

## The risk of early suicide and diagnostic issues in Cotard's syndrome associated to self-starvation

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**Summary. Background and objective.** Cotard's syndrome is a rare neuropsychiatric disorder in which the patient holds nihilistic delusions concerning his/her own existence, including the conviction of being dead or having lost parts of the body. There are occasional reports of Cotard's syndrome being accompanied by nutritional deficiencies or self-starvation. **Methods.** The authors describe the peculiar case of a 40-year-old man who developed severe malnutrition within a few months. At first, a diagnosis of anorexia nervosa was made. The man was admitted to the hospital where other significant psychopathological symptoms emerged. **Results.** One of the consequences of Cotard's syndrome is self-starvation because of negation of existence of self. The presented case points out that, although Cotard's syndrome has been reported to be associated with various organic conditions and other forms of psychopathology, loss of appetite and nutritional deficits can erroneously lead to mistake this diagnosis for anorexia nervosa, thus underestimating the high risk of these patients of committing suicide following hospital discharge. **Conclusion.** Taking into account its rarity and possible subdiagnosis, as a distinct clinical entity the aim of this case report is to emphasize that these patients may initially be addressed to general practitioners, due to the dysmetabolic consequences of malnutrition, rather than to psychiatrists. An early recognition of signs indicative of Cotard's syndrome can be vital to prevent the situation from worsening. In fact, missed diagnoses can put these patients at an higher risk of suicidal behaviour.

**Key words.** Cotard's syndrome, psychiatry, self-starvation, suicide.

*Il rischio di suicidio precoce e le problematiche diagnostiche inerenti la sindrome di Cotard associata al digiuno.*

**Riassunto. Scopo.** La sindrome di Cotard è un raro disturbo neuropsichiatrico caratterizzato da gravi deliri nihilistici, inclusa la convinzione di essere morto o di aver perso parti del corpo. Rari in letteratura sono i casi inerenti l'associazione tra sindrome di Cotard e digiuno autoindotto. **Metodi.** Si riporta il caso peculiare di un uomo di 40 anni che, nell'arco di pochi mesi, sviluppò uno stato di grave malnutrizione. In un primo momento fu posta diagnosi di anoressia nervosa e l'uomo fu ricoverato in ospedale, ove in breve tempo insorsero anche sintomi psicopatologici. **Risultati.** Una delle conseguenze della sindrome di Cotard è rappresentata dal digiuno autoindotto derivante dalla negazione della propria esistenza. Il caso in esame sottolinea come, sebbene sia riportata in letteratura un'associazione tra la sindrome di Cotard e varie condizioni organiche così come alcuni disturbi mentali, la perdita di appetito e i deficit nutrizionali possono indirizzare a una errata diagnosi di anoressia nervosa. **Conclusioni.** Considerate la rarità e la possibile sottodiagnosi della sindrome di Cotard, si sottolinea l'eventualità che i pazienti affetti possano essere inizialmente indirizzati a medici di famiglia per le conseguenze dismetaboliche della loro malnutrizione, piuttosto che direttamente a uno psichiatra. Un riconoscimento precoce dei segni indicativi della sindrome di Cotard risulta fondamentale per evitare che una mancata o ritardata diagnosi esponga questi pazienti a un rischio maggiore di atti anticonservativi soprattutto nel periodo post-dimissione ospedaliera.

**Parole chiave.** Digiuno, psichiatria, sindrome di Cotard, suicidio.

### Introduction

Cotard's syndrome is a rare neuropsychiatric condition, first mentioned in 1882 as "délire de negation" for patients who have a negating attitude of denying the existence of self or world. It is characterised by anxious melancholia, ideas of damnation or possession, a higher propensity to suicide ideation and deliberate self-harm, and nihilistic delusion of non-existence concerning one's own body or various aspect of self, like denial of being alive, of capacity to walk or to eat<sup>1</sup>.

