Severe psychiatric disturbance and attempted suicide in a patient with COVID-19 and no psychiatric history

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SUMMARY
A previously fit and well 37-year-old male healthcare worker presented with confusion, psychotic symptoms and a suicide attempt in the context of a new COVID-19 diagnosis. Following surgical interventions and an extended admission to the intensive care unit, he made a good recovery in terms of both his physical and mental health. A number of factors likely contributed to his presentation, including SARS-CoV-2 infection, severe insomnia, worry, healthcare worker-related stress, and the unique social and psychological stressors associated with the COVID-19 pandemic. This case highlights the need to further characterise the specific psychiatric sequelae of COVID-19 in community settings, and should remind general medical clinicians to be mindful of comorbid psychiatric symptoms when assessing patients with newly diagnosed COVID-19.

BACKGROUND
COVID-19, caused by SARS-CoV-2 infection, remains an emerging disease with poorly defined psychological sequelae. Previous reports have identified that confusion, low mood, anxiety and insomnia are associated with severe coronavirus infection, although the precise risk factors and mechanisms by which these symptoms develop are unclear.

It has been speculated that healthcare workers may be especially vulnerable to the neuropsychiatric manifestations of COVID-19 due to work-related stress, bereavement and their increased risk of infection. Emerging evidence suggests healthcare workers may be at greater risk of depression, anxiety and insomnia during the COVID-19 pandemic, although the prevalence of severe psychiatric symptoms among healthcare workers has not been thoroughly investigated.

We present the case of a 37-year-old healthcare worker presenting with severe psychiatric disturbance and attempted suicide following SARS-CoV-2 infection. We explore a number of potential contributing factors including encephalopathy, severe worry, ethnicity and work-related stress. The case highlights the importance of vigilance towards psychiatric symptoms in patients with SARS-CoV-2 infection in both inpatient and community settings.

CASE PRESENTATION
The patient is a 37-year-old married man with two young children. Prior to this admission, he had no notable medical or psychiatric history, took no regular medications and had no allergies. He is a mental health nurse and works in the UK, where he has raised a family and lived for a number of years. He is of Black ethnicity. Regarding family history, his sister, aunt and grandfather were described as having experienced psychotic episodes, although the circumstances surrounding these and any subsequent diagnoses are not known.

During the COVID-19 pandemic, the patient experienced a 5-day history of fever, cough, breathlessness and myalgia. He experienced severe insomnia during this period, and reported feeling worried that he may infect his family. He had recently lost a number of patients to COVID-19 in the facility he worked at, which had been severely affected by the pandemic. Later, the patient would recall that he became preoccupied with biblical passages during this period, believing they were connected to the events happening in his life.

After self-isolating at home in line with current guidance, an ambulance was eventually called in relation to his worsening breathlessness. He was assessed by paramedics at home. It was agreed that he did not require hospital review, and he was advised to self-isolate at home.

That night, the patient’s family noted that he became increasingly confused and began acting bizarrely. He reported that he had both seen and heard the devil, and was also observed responding to auditory hallucinations. During the night he became increasingly anxious and was specifically preoccupied with dying and concerned he would infect his family. At approximately 04:00, he began to clean out the garden shed to sleep in, in order to be safely distanced from his children. In a phone-call with a family member, he was reported as being ‘confused’ and ‘paranoid’. He was also incontinent of urine.

Later that morning, the patient presented to the emergency department of a local hospital with ongoing concerns about his breathlessness. Clinical assessment, bloodwork and imaging (chest radiograph and CT of the head) did not indicate a need for admission. A swab test for SARS-CoV-2 was taken, and the patient was advised to return home and continue self-isolating. His family raised concerns about his mental state, but recall that no formal psychiatric assessment was performed.

