Cotard's syndrome and major depression with psychotic symptoms

Rev Bras Psiquiatr. 2013;35:212
doi:10.1590/1516-4446-2012-1044

Dear Editor,

Cotard's syndrome is a rare clinical event, characterized by negation delusion (individuals feel major changes in their bodies and deny the existence of one or several parts of their organs or bodies) and nihilistic delusion (individuals believe that they or all people are dead).[1] First described in 1880 by Jules Cotard as negation delirium,[2] the term Cotard's syndrome was proposed in 1893 by Emil Regis.[3] We describe the case of a patient admitted to the psychiatric ward of Hospital Ulysses Pernambucano, in Recife, northeastern Brazil and diagnosed with Cotard's syndrome.

M., 59 years old, male, was brought to the psychiatric emergency service of the hospital with complaints of insomnia, soliloquy, attempts to escape from home, suicide attempts by throwing himself in front of moving cars, and nonsense talk. He had dropped out of drug treatment two months earlier. The patient reported hearing voices making comments about him and giving him commands, as well as the existence of animals eating his body. He informed that he no longer had a body, but rather only a spirit, as he was already dead. He did not fear anything, as no one could kill him again (*sic*). Upon clinical examination, he was barefoot, wearing only shorts (no shirt), showed an unkempt beard and poor hygiene. He also showed alert consciousness, partial disorientation to time, a suspicious attitude, worn-out appearance, personal self-reference, deeply depressed mood, psychomotor retardation, insisting that he was not worth anything, that nobody wanted him there for 60 days already, and that he was paying for what he had done wrong. He also reported not having blood pressure, or blood, and that his body was broken, and that something very bad was about to happen. The patient was diagnosed with Cotard's syndrome secondary to major depression with psychotic symptoms. He was treated with imipramine 150 mg/day and risperidone 4 mg/day for 60 days, and was discharged asymptomatic afterwards.

Even though this disorder was first described by Cotard as a new type of depression, Regis later proposed that this syndrome could be associated with several medical conditions, e.g., psychotic depression, schizophrenia, neurosyphilis, and multiple sclerosis.[3,4] Comorbidity between Cotard's syndrome and Capgrass syndrome (individuals believe that family members have been replaced with doubles) is also common.[4] Currently, Cotard's syndrome is no longer classified as an independent disorder in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR) or in the International Classification of Diseases, Tenth Revision (ICD-10). Rather, in the DSM-IV-TR, nihilistic delusion is classified as a mood-congruent delusion within a depressive episode with psychotic features.[4]

It is important to emphasize that our case was absolutely compatible with the different descriptions available in the literature for Cotard's syndrome, with features such as a depressed mood, nihilistic delusion, and delusions of guilt and immortality.[5]

Treatment of Cotard's syndrome should focus on the underlying condition. Even though electroconvulsive therapy has been the treatment most frequently indicated in the literature, some reports of the combined use of psychotic and antidepressant drugs can also be found when psychotic depression is the underlying illness. Despite the absence of reports describing the combined use of imipramine and risperidone, the therapy was effective in remitting psychotic depression symptoms in our patient.

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Submitted 06 Dec 2012, accepted 08 Dec 2012.

Disclosure

The authors report no conflicts of interest.

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The utility of intravenous clomipramine in a case of Cotard's syndrome

Rev Bras Psiquiatr. 2013;35:212-213
doi:10.1590/1516-4446-2012-1040

Dear Editor,

We present a case of Cotard's syndrome in a 50-year-old female patient with no known prior history of medical or psychiatric illness. The patient went to the emergency department accompanied by a family member. She had been experiencing progressive depressive symptoms

for 2 months. The patient presented with sadness, anhedonia, fatigue, insomnia, apathy, feelings of self-depreciation, and emotional instability, which was not related to any life-events. In the previous week, she started to feel hopelessness and anger; she also believed that her body was putrid. The mental state examination revealed depressive mood associated with psychomotor retardation, ruminative thoughts of death, delusional ideas of ruin, nihilistic delusions concerning her own body, and absence of insight. Physical and neurological examination, basic blood investigations, cerebral computed tomography, illicit drug screening, and electroencephalography showed no relevant alterations. There was no personal history of substance misuse.

She was admitted to the psychiatric department. Initial treatment consisted of paroxetine 20 mg/day and olanzapine 15 mg/day. After 4 days, there was no therapeutic response and her depressive symptoms were aggravated, showing mutism and poor collaboration. Because the standard oral antidepressant failed and the patient refused to feed and take oral medication, glucose-saline solution and intravenous clomipramine were started. Clomipramine is one of the few antidepressants that are available for parenteral administration. Increments of 25 mg of clomipramine were added daily reaching the maximum dose of 100 mg/day after 4 days. At this time, the patient showed improvement in her clinical status and began to feed normally. We started oral clomipramine, which was raised to 150 mg/day with increments of 25 mg/day in two divided doses, and discontinued intravenous clomipramine (also 25 mg/day); the patient also restarted taking olanzapine 10 mg/day.

After 10 more days of hospital stay, there was a progressive and substantial improvement of the clinical status; the depressive symptoms, delusional ideas of ruin, and nihilistic delusions concerning her own body were in remission. The patient was discharged and referred to psychiatric outpatient treatment maintaining oral clomipramine 150 mg/day and olanzapine 10 mg/day.

In our clinical experience, we found that intravenous clomipramine can be useful to treat resistant-depression and obsessive compulsive disorder when standard oral antidepressant treatment fails.[1] The limited available literature also suggests that it can promote an apparent faster clinical improvement compared with oral antidepressants.[2-6] The low demethylation that results from the avoidance of the first-pass effect on hepatic metabolism led to a higher ratio of serotonergic clomipramine vs. noradrenergic metabolite desmethylclomipramine[5]; therefore higher drug plasma levels promote more bioavailability and enhanced selective 5-HT potency when intravenous clomipramine is used instead of oral formulation.[5] Other hypotheses, such as the placebo effect of the intravenous route or allowing the response to oral antidepressants, have also been proposed.[5]

Usually, the starting dose is 25 mg diluted in 500 mL of NaCl 0.9%, administrated by slow infusion over 90 minutes. This can be increased to 250-300 mg by increments of 25 mg/day during 10-14 days. Monitoring of pulse, blood pressure, and electrocardiogram are essential due to potential cardiac toxicity. Other side effects present in oral formulation, such as nausea, sweating, abdominal distress or restlessness, are likewise common.

In spite of the previous period of a combined treatment with paroxetine and olanzapine, the rapid and substantial improvement after starting treatment with intravenous clomipramine may indicate the existence of a specific effect of intravenous clomipramine on Cotard's syndrome. As observed in cases of resistant-depression, this may indicate that Cotard's syndrome can be successfully treated with intravenous clomipramine, especially in situations where there is significant feed refusal and negativism. Additionally, it may be a more rapid and effective alternative to the standard oral antidepressant and antipsychotic treatment.

Despite some concerns about its side effects and toxicity, considering intravenous clomipramine as a very effective and rapid acting agent in treatment-resistant or severe cases of depression with psychotic features, such as Cotard's syndrome, raises much interest in clinical practice and needs more investigation.

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Submitted 05 Nov 2012, accepted 02 Dec 2012.

Disclosure

The authors report no conflicts of interest.

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