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Hyperkinetic Delirium as First Prodomal Symptom of Severe Respiratory Failure in A Patient with Sars-Cov-2: The Implementation of a Rapid Screening to Prevent This Dramatic Multiple Involvment in The Covid-19 Era

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1. Abstract

In December 2019, the novel coronavirus disease-19 (COVID-19), a viral illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), prompting the World Health Organization (WHO) to declare a global pandemic.

The SARS-CoV-2 pandemic has already infected more than 123 million people worldwide and resulted in 2.7 million deaths.

Recent reports suggest that though originally described as a respiratory virus, SARS-CoV-2 has now been shown to have multiple organ involvement.

The new SARS-CoV-2 shows, not only pulmonary tropism but also, neuro-tropism which results in delirium in the acute phase illness particularly in the older age groups.

The current assessment for COVID-19 in older people does not routinely include screening for delirium. Implementation of a rapid delirium screening tool is necessary because, without screening, up to 75% of cases can be missed.

This Case Report describes a clinical scenario of Hyper-Kinetic Delirium as First symptom of Severe Respiratory Failure in a patient with diagnosis of Sars-Cov-2.

2. Background

In December 2019, the novel coronavirus disease-19 (COVID-19), a viral diseases caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), prompting the World Health Organization (WHO) to declare a global pandemic [1].

The SARS-CoV-2 pandemic has already infected more than 123 million people worldwide and resulted in 2.7 million deaths.

Recent reports suggest that though originally described as a respiratory virus, SARS-CoV-2 has a multiple organ involvement [2].

The new SARS-CoV-2 shows neuro-tropism which results in delirium in the acute phase illness particularly in the older age groups.

Currently Sars-Cov-2 in older people does not routinely include screening for delirium. Implementation of a rapid delirium test tool is necessary because, without screening, up to 75% of cases can be missed.

This Case Report describes a clinical scenario of Hiperkinetic Delirium as First Prodromal Symptom of Severe Respiratory Failure in a patient with diagnosis of Sars-Cov-2 and multiple comorbilities.

3. Description

Our Italian patient 78-year-old men, developed anxiety, agitation, inattention, confusion, depressed mood, impaired memory and insomnia on December 17, 2020.

On December 18, 2020 he was admitted immediately in the Hos-

pital after Sars-Cov-2 diagnosis and rapid screening tool 4AT < 3 positive for Delirium (the 4AT is designed as symptoms of delirium is suspected. A score of 1-3 suggests cognitive impairment and more detailed cognitive. Rapid screening 4AT is a well-validated tool that shows good diagnostic accuracy with a pooled sensitivity of 0.88 (95% CI 0.80 to 0.93) and pooled specificity of 0.88 (95% CI 0.82 to 0.92) in older ≥65 years).

Sars-Cov-2 has been diagnosed by fever up to 38.5 degrees C, asthenia, myalgia, dyspnea, cough, anosmia and dysgeusia.

Computed tomography (CT) imaging of her chest showed multiple and bilateral ground-glass opacities located in both sub-pleural and apico-basal spaces (especially on the right). Nasopharyngeal swab specimens were collected to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid. The swab specimens were tested by real-time reverse transcriptase–polymerase chain reaction; a positive result was received 1 days later on 19 December 2020.

Our patient was diagnosed with Iperkinetic Delirium and Sars-Cov-2.

Delirium diagnosis as First Prodomal Symptom of Severe Respiratory Failure in our patient with Sars-Cov-2 and the implementation of a rapid screening is crucial to prevent this dramatic multiple organ involviment.

He received for Sars-Cov-2 pneumonia and respiratory failure high-flow O2 therapy with Ventimask; 400 mg of moxifloxacin I.V daily for 3 days; methylprednisolone three i.v. boluses of 200mg; Tocilizumab was given in a single i.v. 400-mg dose; prophylactic enoxaparin was prescribed (she no presented thrombotic events), inhalated long-acting bronchodilator and steroid, correction of hydro-electrolyte imbalance.

