasia and known right bundle branch block who presented with disequilibrium, loss of balance and difficulty walking for three days prior to initial presentation. He described his disequilibrium as an ‘early fainting spell’. Interestingly, he denied cough, fever, dyspnea, use of any new medications, headache, recent sick contacts, palpitations, gastroenteric symptoms, or any similar previous episodes.

On presentation, he was afebrile, hemodynamically stable, and did not require any supplemental oxygen. The patient was evaluated for syncope with an electrocardiogram showing normal sinus rhythm, started on continuous telemetry, and orthostatic pressures were found to be negative. On physical examination he had a positive Romberg’s sign, an unsteady gait, profound general weakness with malaise. Cardiac and pulmonary examinations revealed normal bronchial and vesicular breath sounds, adequate air entry, no adventitious breath sounds, regularly spaced s1s2 and no audible murmurs. His initial laboratory values demonstrated white blood cell count of 4.6 thousand/uL with mild thrombocytosis at 519,000/uL. His creatinine level was 1.40 mg/dL, which was elevated compared to baseline of 1.20 mg/dL and troponin I level was undetectable. Chest X-ray on admission revealed a mild interstitial prominence that was suggestive of possible chronic lung disease without any clear evidence of infectious etiology [IMAGE 1]. On chart review, he was noted to have an echocardiogram showing an ejection fraction of 65% with no structural or valvular abnormalities. Moreover, on initial workup, Computed Tomography of the head was negative for acute process.

He was admitted to the general medical unit for additional workup and continuous observation. Overnight, there were no abnormal telemetry alarms, and repeated labs were not remarkable. The following day, Magnetic Resonance Imaging (MRI) of the brain showed diffuse age appropriate atrophy of the cerebral and cerebellar regions, along with chronic microvascular changes. At this point, the patient’s symptoms persisted with an unclear etiology. He was continued on normal saline infusion for maintenance fluid, plans for further outpatient workup of his disequilibrium was anticipated and plans for discharge to a skilled nursing facility was underway.

Within 24-48 hours later, the patient began to experience progressive dyspneic episodes, respiratory distress, he was placed on a nasal canula at 2L/min oxygen flow and his repeat chest X-Ray showed an interval progression of the interstitial disease concerning for atypical pneumonia [IMAGE 2], and thus antibiotic therapy for community acquired pneumonia was initiated using ceftriaxone and azithromycin. His dyspnea continued to progress over the course of hours, requiring 8 L/min of supplemental oxygen and the patient was transferred to a higher level of care. A complete septic workup for pneumonia was negative, including a complete 12 panel respiratory

viral PCR workup. Considering the current ongoing-pandemic, the patient was evaluated for SARS-CoV-2 virus. Repeated labs now demonstrated, lymphopenia at < 15% lymphocytes, and CRP level was found to be elevated to at 195.4 with an estimated sedimentation rate of 42.

Arterial blood gas on 10 Liters/minute of high flow nasal canula indicated respiratory alkalosis with profound hypoxemia, pH: 7.44, pCO<sub>2</sub> 31 and pO<sub>2</sub>: 41. The patient was intubated and placed on mechanical ventilation and transferred to the intensive care unit. Chest X-Ray was performed post-intubation which showed appropriate placement of the endotracheal tube and worsening bilateral pulmonary infiltrates [IMAGE 3]. The patient's antibiotic regimen was escalated with vancomycin and cefepime in anticipation for the SARS-CoV-2 virus PCR results. A CT-scan of the chest was performed which showed bilateral diffuse central and peripheral ground glass opacities [IMAGE-4]. The same day the patient's respiratory failure progressed, requiring additional positive end expiratory pressure (PEEP) of 10, with FiO<sub>2</sub> of 80%. The patient was diagnosed with severe acute respiratory distress syndrome (ARDS) with a PaO<sub>2</sub> to FiO<sub>2</sub> ratio of < 100.

The following morning after this respiratory decline, the test results confirmed SARS-CoV-2. The patient's disease progressed into multi-organ failure indicated by transaminitis, poor urine output, a creatinine level of 3.00 mg/dL and an elevated troponin which peaked at 0.46 ug/mL. The patient continued to require mechanical ventilatory support and progressed to worsening PaO<sub>2</sub> to FiO<sub>2</sub> ratio over the course of the next three day, and later expired due to severe hypoxemia and complications of septic shock due to SARS-CoV-2 related ARDS.

## **DISCUSSION:**

We are gaining substantial information of this novel Coronavirus regarding its epidemiology, presenting early symptoms, transmissibility, incubation period and CT findings. We know that fever, cough, headache, fatigue, and gastrointestinal upset have been described as the most common presenting symptoms along with CT Chest findings of bilateral lung opacities<sup>iii</sup>. CT findings are documented to be more sensitive in detection of 2019-nCoV infection in a series of 1014 cases<sup>iv</sup> and we have made great progress in diagnosing 2019-nCoV Pneumonia. Furthermore, as the number of cases rise worldwide, people who are generally susceptible have been identified as being of advanced age and having prior comorbidities such as diabetes and hypertension<sup>v</sup>. Moreover, molecular techniques and sequencing have been utilized to diagnose new cases of severe pneumonia related to this novel virus.<sup>vi</sup> We must continue to gain more information regarding its atypical symptoms including the central nervous system.

