

Onset psychosis and PTSS after severe respiratory symptomatology caused by SARS-CoV-2 infection: a case report

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Summary. Covid-19 is an infective respiratory illness caused by a novel virus, which might present different degrees of severity: from mild or even asymptomatic carriers to severe pneumonia, requiring intubation and intensive care unit (ICU) management. SARS-CoV-2 may cause also central nervous system involvement, including psychiatric manifestations. Some cases of psychosis apparently covid-related have been reported since the start of the pandemic; we will briefly review some of them here, then we will report a case concerning a patient with emerging psychosis during the disease caused by the virus. Our case describes a man with no prior personal or familiar psychiatric history, who developed delusion and a post-traumatic stress symptoms (PTSS) which required hospitalization in a psychiatric unit. The patient was treated with antipsychotic medications and underwent a brief follow-up.

Key words. Post-traumatic stress symptoms, psychosis, SARS-CoV-2 infection.

Psicosi all'esordio e PTSS dopo una grave sintomatologia respiratoria causata dall'infezione da SARS-CoV-2: un caso clinico.

Riassunto. La malattia da coronavirus (covid-19) è una sindrome respiratoria di natura infettiva causata da un virus di nuova scoperta, che può manifestarsi con diversi livelli di gravità: da casi asintomatici a casi di polmonite anche severa, tanto da richiedere intubazione e ricovero in terapia intensiva. SARS-CoV-2 può causare anche il coinvolgimento del sistema nervoso centrale, comprese le manifestazioni psichiatriche. Sono stati riportati in letteratura diversi casi di psicosi apparentemente correlata alla covid-19; in questo lavoro ne passeremo in rassegna alcuni per poi descrivere il caso clinico di un paziente che ha presentato l'esordio di una sintomatologia psicotica durante il decorso della covid-19. L'uomo, che non aveva precedenti anamnestici né familiarità per patologie psichiatriche, ha sviluppato ideazione delirante e sintomi da stress post-traumatico che hanno richiesto un ricovero in ambiente psichiatrico. Il paziente è stato trattato con farmaci antipsicotici ed è stato sottoposto a breve follow-up.

Parole chiave. Infezione da SARS-CoV-2, psicosi, sintomi da stress post-traumatico.

Introduction

Corona virus disease (covid-19) is a respiratory syndrome caused by a novel coronavirus (SARS-CoV-2) first detected in Wuhan, China, in December 2019, then declared to be a global health emergency and a pandemic by the World Health Organization (WHO) on March 11, 2020^{1,2}. This illness can affect every age group, ensuing in an extensive spectrum of various clinical manifestations. In addition to the most widespread symptoms (fever, dry cough, fatigue, arthralgia and chest pain)³⁻⁶, some patients might also present atypical symptoms, including neurological and psychiatric manifestations, due to the neuroinvasion of SARS-CoV-2 demonstrated in autopsies^{7,8}. In the cohort of psychiatric symptoms related to SARS-CoV-2 infection, cases of psychosis have also been described. The nature of this association still remains unclear.

It could be caused by three mechanisms: the specific impact of the pathogen, depending by the virus' direct neurotropism or the consequent neuroinflammation or post-infective sequelae; the social, cultural and psychological circumstances related to the pandemic; the interventions that the patient undergoes (hospitalization, intubation, medicines such as corticosteroids, sedatives and anesthetic agents)⁹. Several reported cases of psychosis associated to the covid-19 can be labeled as reactive to the pandemic stress, but not caused by the virus, because patients were not infected¹⁰⁻¹⁵. The psychological impact of the spread of the virus, and the augmented risk of psychosis that ensued, is witnessed by the consequent 25% increase in first episode psychosis compared with the same period of the previous year¹⁶.

As far as reported cases of psychosis in patients infected with SARS-CoV-2 are concerned, it remains unclear whether the "psychosis" occurred as a dis-

tinct disease or as part of a more extensive modification in the mental state with a well-known physiological cause. In fact psychotic symptoms are extremely prevalent in delirium¹⁷, which in turn is highly widespread in critical illness in general, including covid-19¹⁸.