Because it is often encompassed in different neurological and psychiatric disorders, complicating and worsening their symptomatic frameworks and making more difficult their treatments, the nosographic characterization of Cotard's syndrome remains elusive and its epidemiology is still uncertain<sup>2</sup>. The first evidence-based classification of the disorder resulted from a retrospective factor analysis of 100 cases in the literature conducted by Berrios and Luque<sup>3</sup>, who identified three categories: a form of psychotic depression; type-I Cotard's syndrome, with a prevalence of nihilistic delusion and few depressive episodes; and type-II Cotard's syn-

drome, which includes depression, anxiety and auditory hallucinations.

The most recurrent symptoms reported in subjects were: depression (89%), nihilistic delusion regarding the body (86%) and existence (65%), hypochondriac delusion (58%) and delusion of immortality (55%)<sup>4</sup>. Nihilistic delusion may include hypochondriac thoughts of non-existence or ruin of several organs, of the whole body, of the soul, and the idea of inability to die. There are occasional reports of Cotard's syndrome being accompanied by nutritional deficiencies secondary to voluntary severe starvation attributed to depressive illness or the psychopathology of denial of their existence.

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### Case presentation

A 40-year-old man, who had no previous history of psychiatric disturbance, was admitted to the hospital for a severe state of malnutrition. In the previous months, he had adopted a carbohydrate-free diet, facing sudden loss of appetite and subsequent weight loss. During his hospitalisation, he repeatedly refused to undergo psychiatric evaluation and was soon discharged. Seven months later, the man was admitted again to emergency department (ED) for hyporexia and rhabdomyolysis; his weight was 38 kg and his body mass index (BMI) was 15. Several blood bio-humoral abnormalities were found, including anaemia, hypoglycaemia, hyponatraemia with hyperkalaemia, hypomagnesaemia and alterations of the thyroid axis.

According to his family, he had always been in good health and had never suffered from any episodes of depression. Only recently he appeared more introverted, socially isolated and stopped eating appropriately.

This time, nutritional therapy was administered and the patient underwent psychiatric assessments, upon suspicion of an eating disorder. The man was poorly oriented and unable to carry a conversation, merely repeating "I'm dead" several times. On subsequent psychiatric evaluations, he appeared more collaborative, not showing illusions or hallucinations. He presented depressed mood, emotional closure and demotivation regarding his physical debilitation. A week later, stereotyped purposeless gestures and psychomotor agitation suddenly emerged, accompanied by command-type auditory hallucinations telling him he had to "save the world", and by an aggressive behaviour towards hospital staff. On the basis of history and examination, valproate (250 mg), a mood stabilizer medication, was administered resulting in minimal improvement. Computed tomography and magnetic resonance neuroimaging revealed the presence of diffuse left cerebellar and sub-tentorial cortical atrophy, while

electroencephalography (EEG) showed a theta-delta sequence.

As nihilistic delusions regarding his body surfaced (the patient claimed to be on the verge of death, following the expulsion of the bladder through the anus), an antipsychotic (aripiprazole 2.5 mg) was added to the therapy. Despite treatment, psychomotor agitation worsened and all the symptoms were attributed to delirium, induced by metabolic encephalopathy secondary to lack of nutrients and probably triggered by forced alimentation. Throughout hospitalization, the patient remained in the internal medicine department, as a relocation to the psychiatry department was not considered necessary. After seven days, valproate and aripiprazole were stopped and intramuscular promazine hydrochloride was administered. When the patient was found standing at the window, gazing into space, a psychiatric evaluation was performed, during which he consistently denied suicidal ideations or thoughts of self-harm but admitted the presence of bizarre themes of guilt towards his relatives.

On the basis of symptoms evolution, a diagnosis of Cotard's syndrome was suspected; the recourse of physical contention for the patient appeared necessary in order to prevent him from self-harming. After six weeks, his laboratory parameters stabilised and his weight increased. He was therefore transferred to a rehabilitation facility for patients with eating disorders; although he appeared tired and demoralised after his long hospitalisation, he showed no apparent intention or plan to harm himself. Nevertheless, after only two days, the man committed suicide by throwing himself from the building.