Respiratory involvement of the human Coronavirus has been clearly established since the 1960s and the exacerbation of neurological diseases and CNS involvement was later described in the 1980s. Although, mechanism for this is poorly understood, it is thought to involve autoreactive immune cells along with degeneration and infection of the murine CNS.<sup>vii</sup> In addition, autopsy studies in 2004 have detected the coronavirus in neurons. This may provide an explanation for the invasive nature of this virus and its neuronal and psychologic abnormalities as seen in SARS-2004 patients. Previously, these neurologic symptoms were attributed to the social pressure experienced in an epidemic.<sup>viii</sup>

Prior to this case report, none have described a case of neurological involvement and central disequilibrium with this novel virus, SARS-CoV-2. Although we do not know exactly where SARS-CoV-2 falls on the scale of human to human transmissibility, to prevent a worsening pandemic and possibility of exposure breaches in public health systems,<sup>ix</sup> we must further expand our hierarchy of asymptomatic and symptomatic patients to include atypical presentations. By doing so, we will reduce the rate of infections, prohibit the exposure of health care workers seeing a multitude of patients, and expand our knowledge of this novel pathology.

This case sheds light on a possible presenting symptom in patients with subsequent severe ARDS due to SARS-CoV-2 virus. It is important for healthcare systems to broaden the scope of the symptomatology of this disease and identify earlier signs or symptoms in patients presenting with SARS-CoV-2 virus to prevent further life-threatening exposure to health care workers and patients. We would like to add central disequilibrium to this list. We believe these neurological symptoms may be caused by neuroinvasion of the nervous system with SARS-CoV-2. Further studies are required. We call on other centers to recognize these atypical symptoms as early presentation of SARS-CoV-2 virus.

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IMAGE 1: Mild interstitial prominence that was suggestive of possible chronic lung disease but infectious etiology could not be ruled out

