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CASE REPORT

Complex Trauma, Psychosis and COVID-19: A Case Report

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ABSTRACT

Background: Complex trauma is a variant of post-traumatic stress disorder (PTSD), adding symptoms of affect dysregulation, difficulty in relationships, and negative self-perception. Its neurobiology is closely linked to the pro-inflammatory alterations by the disruption of the hypothalamic-pituitary-adrenal axis, which are also described in psychosis, and neuropsychiatric symptoms of the SARS-CoV-2 virus infection.

Aim: To present a case that illustrates the clinical and neurobiological overlap between COVID-19, psychosis, and complex trauma.

Case presentation: A 24-year-old female who initially presented dissociative symptoms evolving into a psychotic episode, after suffering from COVID-19 disease, in whom a history of abuse was later clarified. The clinical case is reviewed, performing a free search of articles for the discussion of clinical and pathophysiological challenges.

Conclusion: Trauma is one of the greatest determinants in mental health, and is associated with several clinical spectra, being necessary to open the phenomenological and physiological debate to understand the sum of effects in patients who present with severe mental illness.

Keywords: post-traumatic stress disorder (PTSD), complex trauma, psychosis, psychotic disorder, SARS-CoV-2, COVID-19

Introduction

Post-Traumatic Stress Disorder (PTSD) is part of the group of disorders classified as stress-related disorders included in the eleventh revision of the International Classification of Diseases (ICD-11), and in which category complex Post-Traumatic Stress Disorder is also included [1]. Each of these two disorders is characterized by a set of symptoms that allow differentiation of the diagnoses. In that sense the main antecedent of Post-Traumatic Stress Disorder is exposure to an event of injury, violence or threat. It has four types of evolution: few symptoms, gradual remission, progressive attenuated symptoms, and chronic symptomatology [2]. Individuals exposed to repetitive or sustained trauma (including child abuse and domestic violence) will develop severe emotional regulation problems, cognitive distortions towards themselves and/or the aggressor, learned helplessness, impulsiveness, dissociative symptoms, substance use[3], somatization, re-victimization and cognitive problems [4], being finally diagnosed with complex trauma (Table 1 and Figure 1). Diagnosis is clinical and difficult; alterations in the hippocampal neuronal processes and reduction of inhibitory frontal networks are known, with an increase in cortisol, disturbing the functioning of the Hypothalamic-Pituitary-Adrenal (HPA) axis, an explanation that made possible therapeutic options [2–4].

Table 1. Post-Traumatic Stress Disorder and complex trauma diagnostic criteria. Diagnostic criteria that must be met for the diagnosis of Post-Traumatic Stress Disorder and the additional symptoms that comprise complex trauma. *Adapted from* [5].

Symptoms to consider Post-Traumatic Stress Disorder
Trauma-associated reactivity: aggressiveness, hypervigilance, insomnia; avoidance of trauma-related stimuli; intrusion symptoms: re-experiencing the event, flashbacks, nightmares; negative cognitions or feelings about self or others; dissociation; due to a history of exposure (direct or indirect) to a traumatic event, an event of injury, violence, or threat [6–8].
Plus:
Re-experiencing, dissociative reactions, and avoidance behavior
Additional symptoms to consider complex trauma:
Alterations in the organization of oneself, dysregulation of affect and impulses, relating difficulty and negative self-perception