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### Discussion

Cotard's syndrome is not currently classified as a distinct clinical and nosological entity in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013) or the International Classification of Diseases (ICD-10, World Health Organization, 2015), and is considered to be an epi-phenomenon of other neurological and psychiatric disorders<sup>5</sup>. It has been suggested that pre-morbid personality features may play a role in the development of this syndrome, since patients with a greater internal attributional style (commonly co-occurring with depression) may be predisposed to develop Cotard delusion<sup>6</sup>. By contrast, patients with a greater external attributional style (e.g. paranoia) are more prone to develop Capgras' syndrome<sup>7</sup>. Although Cotard's syndrome is not listed as a specific disorder in the current classifications, early recognition of its clinical manifestations is essential, in order to safeguard the patient against the increased risk of suicide. In fact, Cotard syndrome vary from ideas of spontaneous destruction of or-

gans, body, and soul to the complete denial of one's existence. Subsequently, some patients may cease to eat and may have increased tendency toward self-mutilation or suicidal behavior.

In the case here described, the man, who had never previously suffered from any mental disorders, showed a strong refusal to eat, so much that he was hospitalised for nutritional therapy. The delirium of Cotard's syndrome emerged only after a prolonged hospitalisation, when the man presented markedly compromised bio-humoral tests and metabolic encephalopathy. A diagnosis of eating disorder (anorexia nervosa) was made and he was transferred to a rehabilitation centre.

However, on the basis of his history and mental examination, his symptoms should have suggested the occurrence of type-I Cotard's syndrome. His nihilistic delusions were manifested in hypochondriac thoughts of non-existence or ruin of several organs, of the whole body (he claimed to be dead and to have expelled his bladder through his anus); these delusions combined with sense of guilt towards his family and of grandeur (he claimed to have to save the world), are described in the literature<sup>1</sup>.

Moreover, the man showed aggressive and violent behaviour towards healthcare personnel, studies describe aggression in patients with Cotard's syndrome as an extremely rare phenomenon<sup>8</sup>. According to neuroanatomical investigations, CT and MRI images of the patient's brain revealed diffuse areas of atrophy, mainly sub-tentorial. Moreover, EEG showed a slowing of brain activity.

Neuroimaging researchers have found no gross structural changes in patients with Cotard delusion. A possible, albeit not exclusive, involvement of the right hemisphere and the frontal lobes has been suggested. In addition, a few investigations have associated Cotard syndrome with multifocal brain atrophy and enlargement of lateral and third ventricles, which may indicate a role for frontotemporoparietal areas in the pathophysiology of Cotard syndrome<sup>1</sup>. By contrast, EEG does not show particular alterations<sup>2</sup>.

In the presented case, the areas of multifocal atrophy detected may have been caused by the patient's state of severe malnutrition. Indeed, some studies have found that the refusal to eat is associated in a variable, though often significant, case of cerebral atrophy<sup>9</sup>, since lack of nutrition can cause neuronal death and alteration of the glial cells<sup>10</sup>.

Moreover, it could also be hypothesised that the brain lesions described may have played a role in the onset of the patient's delusions through a mechanism of anatomical dysregulation of the neural circuits<sup>11</sup>. In this regard, numerous basic neurological conditions that may be associated to Cotard's syndrome have been described: syphilitic infections, strokes, tumours, epilepsy of the temporal lobe, migraine, mental retardation<sup>10</sup>.

Concerning the diagnosis, there are no established criteria for the identification of Cotard's syndrome as a separate disorder in specific patients. Indeed, it has been hypothesised, for example, that the disorder should be regarded as an expansion of depression, a derangement of the bodily scheme, a somatoform disorder or a mixed subtype of paranoid delusion, hypochondriac delusion and delusion of grandeur<sup>2</sup>.

The diagnostic difficulties unfortunately impact on treatment choices. As Cotard's syndrome is, in most cases, associated to mood depression and psychomotor inhibition, its treatment requires the use of antidepressants and mood stabilisers; electroconvulsive therapy has also been found to be beneficial<sup>1</sup>. The literature review reveals in fact that there have been several successful pharmacologic treatments studied for Cotard's syndrome including aripiprazole, amitriptyline, duloxetine, olanzapine, sulphiride, lithium, and combination strategies with selective serotonin reuptake inhibitors, tricyclic antidepressants, and antipsychotics<sup>12</sup>.