The patient was driven home by a family member. On return, he went to the bathroom, stating he would wash to avoid infecting his family. Within approximately 20 minutes, his wife heard loud noises. On investigating, she found that the patient had lacerated his neck and jumped from an upstairs window. Emergency service attended the scene; the patient was heard telling clinicians “this is not me”. He was sedated, intubated, fluid resuscitated and
transferred to a local trauma centre. On arrival, he was noted to have a deep anterior neck laceration (12 cm by 4 cm) and an open wound of his right knee.

INVESTIGATIONS
CT imaging of the patient’s neck and chest revealed pneumomediasinum and surgical emphysema of the neck secondary to tracheal injury, and ground glass opacification and consolidation in keeping with moderate COVID-19. A CT of the head revealed no intracranial pathology. Fractures of the left radius, left ulna, left and right ankles were noted on imaging, alongside a tracheal compression fracture of L1. Bloodwork revealed an elevated white cell count (24.18 x 10^9/L) with lymphopenia (0.51 x 10^9/L), normal C reactive protein (1.5 mg/L) and electrolytes within normal range. Toxicology tests (ethanol, paracetamol, salicylate) were all negative. A SARS-CoV-2 PCR test was positive.

During his subsequent intensive care admission, a repeat CT of the head, cerebrospinal fluid (CSF) studies (lactate, glucose, protein, microscopy, cytology, flow cytology and NMDA receptor antibodies) and serology tests (CASP2R2, LG1, voltage-gated potassium channel and NMDA receptor antibodies, HIV and syphilis) were performed; all were negative.

DIFFERENTIAL DIAGNOSIS
This patient’s case likely represents either a manifestation of either delirium, a single acute psychotic episode or a manic episode in keeping with bipolar affective disorder. Factors supporting a diagnosis of delirium include the lack of any personal psychiatric history, the rapid onset of symptoms, quick recovery, amnesia and predominance of confusion throughout the event. Meanwhile, the patient’s family history of psychotic episodes may support the diagnosis of a single acute psychotic episode. A manifestation of bipolar-spectrum illness is also possible, given the patient’s apparent decreased need for sleep, increased energy and psychotic symptoms. Regardless, the underlying causes are similar; SARS-CoV-2 infection, severe insomnia, stress, preoccupation and worry are likely to have contributed to the patient’s mental deterioration.

TREATMENT
The patient was taken to operating theatres for an anterior tracheal repair and tracheostomy. The injury was noted to involve very deep lacerations of his larynx and neck resulting in severed cricothyroid joints, an open hole in the airway and bilateral external jugular venous haemorrhage. After surgery, he was kept sedated and admitted to the intensive care unit for ongoing support. Orthopaedic open reduction internal fixation and manipulation under anaesthesia were performed for his left radius and ankle fractures 2 days later.

The patient’s intensive care admission was complicated by haemodynamic instability, line sepsis, renal failure, refeeding syndrome and agitation. When sedative agents were reduced, he was noted to be agitated on a number of occasions, resulting in him pulling out his tracheostomy tube. Difficulty weaning sedative agents (propofol and fentanyl) contributed to a prolonged 32-day admission.

Regular olanzapine was commenced alongside PRN diazepam. The latter of these was introduced to facilitate weaning from intravenous sedatives rather than for primary treatment of psychiatric symptoms. Intravenous sedation was gradually weaned and the patient eventually began to wake safely. Communication was difficult due to the patient’s tracheostomy and oxygen requirements, however he smiled when family members visited and video-called, and he engaged with staff appropriately. At a bedside assessment, using a whiteboard to communicate, he calmly introduced himself to the consultant psychiatrist. He was orientated to being in hospital and the current year, and retained information about the exact date. The patient had no recollection of events leading to admission and was surprised to discover that he had jumped from a window. Although appearing tearful at times, he showed no signs of overt distress. He denied any current suicidal thoughts and expressed eagerness to recover and see his family.

The patient was weaned off oxygen support and stepped down to ward-level care. He remained settled, and worked cooperatively with physiotherapists both on and off the ward. His speech improved, and the psychiatry team assessed him on a number of occasions during this period. The patient recalled experiencing frightening disorientation, paranoia and hallucinations on the intensive care unit. It was explained that these are common features of delirium.