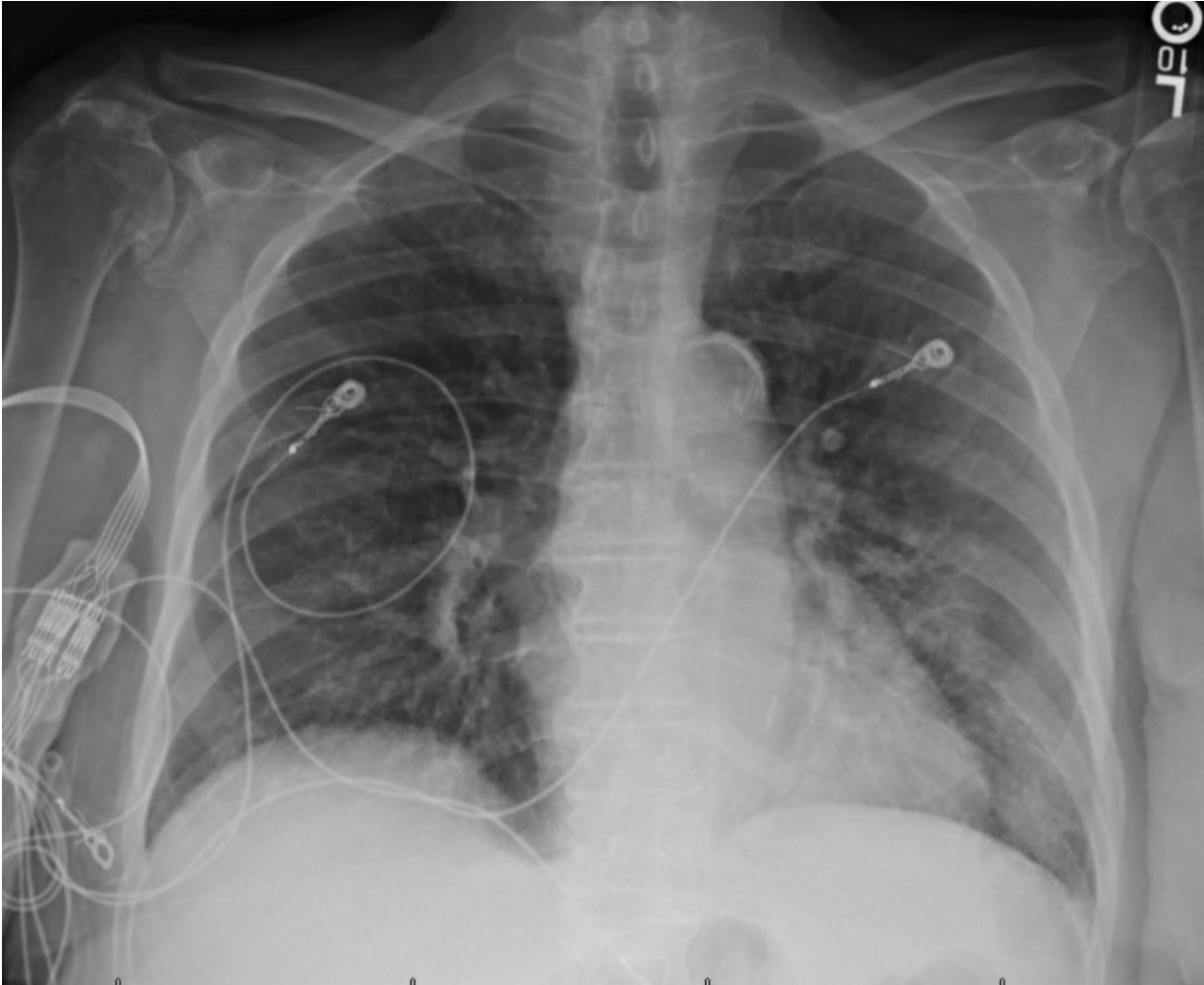


IMAGE 2: Interval progression of the interstitial disease concerning for atypical pneumonia

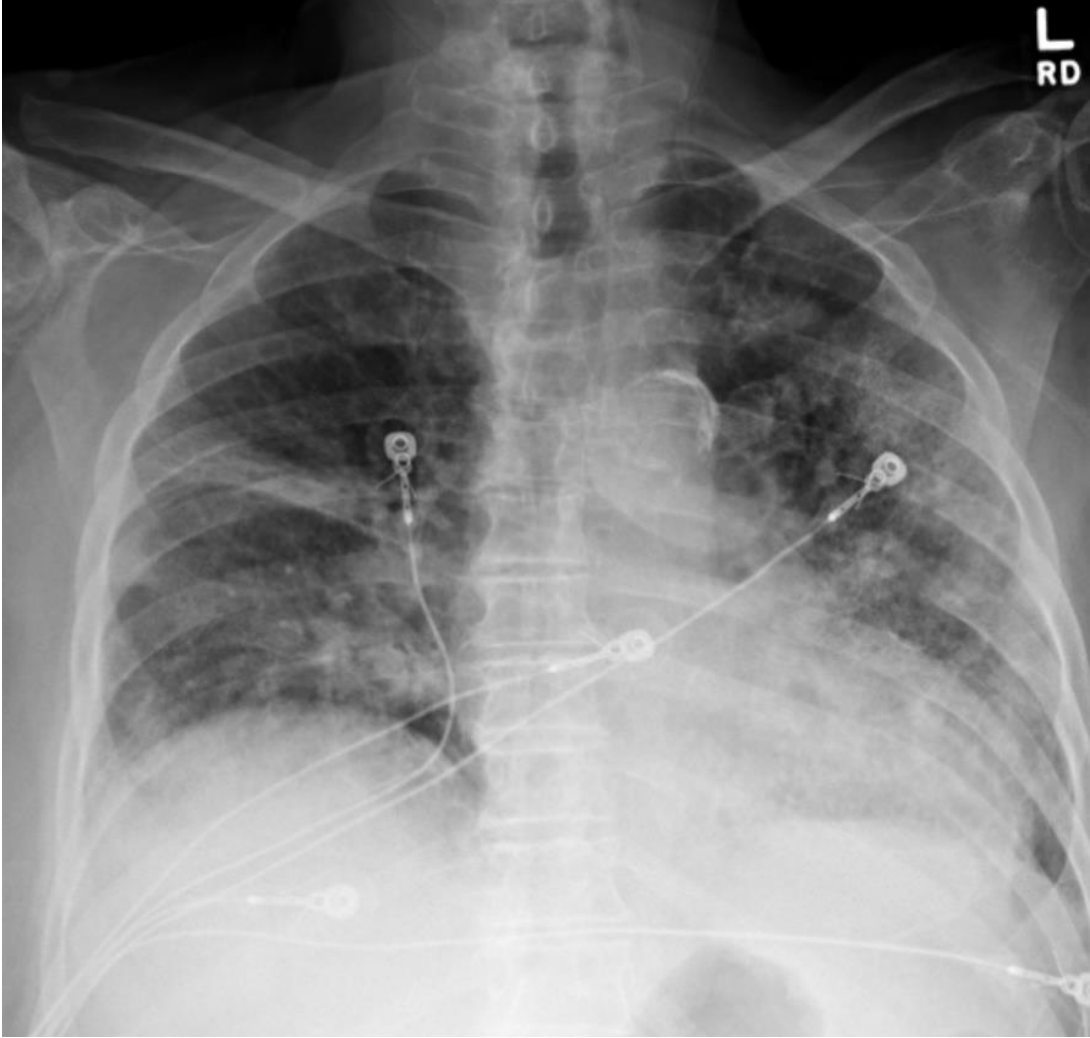


IMAGE 3: appropriate placement of the endotracheal tube and worsening bilateral pulmonary infiltrates



IMAGE 4: Bilateral Diffuse Central and peripheral ground glass opacities with interval areas of sparing