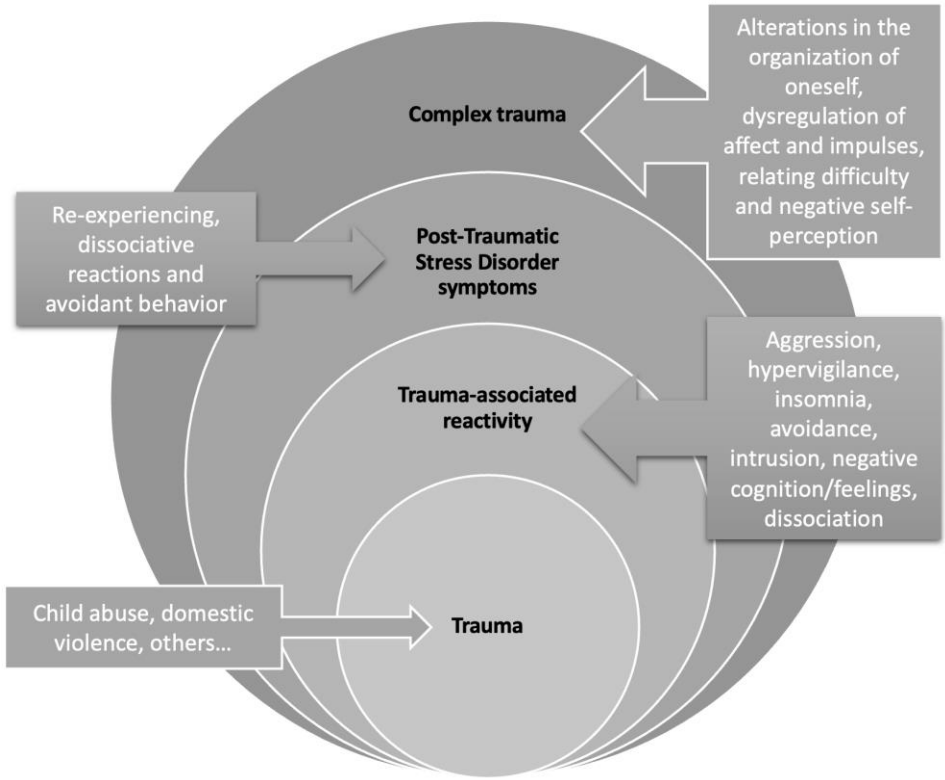

Figure 1. Dimensional relationship between symptoms associated with trauma and complex trauma

Confinement, social distancing and concerns due to the SARS-CoV-2 virus pandemic are considered potential traumatic events [9,10], coursing or not with COVID-19, so we can find symptoms of Post-Traumatic Stress Disorder as an emotional response to the pandemic, or as a direct sequel to the infectious disease [11]. The high affinity of the virus to the Angiotensin-Converting Enzyme-2 (ACE2), also expressed in the Central Nervous System (CNS), implies an acute inflammatory response, with interleukin and interferon activity due to an adaptive immune response [12–14]; by hematogenous dissemination, retrograde neuronal transport and passage through the cribriform plate, this phenomenon explains the presence of neuropsychiatric symptoms, in which between 40-88% of patients with severe COVID-19 present neurological symptoms, neurodegeneration, neuroinflammation and demyelination [11,12]. Among the post-COVID psychiatric manifestations, there are depressive, anxious, traumatic symptoms, insomnia and psychosis, including dissociative manifestations [15–18].

The overlapping of neurobiological phenomena between Post-Traumatic Stress Disorder and SARS-CoV-2 virus infection can generate mixed clinical pictures that are difficult to diagnose and have a poor response to treatment. In addition to what has been pointed out by several investigations on the psychosocial impact of the COVID-19, pandemic and its consequences on mental health have been a challenging and stressful crisis that has increased the risk of exposure to trauma, especially in vulnerable populations, such as those with pre-existing mental illnesses, those who have been previously exposed to trauma, or those who have suffered severe and prolonged trauma, the latter constituting a complex trauma, and in which case psychological responses that meet the diagnostic criteria for Post-Traumatic Stress Disorder (symptoms of intrusion, avoidance of trauma-associated stimuli, dissociation, trauma-related reactivity, negative cognitions or feelings about self or others) are present[19], as well as additional symptoms, such as altered affect and impulse disturbance, altered self-perception and perception of others, severe dissociation, difficulties in relating, and somatization, mainly [7,8,20,21].