In the case presented, only a low-dose neuroleptic and mood stabilizer medication were prescribed, and only for seven days. This reveals that an omnicomprehensive evaluation of the patient's symptoms (depressive symptoms and delusion of being dead) was lacking. Moreover, absolutely no attention was paid to a major concomitant symptom, i.e. that of sitophobia (refusal to eat), which is the principal indicator of the presence of a deep delusional conflict linked to the perception of the absence of integrity of his body<sup>13</sup>. Instead, the diagnosis appeared incomplete and focused only on the eating disorder.

The sudden onset of refusal to eat, in the case of an adult male, when associated to delusion of grandeur, should immediately arouse suspicion of the presence of a bipolar syndrome, and specifically of a mixed state. But sitophobia appears to be somewhat common in Cotard's syndrome, and is often associated to the delusional conviction of being dead, thus impacting negatively on the subject's general state of health.

In this case, the difficulty of a correct psychopathological classification derives from a rather fragmented clinical path, in which it was not possible to clarify whether the state of malnutrition was secondary to an eating disorder or linked to an organic alteration (anemia, deficiency deficits, thyroid alterations). In addition, the depressive aspect and self-injurious potential was not investigated.

The elements suggesting a Cotard's syndrome were represented by nihilistic delusion regarding his body and the refusal to eat, with alterations in blood chemistry and the thyroid axis that incremented the complexity of the diagnosis. According to the literature, electrolytic and/or hormonal misbalances are

non-specific indicators for the diagnosis of Cotard's syndrome; low hemoglobin, hypoproteinemia and hypoalbuminemia, indeed, can be commonly found not only in other psychiatric disorders (such as AN, major depression) but also in several organic diseases (ascites, renal failure).

Moreover, compared to the instrumental findings, while the literature indicates the presence of structural changes in the right hemisphere, in this case the abnormalities appeared to be in the left hemisphere, as a variance with respect to the most common descriptions. The prescribed therapies were also clearly inadequate, since they were completely insufficient in terms of dosage and duration of treatment.

In the case described, the patient's clinical course ended in very early suicide – less than one month after the appearance of the first delusion and during hospitalisation to treat an eating disorder, when psychiatric medications had been suspended. The man committed suicide when his clinical condition (hydro-electrolytic and metabolic balance) had stabilised and no psychotic phenomena were in progress, though his depressive symptoms (tiredness and demoralisation) persisted.

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### Limitations of the study

Cotard's syndrome is an uncommon psychiatric condition. As a result, current information is mainly based on reports; few studies have analyzed case series with few patients. To our knowledge, the study that retrospectively examined the largest number of cases was a study by Berrios and Luque<sup>3</sup>, who reviewed 100 cases of patients with this syndrome reported between 1880 and 1993. The restriction of publications to case reports is a potential pitfall making it challenging to identify general conclusions on course, pathophysiology, or treatment<sup>14</sup>.

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### Conclusions

Cotard's syndrome is a phenomenological diagnosis which may constitute the expression of various underlying disorders, both organic and psychiatric, for which there are several successful phar-

macologic treatments. Patients who display nihilistic delusion and depressive episodes with psychotic features have increased tendency toward self-mutilation or suicidal behaviour. It is therefore essential to reach an early and accurate diagnosis, in order to establish a proper treatment and to implement measures to prevent possible suicide. This case highlights characteristics of Cotard syndrome with the goal of providing insight into a seemingly rare syndrome, showing that a diagnosis of Cotard's syndrome has to be considered in patients who manifest nihilistic delusions concerned with the body concomitantly with sitophobia. The differential diagnosis between a delusional behaviour associated with Cotard's syndrome and the dysmorphophobic prevalent ideas linked to the body image typical of eating disorders is essential. Safety measures have also to be required due to the possible dramatic symptomatology.

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

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