Delirium is the most common problem associated with intensive care unit (ICU) admission as part of a cluster of symptoms called “post-intensive care syndrome” (PICS), including new or worsening physical, cognitive, or mental impairments in a patient following critical illness or intensive care¹⁹. Mechanical ventilation can affect cognition too²⁰. Therefore, it can be useful to distinguish the cases in which the psychosis is attributable to organic conditions, from the ones in which this happens without severe respiratory illness, blood gas or electrolyte disturbances, sepsis, and iatrogenic causes.

Correa-Palacio et al.²¹ reported a case of psychosis developed around 2 weeks after covid-19 somatic symptoms, in a patient with no prior personal or familial history of psychiatric diseases. The patient had also been treated with corticosteroids, which are a well-known risk factor for psychotic complications²².

An interesting case, without the bias of corticosteroids treatment, is the one reported by Smith et al.²³, concerning a patient with poor symptomatic SARS-CoV-2 infection who had no prior personal or familial history. The patient presented insomnia and persecutory delusions after the covid-19 diagnosis. The symptomatology regressed over two weeks and remained symptom-free despite discontinuing risperidone in the community.

In the series reported by Parra et al.²⁴, the ten patients included, with no prior psychiatric history, presented a first-onset psychosis after about two weeks of somatic covid-19 symptoms, and their delusions persisted longer than the confusional symptoms described for some of them.

Some cases where patients presented mild or no symptoms at all, in addition to psychiatric manifestations, have been described to support the hypothesis that the viral infection or the consequent inflammatory activation would rise psychotic symptoms.

The cases reported by Ferrando et al.²⁵ presented new and recent-onset of severe anxiety, agitation, paranoia, disorganized thinking and hallucinations, without severe covid-19 symptoms, except for cough, body aches, chills, and nausea.

Instead, the patients of the series reported by Lanier et al.²⁶ presented none of the typical covid-related respiratory or gastrointestinal symptoms or disturbances in taste and smell. The patients manifested only psychiatric symptoms such as extreme anxiety, agitation, suspiciousness, disorganized thinking and two of them presented hallucinations, too.

Case report

In November 2020 O.M., a Caucasian 39-year-old man, comes to our psychiatric ward, transferred from a center of infectious diseases, where he had been hospitalized for a total of 30 days. He had a respiratory failure due to bilateral interstitial pneumonia caused by SARS-CoV-2 which had necessitated the use of orotracheal intubation and invasive mechanical ventilation. From the clinical documentation we learned that the patient, during his stay at the Intensive Therapy (IT) department, had taken steroid therapy with subsequent tapering, enoxaparina sodium and empirical antibiotic therapy (ceftriaxone with subsequent switch to piperacillin/tazobactam). He was extubated after 17 days with progressive improvement of the general conditions, with a significant weight reduction (about 10 kg) and the persistence of sinus tachycardia, for which therapy with betablocant was set. During the long hospitalization the patient had not been able to see or hear his family members. Despite the clear improvement of the internistic aspects and the definitive clinical recovery from SARS-CoV-2, the patient presented an exacerbation of the psychopathological conditions with worsening of restlessness and the occurrence of delusional ideas that required admission to psychiatric ward. When he reached our observation, O.M. was alert, oriented in time, he appeared quiet, but suspicious in the interaction with others, he was tendentially mutable with emotional confusion and he had the firm conviction that all his family members had died during the period of his stay in it. He was unaffectionate, not reassuring, constantly he recalled the images of both the traumatic events of hospitalization and the delusional idea of the death of his family members. He was not critical about this thought, despite the contrary information provided by the Health. The patient's psychiatric history was negative, there was no evidence of alcohol or drug use nor the presence of previous organic diseases. During the hospitalization the patient was treated with antipsychotic therapy (olanzapine 10 mg/day), but he had a marked improvement when he met his relatives in the ward; furthermore, he was allowed to contact them by phone daily. During the stay Mr. O.M. was also subjected to a psychodiagnostic evaluation, aimed at assessing psychological functioning, symptoms of clinical relevance and possible dysfunctional personality traits: Millon Clinical Multiaxial Inventory III (MCMI-III) and Minnesota Multiphasic Personality Inventory 2 (MMPI-2). Both evaluations did not reveal any clinical relevance, thus showing a good current and previous functioning. Also the scores at the Brief Psychiatric Rating Scale (BPRS), administered a first time entry on the admission and a second time release after eight days,

showed a significant clinical improvement. The stay lasted nine days and there was a rapid and complete resolution of the delusional symptoms, so the patient was discharged in good general condition, with the indication to go to outpatient services. During the three following months the patient continued the prescribed therapy, his clinical outcomes confirmed to be good, restoring his previous functioning and he was able to go back to work.