On the other hand, several studies have described that isolation, social distancing, fear of becoming infected or infecting others or the economic impact of the coronavirus pandemic have increased the incidence of acute new-onset psychotic disorders [22,23]. According to some research, acute psychosis, with or without other symptoms, may be a potential presentation of COVID-19 [24], or SARS-CoV-2 infection may increase the likelihood of developing neuropsychiatric symptoms and even amplify the effects of risk factors associated with an increased risk of psychosis experienced after infection [23,25]. A systematic review of case reports of adult patients with psychosis and antecedent or concurrent COVID-19 has also found reports of patients with a psychiatric history, patients with substance use, and others with a comorbid medical condition, some of whom have required psychiatric institutionalization [26]. In cases of acute psychotic disorders, psychosocial distress generated by the COVID-19 pandemic has resulted in clinical symptoms such as hallucinatory syndrome, delusional syndrome and COVID-19-focused delusional syndrome [27], or psychotic manifestations due to psychological stress caused by fear of infection, in which patients present with sleeping difficulties, hallucinations, delusions, disorganized speech and disorientation, symptoms that remit with antipsychotic treatment [28]. A multicenter observational study of patients with brief psychotic disorders triggered by COVID-19 crises, who met Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for "brief psychotic disorders with marked stressors", found that about a quarter of the patients showed suicidal symptoms and almost half had symptoms of first-degree schizophrenia [29].

Considering the above, the aim of this article is to present a case showing the clinical and neurobiological overlap between COVID-19, psychosis, and complex trauma in a young female patient.

Case Presentation

The case report was prepared by collecting clinical information from the patient's hospital and ambulatory records, with the prior signature of the informed consent. A 24-year-old female, who has a history of an unspecified anxiety disorder for about six years, which was treated with Fluoxetine 20 mg/day for an undetermined time, with unknown adherence, but with apparent good evolution, as well as a recent SARS-CoV-2 infection resolved about three weeks ago, having presented minor respiratory symptoms, but receiving management with Dexamethasone, of which at least a 6 mg dose applied intramuscularly is known, although it cannot be established with certainty time and total dose of treatment. She arrives at the emergency service accompanied by her psychotherapist, due to a clinical picture of at least six days of evolution, which began during a vacation trip she was taking with her partner and in-laws, showing high levels of anxiety upon assuming that there was hostility and

jealousy in the treatment by their partner. A few days after starting the trip, the patient presented an experience of sexual abuse by her partner (an event that could later be established as not having occurred), observing her in-laws as passive witnesses of it, describing feeling under the effect of some substance which she inferred as furtively supplied (due to drowsiness, weakness, memory disturbances), initiating a dissociative experience of de-realization with which she finally interprets the event as hallucinatory, for which she makes no further mention of it during the trip.

She reports that during her return she was unaware of her travel group (a probable phenomenon of misidentification), with the persistence of de-realization, presenting delusional paranoid ideas of harm, so, helped by airport personnel, she made the trip alone, and through her psychotherapist and close relative, she was admitted to the psychiatric ward, due to the prolongation of dissociative symptoms and disorganized behavior. During her stay, she developed a structured delusion in which she accused her father and a group of people of repeated sexual abuse over the last eight years, adding cenesthetic hallucinations, periods of re-experiencing sexual aggression and disorganized behavior, keeping napkins with saliva to present them as evidence of the abuse. The patient received antipsychotic initial treatment with Haloperidol, 5 mg in 24 hours, which was suspended due to the presence of orolingual dystonia that resolves with the use of 50 mg of Diphenhydramine, replacing management with Olanzapine that reaches up to 15 mg/day throughout the following week, seeking final change to Aripiprazole, which is titrated up to 22.5 mg/day, with the intention that this would be his outpatient treatment due to concerns about the metabolic impact of Olanzapine.

Basic laboratory studies were performed, Complete Blood Count (CBC), 6-item blood chemistry, lipid profile, liver function tests, thyroid profile, serum electrolytes, rapid Human Immunodeficiency Virus (HIV) test, pregnancy test, COVID test and a profile of sexually transmitted diseases, as well as a magnetic resonance imaging of the skull, with no pathological findings; his conventional electroencephalogram reported mixed fast and slow diffuse rhythms, without focalizations. A lumbar puncture was also performed (after neurological consultation [without evident deficit]), with no laboratory abnormalities, as well as a negative COVID-19 test. A gynecological consultation was requested due to pseudocyesis, performing a transvaginal ultrasound with no evidence of pregnancy and with a negative human chorionic gonadotropin result. Upon indirect questioning, her parents commented that, five years earlier, she experienced sexual abuse by a former partner (possibly in a group setting), during a stay abroad, accompanied by forced use of substances and psychological abuse that ended in economic threats, requiring admission to a psychiatric hospital to obtain her return to the country (she lived with the mother of the abuser), during which it has been reported the diagnosis of bipolar disorder, without maintenance treatment (there is no clinical summary; related symptomatology is denied) (See Figure 2).