The patient had a history of ischemic heart disease, arterial hypertension, type II insulin-dependent diabetes, prostatic adenoma, chronic vascular encephalopathy, hypokinetic syndrome.

Biochemistry test indicated leucocytes 9.58 × 10 3c/µl (reference 4–11 × 103c/µl), D-dimer 3.3 µg/ml (reference 0.1–0.5 µg/ml), C-re-active protein 329 mg/l (reference 0–5 mg/l), pro-calcitonin 6.72ng/ml (reference 0–0.1 ng/ml), lactate dehydrogenase 316u/l (reference 135–225 u/l) and lactic acid 3.6 mmol/l (reference 0.5–1 mmol/l).

The response to treatment was initially refractory. During hospitalization, probably due to prolonged immobilization and social and family isolation (except for some video calls), episodes of hyperkinetic delirium with acute and fluctuating attention deficit, altered cognitive status, alternating agitation and drowsiness, psycho-motor activity disorders, alterations in sleep-wake rhythm, disorientation, perception disorders with hallucinations, have been intensified.

Iperkinetic Delirium has been treated in the initial severe phase with a benzodiazepine (Midazolam 5mg/ml) with benefit. Antipsychotic treatment with haloperidol (15 drops 3 times/day), then suspended for Qtc lengthening (490 ms); for treatment of sleep disorders Lormetazepam 10 drops in the evening and melatonin 1.5–6 mg/day administered during the evening time. Although sedatives such as hypnotics and benzodiazepines can help sleep deprivation, they can exaggerate symptoms of delirium and also are associated with increased risk of respiratory depression in older people.

Fortunately, January 15, 2021 our patient was PCR negative and he has after Computed Tomography (CT) imaging of her chest a complete resolution of bilateral areas of altered density a ground glass after treatment (Figure1).

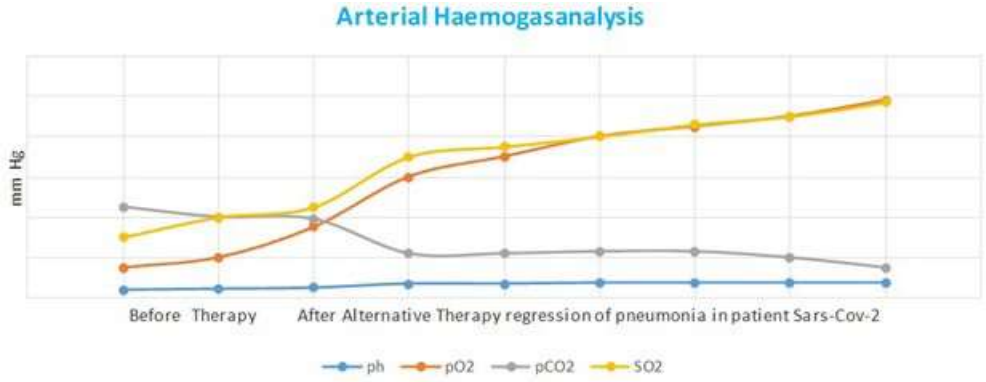

Figure 1: Arterial Haemogasanalysis

Note: This figure shows Arterial Haemogasanalysis before Antiviral and Antimicrobial Agents for Sars-Cov-2 and After Therapy with regression of pneumonia.

Suspended the current antibiotic therapy and antipsychotic for Iperkinetic Delirium, continue with melatonine, starts from 16/01 therapy with Vancomycin 125 mg q.i.d. for 10 days with resolution of symptoms and respiratory failure.

4. Discussion

Delirium is a potentially fatal acute brain dysfunction that is characterised by inattention and fluctuating mental changes. It is indicative of an acute serious organ failure or acute infection or the first symptom of severe respiratory failure in older persons with

multiple comorbilities, frailty and Sars-Cov-2.

