

Change of Neuropsychiatric Symptomatology After Novel HCV Eradication Treatment

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Introduction

A large number of neurological complications occur in patients with chronic Hepatitis C Virus (HCV) infection independently of liver disease, including metabolic, inflammatory and autoimmune conditions affecting the Central Nervous System, as well as the Peripheral Nervous System and muscles [1,2,3]. HCV has been confirmed as both a hepatotropic and lymphotropic virus. Consequently, the liver is not the only target of HCV infection, so that several other organs and tissues are also likely to be involved [4,5]. The term "HCV syndrome" was coined to include both hepatic and extra-hepatic manifestations of HCV infection [6,7].

Therefore, the detection of defective central serotonergic and dopaminergic neurotransmission in some HCV patients with neuropsychiatric symptoms and mild or no liver disease has suggested a possible role for HCV in inducing dysfunction in selective aminergic systems [3,5,8].

Over the last few years, a number of factors, including associated comorbidities, alcohol misuse, substance abuse, interferon treatment, and HCV itself, have been investigated to assess their role as deteriorating or causative contributors to HCV-associated neurocognitive disorder (HCV-AND) [3]. Available data suggest that HCV-AND is unrelated to advanced liver disease, and therefore, the nature of this condition is distinct from the potentially reversible neuropsychological/neurophysiological complications observed in individuals with minimal hepatic encephalopathy, i.e., with biopsy-proven compensated cirrhosis or portalsystemic encephalopathy [3,4,5].

The aim of this study is to present a case report of a patient with Attention Deficit Hyperactivity Disorder, heroin and cocaine dependence that after the novel treatment for the eradication of HCV, present a change of neuropsychiatric symptomatology with the development of psychotic spectrum symptoms and suicidal plan.

Method

Case presentation

RZ, a 44-year-old Caucasian Lady woman affected by ADHD, heroin and cocaine dependence, is known to our clinic for few hospitalizations in a context of acute substance intoxication, and is now referred to our clinic due to the occurrence for the first time of a severe psychotics symptomatology and with suicidal planning. She had a negative Her family history was negative for any mental psychiatric disorder. She had a positive precedent history of suicide attempts made through intentional drugs

ingestion. There is past history Since adolescence the patient suffered from polysubstance use of substance use/abuse (heroin, cocaine, cannabinoids, alcohol) in a context of an ADHD syndrome associated with multiple suicide attempts through intentional drugs ingestion. The diagnosis of ADHD (according to DSM-5) was made for the first time in adulthood at our clinic after collecting significant anamnestic data such as among which: the presence of symptoms of inattentiveness, hyperactivity and impulsiveness, the paradoxical response to therapy with typical neuroleptics (agitation with haloperidol, zuclophentixole and, risperidone for example, agitation and insomnia with lorazepam), a school history of inattentiveness and hyperactivity with multiple school notesdisciplinary reports and expulsions, the 'calming' effect with the use of cocaine stimulants, underachieving in social activities, difficulty in relationships with partners interpersonal difficulties (Based on the types of the presented symptomatology met the criteria for an presented symptoms we purpose a diagnosis of ADHD with combined presentation). In the past sShe had never developed threshold or subthreshold psychotic spectrum symptoms in the past. She had no any particular somatic problem diseases, except for HCV infection known for at least 20 years (da quanto tempo?). She was treated, Bbefore HCV eradication treatment, Ms RZ was treated with Methadone 100 mg per day, Topiramate 100 mg per day, Methylphenidate 40 mg per day with a good outcome and with an improvement of ADHD specific symptomatology and a complete abeyanceremission of psychotropic substance use (cocaine, cannabinoids and alcohol). (with both improvement of ADHD specific symptomatology and substance abuse?).

In the last year she was treated with a novel HCV treatment with sofosbuvir, daclatasvir and ribavirin for 3 months with attaining a complete eradication of HCV infection. In the context of this treatment (at During the second month of HCV treatment) she started to present subthreshold psychotic symptoms like interpretativeness, diffidence mistrust (non so se esiste come termine inglese) and suspiciousness. After two months, subsequently to the end of the HCV eradication treatment, she developed an acute psychoticsic episodeis with paranoid delusions, imperative auditory hallucinations, psychomotor activation with agitation, perplexity, anxiety, as well as suicidal thoughts with planning. During this period of timeepisode the patient continued the psychopharmacological therapy mentioned above, with the same posology, and she reintroducewith a new relapse in the use of cocaine and cannabinoids without the knowed relaxant and calming effects

that she had experienced in the past. (usava anche sostanze?faceva la sua terapia? Ha fatto un neuroimaging? Secondo me va specificato). Because of Due to the aforementioned symptomatology she was, and for this reason she was hospitalized admitted to our clinic and, So we treated with First and Second Generation Neuroleptics Antipsychotics (Pipamperone 80 mg per day and Paliperidone 12 mg per day), Methadone 100 mg per day, Topiramate 100 mg per day and we associated with abruptly interruption of Methylphenidate with reaching only an only partial resolution of the described psychotic and suicidal symptomatology clinical picture. (which ones?). After three months of continued treatment we achieved she showed the complete psychotic and suicidal symptomatology remission of the psychotic and suicidal symptomatology. We never use Psychostimulant medications were never reintroduced in the future in the subsequent evaluations. To rule out any organic diseases, after during the admission hospitalization we performed a cerebral CT and a Cerebro Spinal Fluid analysis, which showed no pathological findings that didn't show particularity. After we have reached reaching the remission of the symptomatology remission, we also performed a cerebral MRI, which did not show particular structural morphological alterations.