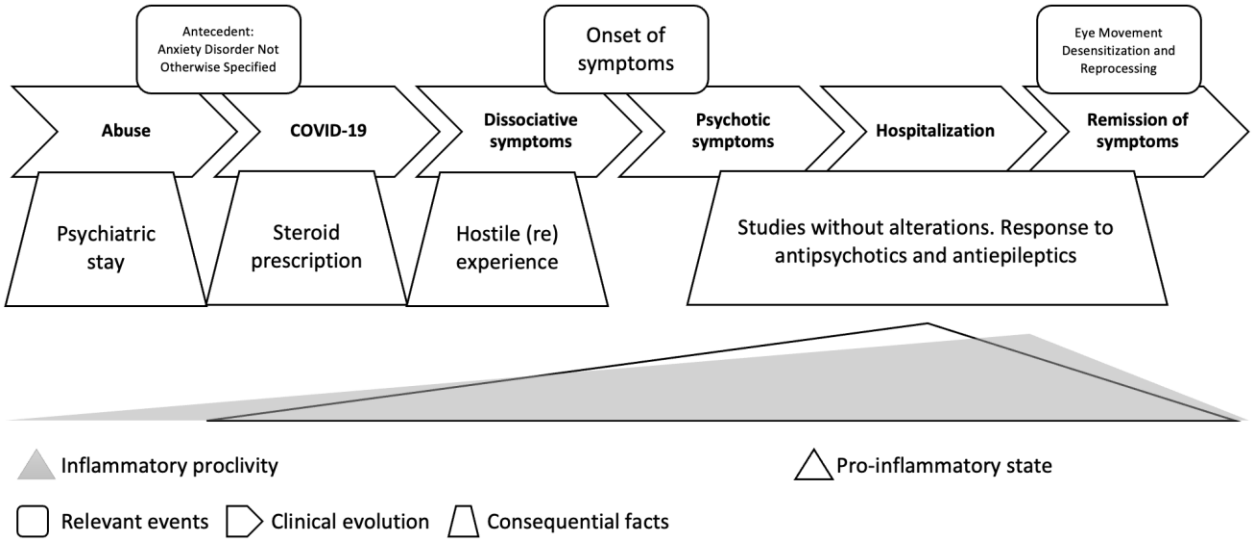

Figure 2. Symptomatic Chronology and Probable Course of the Inflammatory State for the Clinical Case. The sequence of events, evaluations, stays, hospitalizations, and studies performed on the patient are shown; which are part of the background, the onset of symptoms and treatments for the diagnosed diseases; as well as the probable inflammatory state over time.

After the pharmacological response, adding Pregabalin and Semisodium valproate (both during the hospital stay), she presented significant improvement, with which the patient identified re-experiencing the abuse while being with her current partner. Upon her discharge, she completed the transition to Aripiprazole and Lamotrigine, starting outpatient management with Eye Movement Desensitization and Reprocessing (EMDR) therapy, continuing her Cognitive Behavioral Therapy (CBT). She did not tolerate the use of antipsychotics (she presented akathisia, even with paliperidone), so it was finally discontinued, maintaining the use of Lamotrigine for about six more months, subsequently discontinued from 50 mg every 12 hours, ending her management with Eye Movement Desensitization and Reprocessing and continuing neuropsychiatric follow-up, remaining asymptomatic and fully recovering her academic and social functioning. A diagnosis of complex trauma is suspected -with the acute psychotic episode-, possibly triggered by COVID-19.