Discussion and conclusions

Data in the literature show an increased risk of psychiatric sequelae in patients who have had a covid-19 infection in the period between 14 days and the following 90 days, with an approximately doubled risk to receive a new diagnosis (by 5.8%). The most frequent psychiatric diagnoses are anxiety disorders, adaptation disorder, post-traumatic stress disorder and panic. Main psychiatric diagnoses develop largely in younger subjects²⁷.

The underlying mechanisms are unknown and require further investigation, although it has been suggested that the association between covid and psychiatric manifestations could be mediated by biological factors directly related to covid-19²⁸. In a recent review were reported patients who had psychiatric manifestations during the course of SARS-CoV-2 disease, they had also previously been treated with antiviral and corticosteroid therapy. Half of the patients had undergone intensive care (for a mean of 15.5 days), the 80% of patients had a complete remission from the psychotic symptoms, whom appeared more than two weeks after the first somatic manifestation attributed to covid-19 and solved in less than two weeks²⁴.

Environmental factors also play a fundamental role: the covid-19 special units in hospitals are characterized by the isolation of patients, the use of extensive personal protective equipment and no possibilities to be visited by relatives²⁹. Several hypotheses have been advanced to explain how PTSD/PTSS emerges in patients with covid-19: it is known that the severity of the disease and the ICU hospitalization are risk factors themselves, but there are emerging reports of a burden significant psychological trauma in patients who have developed covid-19, even in a mild form³⁰.

Mr O.M. developed alterations and distortions of thoughts associated with erroneous beliefs of reality that continued after the period of ICU and post-intensive hospitalization. Based on the present literature, we hypothesize that the conditions of environmental deprivation characteristic of covid-19 departments may have a role in the onset of delusional symptoms of our patient, the content of which was characterized by themes isomorphic to the sensory deprivation, experience to which patients with covid-19 are exposed. During the

stay in the psychiatric ward he also had vivid memories and a traumatic recall of delusional content, in particular that all the family members were dead, compatible with PTSS. These symptoms were quickly disappeared with antipsychotic medications and meeting his family. Three-month follow-up showed good recovery. Given the limited number of follow-up studies present in literature about similar cases, it is necessary to carry out further investigations to clarify the connection between onset of psychiatric symptoms and covid-19. In conclusion, the more appropriate treatment for this condition needs to be identified yet.

Conflict of interests: the authors have no conflict of interests to declare.

References

1. World Health Organization (WHO). Statement on the Second Meeting of the International Health Regulations Emergency Committee Regarding the Outbreak of Novel Coronavirus (2019-nCoV). Geneva: WHO, 2005.
2. World Health Organization. WHO Director-General's Opening Remarks at the Media Briefing on COVID-19. Geneva: WHO, 2020.
3. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine* 2020; 21: 100331.
4. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708-20.
5. Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. *JAMA Netw Open* 2020; 3: e205619.
6. Wang Z, Chen X, Lu Y, Chen F, Zhang W. Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. *Biosci Trends* 2020; 14: 64-8.
7. Natoli S, Oliveira V, Calabresi P, Maia LF, Pisani A. Does SARS-Cov-2 invade the brain? Translational lessons from animal models. *Eur J Neurol* 2020; 27: 1764-73.
8. Arabi YM, Balkhy HH, Hayden FG, et al. Middle East respiratory syndrome. *N Engl J Med* 2017; 376: 584-94.
9. Han D, Wang C, Feng X, Wu J. Delirium during recovery in patients with severe COVID-19: two case reports. *Front Med* 2020; 7: 573791.
10. D'Agostino A, D'Angelo S, Giordano B, et al. Brief Psychotic Disorder during the national lockdown in Italy: an emerging clinical phenomenon of the coronavirus pandemic. *Schizophr Bull* 2021; 47: 15-22.
11. Chandra PS, Shiva L, Nagendrappa S, Ganjekar S, Thippeswamy H. COVID 19 related psychosis as an interface of fears, socio-cultural issues and vulnerability-case report of two women from India. *Psychiatry Res* 2020; 290: 113136.
12. Rivas VCMO, Hernández-Huerta D, Silva CPD, Gómez-Arnau J. Reactive psychosis in a health care worker during the COVID-19 pandemic. *Prim Care Companion CNS Disord* 2020; 22: 20102692.
13. Huarcaya-Victoria J, Herrera D, Castillo C. Psychosis in a patient with anxiety related to COVID-19: a case report. *Psychiatry Res* 2020; 289: 113052.
14. Fischer M, Coogan AN, Faltraco F, Thome J. COVID-19