Delirium may be a prodromal symptom of infection or hypoxia before respiratory failure occurs.

Our elderly patient has ischemic heart disease, arterial hypertension, type II insulin-dependent diabetes and as first symptoms has been anxiety, agitation, inattention, confusion, depressed mood, impaired memory and insomnia. Rapid screening test and early Sars-Cov-2 diagnosis can prevent the dramatic multiple organ involvement with severe respiratory failure. This clinical setting is also associated with prolonged hospital stay, long-term cognitive decline and increased mortality in older people with comorbily [3].

Recently, a British study has found that delirium is common in hospitalized patients with COVID-19, yet under-recognized and is associated with functional impairment in the medium term. Out of a total of 71 patients, 31 (42%) had delirium, of whom only 19 had been recognized by the clinical team. Physical function was substantially worse in people after delirium (− 39 points on functional scale/166, 95% CI −92 to −21, p = 0.01) [4].

The possible causes of delirium in COVID-19 patients are likely multifactorial that include Central Nervous System (CNS) invasion by the virus. The SARS-CoV-2 enters human cells via the Angiotensin-Converting Enzyme (ACE2) receptors which are expressed in various organs including the brain. Entry route for the virus into the brain may be directly through intra-nasal access via olfactory nerves, with a possible anosmia as an early symptom, or indirectly by crossing the blood-brain barrier via haematogenous or lymphatic spread.

Non-pharmacological approaches for delirium prevention and management should be considered first, if possible, before pharmacological intervention. Clinicians should start with identification of high-risk group of patients with risk factors for delirium such as older age, multiple comorbidities, pre-existing cognitive dysfunction, depression and polypharmacy. Alleviating precipitating factors for delirium as possible may help reduce the risk. For example, sleep deprivation can be a precipitating fact as well as a consequence of delirium. Although sedatives such as hypnotics and benzodiazepines can help sleep deprivation, they can exaggerate symptoms of delirium and also are associated with increased risk of respiratory depression in older people. It has recently been shown that melatonin or melatonin receptor agonists can reduce prevalence of delirium, length of ICU stay and improve quality of sleep [5]. Melatonin has also shown other anti-inflammatory, anti-oxidant and immune-enhancing properties that may help reduce the risk of infection-related progression to acute respiratory distress syndrome. Other precipitating factors such as hypoxia, pain, constipation and urinary retention should be avoided or promptly treated as possible. Reduction of the impact of isolation by allowing face-to-face family contact through social media and the use of orientation cues may help. Frequent inquiry about patients' comfort and satisfaction and keeping them up to date with the progress of their condition and stage of treatment are important. The negative impact of the PPE can be minimized by using a name badge or a picture of the person looking after the patient. Early physiotherapy input and early mobilization as able is vital in speeding up recovery [6].

Our Sars-Cov-2 patient with hyperkinetic delirium, severe respiratory failure, pneumonia and multiple comorbilities (ischemic heart disease, arterial hypertension, type II insulin-dependent diabetes) responding to therapy with regression of pneumonia and severe respiratory failure. Pharmacological therapy for Hyperkinetic Delirium has been complicate for multiple comorbilities (benzodiazepines for exaggerate symptoms and agitation; antipsychotic treatment with haloperidol has been suspended for Qtc lengthening (490 ms).

Actually our patient responding to benzodiazepines (Lormetazepam) for sleep deprivation and melatonin therapy had reduced the risk of infection-related progression to acute respiratory distress syndrome.

5. Conclusion

Currently Sars-Cov-2 in older people does not routinely include screening for delirium.

Delirium may be the first prodromal symptom of infection or hypoxia before respiratory failure.

Rapid screening test to identify COVID-19 patients with delirium may be crucial for the prevention of severe respiratory insufficiency.

Future prospective studies will be crucial to explore the long-term impact of Delirium and to activate protocols and early screening to prevent severe respiratory consequences in persons with Sars-Cov-2.

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