Discussion

This report presents a case recounting the history of an ongoing episode of abuse in early life. After experiencing a stressor, anxious symptoms were triggered, progressing to re-experiencing and delusional ideas, dissociative reaction and cognitive alteration, a clinical picture that suggests a direct relationship with the trauma [30] . Among the prominent symptoms in this case, we find paranoid delusion (closely related to abuse), misidentification phenomenon and disorganized behavior, which can be consistent with a subtype of Post-Traumatic Stress Disorder; it is unfortunate no to have a clear history of symptoms in the recent period after the abuse that help to determine the presence of traditional Post-Traumatic Stress Disorder symptoms [31]. Complex trauma is integrated as a suspicion into the hospital evolution record, since it has been described that certain social interactions can trigger traumatic reactions, and the experience with the current partner during the crisis has likely been interpreted as a new condition of abuse [30]. COVID-19 infection should be considered, being known that approximately a third of these patients develop neuropsychiatric symptoms, including mood disturbances, anxiety and psychosis. In addition, in adult patients with incident psychosis and antecedent or concurrent COVID-19, it has been reported that delusions were the most common psychiatric sign (92% of cases, 44 cases in total) [26], which coincides with one of the symptoms highlighted in the case we describe. Also, an increase in trauma-related disorders has been noted in patients with COVID-19, developing distressing memories that contribute to the establishment of Post-Traumatic Stress Disorder [11]. Additionally, there is a history of management with dexamethasone, adding another risk factor for the development of psychosis, given the evidence that steroids may be a causal agent, although its pathophysiology is not yet fully established [33].

Risk factors have been reported in patients who have been victims of abuse to progress to psychosis, such as alterations in the Hypothalamus-Pituitary-Adrenal axis. In this case, the history of physical, emotional and sexual abuse during adolescence, with the possibility of manic symptoms and subsequent amnesia of the event, is related to an increase in adrenergic responses [34]. We also consider the condition of the event memory encoding process: the sensory stimuli of a non-traumatic situation are initially encoded as perceptual memory through subcortical structures such as the amygdala; this memory is inaccessible to voluntary retrieval and is usually eliminated as soon as it is coded as episodic memory, which implies a representation in a temporal space of how and when the event occurred, in the medial temporal lobe, hippocampus and prefrontal areas; finally, they are integrated into semantic memory, which implies the abstract meaning of oneself, derived from specific knowledge and learned sociocultural values [34]. In a traumatic context, perceptual memory is increased, therefore, when episodic memory of the same event is recovered, sensory-perceptual stimuli will be experienced with greater intensity, without recovery of the memory at will [34].

Psychotherapy is indispensable; the Eye Movement Desensitization and Reprocessing option has been approved by the American Psychological Association, although it is controversial. However, there is recent evidence that shows good results in Post-Traumatic Stress Disorder, and it is necessary to continue the debate on whether it is a better intervention than Cognitive Behavioral Therapy [35,36]. Likewise, the use of antipsychotics (first or second generation) is approved for the treatment of psychosis associated with trauma and may have an antioxidant role [31].

Despite the different etiologies of neuropsychiatric disorders, the factors involved in their pathogenesis likely coincide with alterations of neurobiological pathways [37]. The neurobiology of Post-Traumatic Stress Disorder is associated with a deficit in the completion/generalization of fear, as well as a negative threat bias towards neutral or dangerous stimuli; although the mechanisms are not fully defined, it correlates with glutamate

dysregulation, stress-associated synaptic loss in the prefrontal cortex and hippocampus and synaptic gain in the nucleus accumbens and amygdala [37,38]. Sustained response to stress, female sex or predisposing neuronal disorders represent a risk that leads to greater biological alteration, since stressors generate a neuronal response that interrupts glucocorticoid signaling, neuroinflammation, reduction of brain-derived neurotrophic factor (BDNF -which may have a reactive increase-), astrocytes deficit and reduced uptake of glutamate released at the synapse, with extracellular increase and cytotoxicity. This results in a pro-inflammatory state that gives rise to neuronal atrophy in the prefrontal cortex, hippocampus and medial amygdala (in which hypertrophy also has been reported), causing alterations in synapses, behavior, mood and anxiety [38]. This process causes monoaminergic alterations, mainly in norepinephrine, a neurotransmitter that has important activity in the locus coeruleus, amygdala, hippocampus and prefrontal cortex [39], contributing to the presence of psychotic symptoms, due to susceptibility to oxidative stress, deregulation in connectivity and neurotransmission, with changes in the orbitofrontal cortex and hippocampus, as well as dysfunction in the connectivity between the ventral striatum and cortical regions [40,41].