- paranoia in a patient suffering from schizophrenic psychosis - a case report. *Psychiatry Res* 2020; 288: 113001.
15. Valdés-Flórida MJ, López-Díaz Á, Palermo-Zeballos FJ, et al. Reactive psychoses in the context of the COVID-19 pandemic: clinical perspectives from a case series. *Rev Psiquiatr Salud Ment (Engl Ed)* 2020; 13: 90-4.
 16. Hu W, Su L, Qiao J, Zhu J, Zhou Y. COVID-19 outbreak increased risk of schizophrenia in aged adults. *PsyChiaXiv* 2020. Preprint. doi: 10(202003.00003).
 17. Meagher DJ, Moran M, Raju B, et al. Phenomenology of delirium: assessment of 100 adult cases using standardized measures. *Br J Psychiatry* 2007; 190: 135-41.
 18. Helms J, Kremer S, Merdji H, et al. Delirium and encephalopathy in severe COVID-19: a cohort analysis of ICU patients. *Crit Care* 2020; 24: 1-11.
 19. Bryant SE, McNabb K. Postintensive care syndrome. *Crit Care Nurs Clin North Am* 2019; 31: 507-16.
 20. Almeida IC, Soares M, Bozza FA, et al. The impact of acute brain dysfunction in the outcomes of mechanically ventilated cancer patients. *PloS One* 2014; 9: e85332.
 21. Correa-Palacio AF, Hernández-Huerta D, Gómez-Arnau J, Loeck C, Caballero I. Affective psychosis after COVID-19 infection in a previously healthy patient: a case report. *Psychiatry Res* 2020; 290:113115.
 22. Dubovsky AN, Arvikar S, Stern TA, Axelrod L. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. *Psychosomatics* 2012; 53: 103-15.
 23. Smith CM, Komisar JR, Mourad A, Kincaid BR. COVID-19-associated brief psychotic disorder. *BMJ Case Rep* 2020; 13: e236940.
 24. Parra A, Juanes A, Losada CP, et al. Psychotic symptoms in COVID-19 patients. A retrospective descriptive study. *Psychiatry Res* 2020; 291: 113254.
 25. Ferrando SJ, Klepacz L, Lynch S, et al. COVID-19 psychosis: a potential new neuropsychiatric condition triggered by novel coronavirus infection and the inflammatory response? *Psychosomatics* 2020; 61: 551-5.
 26. Lanier CG, Lewis SA, Patel PD, Ahmed AM, Lewis PO. An unusual case of COVID-19 presenting as acute psychosis. *J Pharm Pract* 2020; 897190020977721.
 27. Varatharaj A, Thomas N, Ellul MA, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry* 2020; 7: 875-82.
 28. Sriharan J, Sriharan A. Emerging mental health issues from the novel coronavirus (COVID-19) pandemic. *Journal of Health and Medical Sciences* 2020; 157-62.
 29. Bolton C, Thilges S, Lane C, Lowe J, Mumby P. Post-traumatic stress disorder following acute delirium. *J Clin Psychol Med Settings* 2021; 28: 31-9.
 30. Di Crosta A, Palumbo R, Marchetti D, et al. Individual differences, economic stability, and fear of contagion as risk factors for PTSD symptoms in the COVID-19 emergency. *Front Psychol* 2020; 11: 567367.