We conducted a systematic literature review search with through the principal scientific databases (PubMed, Embase, PsychInfo) using the key terms “HCV”, “eradication”, “psychiatric disorder”, “psychosis”, “psychomotor activation” as well as “agitation”.

The patient followed by our psychiatric service, was assessed with the patient's symptomatology was assessed using the following instruments: the Structured Clinical Interview for the mental diagnosis (SCID-P) for the axis I diagnosis, the Young Mania Rating Scale (YMRS) to determine the mania score, the Hamilton Rating Scale for Depression (HRSD) to determine the depressive score, the Positive and Negative Syndrome Scale (PANNS) to determine the different psychotic symptoms, the Brief Psychiatric Rating Scale (BPRS) and the Symptoms Checklist-90 (SCL-90) to evaluate a broad range of psychological problems and symptoms of psychopathology, the Clinical Global Impression (CGI) scale to evaluate the symptoms severity, the Global Suicide Risk (GSR) to determine the risk factors for suicidality, , CAGE questionnaire, as well as a scale to determine different anamnestic clinical correlates. The assessment was made in during the euthymic phase before the beginning of the HCV eradication HCV treatment (T0), at the admission in our hospital treatment entry after HCV eradication treatment (T1) and at the discharge from the hospital our Clinic (T2).

Results

The assessments were scheduled at baseline (T0), We assess the patient in euthymic phase (T0), at the admission (T1) and at the discharge from the hospitalization (T2). After the HCV eradication treatment (T1) the patient showed we have a significant worsening of psychopathology severity compared to baseline evaluation (T0) the symptoms (BPRS total score at T1 vs BPRS total score at T0 $p > .001$; SCL-90 total score at T1 vs SCL-90 total score at T0 $p < .003$; PANNS total score at T1 vs PANNS total score at T0 $p < .001$; YMRS total score at T1 vs YMRS total score at T0 $p < .003$; HAMD total score at T1 vs HAMD total score at T0 $p < .001$; CGI total score at T0 vs CGI

total score at T1 $p < .001$). and at the discharge we have a significant persistent residual symptomatology (SCL-90 total score at T2 vs SCL 90 at T0 $p < .003$; PANNS total score at T2 vs PANNS total score at T0 $p < .005$; CGI total score at T2 vs CGI total score at T0 $p < .005$). We have a significantly higher score in different Regarding SCL-90, at T1 the patient showed significantly higher scores in the following dimensions compared to T0 dimensions at T1 vs T0 respectively in: anxiety ($p < .001$), interpersonal sensitivity ($p < .001$), hostility ($p < .001$), paranoid ideation ($p < .001$) and psychoticism ($p < .001$).

At T2 assessment the patient showed a significant persistent residual symptomatology (SCL-90 total score at T2 vs SCL 90 at T0 $p < .003$; PANNS total score at T2 vs PANNS total score at T0 $p < .005$; CGI total score at T2 vs CGI total score at T0 $p < .005$).

Discussion and conclusion

To our knowledge As far as we know, in the literature there are no studies that have addressed this theme and, like our case report, and that explain the change of neuropsychiatric symptomatology with the development of a psychotic spectrum disorder and suicidal plan after a HCV eradication treatment in a patient that before was previously diagnosed affected by an with ADHD and polysubstance use disorder (heroin, cocaine, alcohol and cannabinoid) dependence. Despite there are different several studies study that report exactly the opposite of our observation, so as an improvement of the neuropsychological symptomatology after the HCV eradication HCV treatment [9,10,11,12], while we observed a clear change of the symptomatology, the clinical presentation and patient's symptomatology, as well as phenomenology like with a change of the phenotype and clinical expression of the disease. It's acknowledged that HCV has been confirmed as both a hepatotropic and lymphotropic virus [13] Probably We can observe in some cases that the prevalent and the main HCV trophism is for the brain tissues, and it's that HCV has been confirmed as both a hepatotropic and lymphotropic virus [13] and the detection of defective central serotonergic and dopaminergic neurotransmission is correlated with HCV infection, as well as the possible role for HCV in inducing dysfunction in selective aminergic systems. In our case report we observe a complete change in the neuropsychiatric symptomatology, in the answer to the treatment as well as in the severity of suicidal symptomatology. These clinical observations should be taken into consideration in the assessment and follow-up phases, as significant psychiatric and behavioral changes could arise after eradication [14], suggesting the importance of a correct psychiatric evaluation after HCV eradication treatment. Unlike the majority of literature studies that reported an improvement of neuropsychological symptoms after HCV treatment [9,10,11,12], What we observed is a complete different clinical presentation of a symptomatology, with a changing of the psychiatric phenotype from an ADHD spectrum to a psychotic spectrum symptomatology.

Further research is warranted to replicate our clinical and qualitative observations and, in general, quantitative studies in large samples followed up over time are needed.

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