Psychiatric presentations related to SARS-CoV-2 in acute stages are due to the direct inflammatory impact of the virus on the Central Nervous System immune response, causing cognitive, affective, behavioral and perceptual alterations, through an increase in cytokines that contribute to the development of neuronal stress, hippocampal atrophy and release of corticosteroids with hypothalamic stimulation that interferes with brain metabolism, increasing the risk of cognitive deficit, a process similar to that described in Post-Traumatic Stress Disorder and primary psychosis [11–14] (Table 2).

The risk factors for the development of psychosis related to COVID-19 are relatively well established (male sex, medical comorbidity, substance use or mental disorders, prior treatments used or relevant psychosocial stress)[42,43]; however, no distinguishing symptoms of this seem evident, being difficult to exclude Delirium presence. Therefore, preventive actions for Post-Traumatic Stress Disorder and psychosis should be considered on a case-by-case approach, including available interventions. For example, the International Society for Traumatic Stress Studies proposes some psychosocial interventions in children and adolescents during the initial trimester after a traumatic event, showing a significant decrease in symptoms with psychotherapeutic follow-up, with no evidence of pharmacotherapy's utility in this age group[44]. Meanwhile in adults, evidence of benefits for the early use of Hydrocortisone is found, but not for other medications (Propanolol, Oxytocin, Gabapentin, Antidepressants, Antipsychotics, Antiepileptics), as reported by previous studies [44–46], which also emphasize the use of Cognitive Behavioral Therapy focused on trauma (CBT-FT), Cognitive Processing Therapy (CPT), Cognitive Therapy (CT), Eye Movement Desensitization and Reprocessing (EMDR) and Prolonged Exposure (PE)[45–47], as well as suggesting therapies mediated by the use of 3,4-methylenedioxy-methamphetamine (MDMA) as promising[46], considering all factors related to developing acute or post-traumatic stress[48]. Preventive care in psychosis is considerably complex, mainly focused on avoiding exposure to substance use, nutrition or infectious problems in childhood, as well as maternal-fetal health problems[49], but other biological and clinical factors surpass the scope of this paper[49,50].

Table 2. Similarities in symptoms, alterations and treatments of the conditions presented in the case.

	Stress	Affective alterations	Cognitive alterations	Perceptual alterations	Inflammation	Hypothalamus-Pituitary-Adrenal axis dysregulation	Adrenergic disruption	Anti psychotics	Anti depressants	Psychotherapy
Complex trauma	Yes	Yes	Yes	Possible	Yes	Yes	Very possible	Possible	Yes	Yes (CBT - EMDR)
Psychotic episode	Possible	Yes	Yes	Possible	Very possible	Very possible	Very possible	Yes	Possible	Yes (CBT)
COVID-19 disease	Yes	Possible	Possible	Possible	Yes	Very possible	Very possible	Possible	Possible	Possible

- CBT (Cognitive behavioral therapy).
- EMDR (Eye Movement Desensitization and Reprocessing).

Conclusions

Trauma is one of the biggest determinants of mental health, associated with several clinical spectrums in symptomatology and diagnosis. Its sequelae can remain latent for many years, due to factors ranging from the neurological to the psychological, so we can also find a wide variety of triggers.

The neurobiological effects of COVID-19 are closely linked to the inflammatory response, with very similar physiological cascades in trauma and psychosis, so it can be considered a trigger and a cause of mental problems, which can be added to the use of medications such as steroids. These factors generate a high rate of diagnostic and therapeutic confusion, not only for the psychiatrist but for any type of specialist.

The presentation of this case illustrates this complex dynamic, being the reason why the authors have decided to cover it from the clinical and pathophysiological points of view. It is necessary to open the phenomenological and physiological debate, to understand the sum of effects in a patient who presents with a clinical picture of severe mental illness.

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Conflict of interests

The authors declare no conflict of interest.

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Data Confidentiality and Ethical Responsibilities

The authors declare the data collected for this report were authorized from the patient by the signature of an informed consent form, in accordance with all the regulations of confidentiality. Likewise, the protocol for this study was reviewed and approved by the Research Ethics Committee and the Research Committee of the Hospital Español de México on April 8, 2022.

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