OUTCOME AND FOLLOW-UP
The patient continued to have limited recollection of the events leading up to admission, other than recalling severe worry about SARS-CoV-2 infection, insomnia and some religious preoccupation. He discussed the possibility of psychiatric illness openly and was curious towards a diagnosis to explain the events leading to admission. On the ward, he showed no signs of psychosis or suicidality, although did feel inexplicably tearful on occasion, struggled to concentrate while reading and had fragmented memories of the past week. These symptoms improved within days. At further assessments, he remained fully orientated, remembered previous conversations at each assessment and showed no signs of psychiatric illness. The patient’s tracheostomy was decannulated, and he was discharged on olanzapine, with appropriate medical and community mental health follow-up.

Since his discharge, the patient has remained well. On returning home, he initially experienced flashbacks of the events of deliberate self-harm, although these intrusions have now ceased. He is sleeping well, spending time with his family and showing no signs of agitation. He has been counselled on the importance of sleep and vigilance for signs of recurrence, and continues to take olanzapine while awaiting further community mental health review.

DISCUSSION
COVID-19 remains an emerging disease, with unknown psychological sequelae. A meta-analysis of severe coronavirus infection identified both delirium and insomnia to be common among such patients. Delirium was especially prevalent despite the relatively young age of the sample. Likewise, a separate analysis of 40469 patients’ electronic medical records identified insomnia and delirium to be prevalent manifestations of COVID-19.

Neuroinflammation, neurotropic SARS-CoV-2 infection, hypoxia, cerebrovascular events and the effect of steroid treatment have all been speculated to act as biological mediators of psychiatric disturbance in COVID-19, although the difficulty of differentiating delirium and psychosis has been noted. The vast majority of evidence focuses on psychiatric presentations in hospitalised patients and may be less generalisable to those with mild or moderate physical symptoms...
in community settings. In this case, both neuroimaging and CSF studies were normal, although these findings cannot exclude the role of neuroinflammation, neurotropic infection or hypoxia as potential biological mediators of the patient’s psychiatric disturbance.

Evidence supporting an aetiological role for neuroinflammation triggered by COVID-19 includes the finding that patients with psychiatric disorders have elevated serum levels of IgG to human coronaviruses compared with controls, and that this association may be partially specific to psychotic, compared with mood, disorders. Coronavirus strains tested include 229E, HKU1, NL63 and OC43, although to our knowledge, similar studies focused on immunoglobulins against SARS-CoV-2 are yet to be performed.

Neurotropic SARS-CoV-2 infection is also a plausible explanation of the patient’s psychiatric presentation in the above case. The functional receptor by which SARS-CoV-2 enters host cells is the ACE2 receptor, which is expressed in brain endothelium, allowing a plausible mechanism for neurotropic SARS-CoV-2 infection. Peripheral nerve invasion has also been hypothesised as a potential route for neurotropic infection, while neuronal degeneration has been identified in the brains of patients with SARS-CoV infection, suggesting that neurotropism may plausibly mediate the psychiatric manifestations of COVID-19.

The coagulopathy associated with COVID-19 may also represent a potential aetiological factor in this case. Of particular interest are studies which have identified abnormalities consistent with hypercoagulability in patients with psychosis, and proteomic evidence which suggests complement activation and hypercoagulation may precede psychosis in the general population. Although such evidence is limited, if associations between coagulation abnormalities and psychosis are rigorously established, hypercoagulability may represent a plausible mechanism by which COVID-19 mediates its neuropsychiatric sequelae.

A range of unique psychological and social factors associated with the COVID-19 pandemic may also have contributed to the patient’s presentation. Policy measures may detrimentally affect general population’s mental health regardless of infection through social distancing, decreased physical exercise, unemployment, domestic violence, loss of routine and health anxiety. Social stress associated with the pandemic has been implicated in a number of reports of psychotic symptoms in patients without SARS-CoV-2 infection, and preliminary evidence suggests increased rates of new schizophrenia diagnoses in a region affected by the COVID-19 pandemic.

Similarly, social factors may specifically exacerbate the psychiatric consequences of COVID-19 compared with other physical illnesses. Quarantine measures may lead to psychiatric distress and insomnia, while SARS-CoV-2 infection may be associated with greater anxiety symptoms compared with other non-COVID-19 pneumonias. Specific anxieties commonly relate to transmission of the virus to family members and to death. The patient’s occupation as a healthcare worker may have contributed to his presentation. Healthcare workers are thought to be at increased risk of mental ill-health during pandemic situations due to overwork, exhaustion, frustration, bereavement, risk of infection and discrimination. Data from the COVID-19 pandemic suggests frontline healthcare workers, especially nursing staff, appear to be especially at risk of experiencing psychological symptoms and insomnia. Specific to this case, the patient had lost a number of patients to COVID-19 at the facility he worked at, which may have contributed to his psychological distress and influenced the nature of his preoccupation and anxiety relating to the transmission of the virus to family members.

Another potentially relevant factor in the patient’s case is his ethnicity. The emerging literature suggests that COVID-19 disproportionately affects BAME (Black, Asian and minority ethnic) communities in terms of prevalence and mortality, and more recently concerns have been expressed about a potentially disproportionate impact on the mental health of such communities. Posited reasons for a racial disparity in mental ill-health include fear of contracting the virus, bereavement of social contacts and the disproportionate impact of social distancing measures on BAME communities. Although the patient did not report any direct discrimination by healthcare workers during the admission, his ethnicity may have contributed to his presentation through the indirect risk factors previously described in the literature.

Regardless of whether any potential association between COVID-19 and mental illness is mediated through biological, psychological or social factors, this case should make general medical clinicians alert to psychiatric presentations and their associated risk when assessing patients with COVID-19. Of particular concern is a similar case of a man who jumped from a third-floor window during self-isolation with SARS-CoV-2 and a number of reports of nurses attempting suicide during the COVID-19 pandemic. Likewise, psychiatrists should be mindful of the contribution of biological, psychological and social factors associated with the COVID-19 pandemic when assessing patients with primarily psychiatric presentations. Such associations are likely to be multifactorial, may require careful assessment and will likely go beyond the projected rise in post-traumatic symptoms associated with critical illness.

As well as aetiology, the treatment detailed in this case is also relevant to the association between SARS-CoV-2 and its psychiatric sequelae. This case adds to two previous reports of manic or psychotic episodes which have responded well to conventional antipsychotic treatments. This preliminary evidence may reassure clinicians that COVID-19-associated psychiatric presentations are treatable with established pharmacotherapies. However, as aetiological factors are elucidated, it is possible that more specific therapies are identified for presentations involving psychiatric symptoms. For instance, the hypercoagulable state associated with SARS-CoV-2 infection may represent a potential area of future therapeutic interest.

In conclusion, we report on the case of a 37-year-old man with no psychiatric history, who presented with confusion, psychotic symptoms and a suicide attempt in the context of a new COVID-19 diagnosis. We suggest this case may represent delirium, psychosis or a manic episode, and discuss a number of potential precipitating factors including SARS-CoV-2 infection, severe insomnia, worry and healthcare worker-related stress. The array of psychiatric manifestations associated with COVID-19 remains unclear and the majority of literature focuses on secondary psychiatric symptoms among patients hospitalised for severe infection. This case may therefore highlight the need to further characterise the specific psychiatric sequelae of COVID-19 in community settings, which may be in part achieved by performing case-control serological studies as in previous epidemics.

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Contributors Both authors made a substantial contribution to the conception, design, drafting and revising of the article. GG wrote the first draft of the manuscript and UJ supervised the project.
The majority of research literature investigating comorbid psychiatric symptoms in COVID-19 has focused on patients hospitalised for severe infection. There may be an urgent need to characterise the specific psychiatric sequelae of COVID-19 in community settings.

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