Narcolepsy and psychosis; case report

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ABSTRACT

Narcolepsy is an infrequent neurological disorder, included in the catalog of rare diseases. Despite the existence of precise diagnostic criteria, this entity remains underdiagnosed. It is characterized by excessive daytime sleepiness associated with cataplexy; in some cases, hypnagogic or hypnopompic hallucinations, auditory hallucinations, and/or delusional ideation may appear. The occurrence of psychotic symptoms makes differential diagnosis extremely difficult (narcolepsy, schizophrenia, or both). Furthermore, therapeutic management may be complex, since the treatment of one of the disorders may worsen the other. Here we describe the case of a patient with this rare comorbidity, which illustrates the major difficulties associated to both differential diagnosis and therapeutic management once a definitive diagnosis has been reached.

Keywords: Narcolepsy, Psychosis, Hallucination, Differential diagnosis.

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RESUMEN

La narcolepsia es trastorno neurológico infrecuente, incluido dentro del catálogo de enfermedades raras. Pese a la existencia de criterios diagnósticos precisos, se encuentra infradiagnosticada. Se caracteriza por una excesiva somnolencia diurna asociada a cataplejías, y en algunos casos puede aparecer alucinaciones hipnagógicas e hipnopómpicas, alucinaciones auditivas y/o ideación delirante. La presencia de síntomas psicóticos dificulta enormemente el diagnóstico diferencial (narcolepsia, esquizofrenia o la concomitancia de ambas). Además, el manejo terapéutico puede resultar complejo, ya que el tratamiento de una patología puede empeorar la otra. El siguiente caso clínico corresponde a una paciente con esta infrecuente comorbilidad entre ambos trastornos, en el que quedan patentes las importantes dificultades tanto en el diagnóstico diferencial como en el manejo terapéutico, una vez alcanzado el diagnóstico de certeza.

Palabras clave: Narcolepsia, Psicosis, Alucinaciones, Diagnóstico diferencial.

DEAR EDITOR,

Type I narcolepsy is a sleep disorder of neurologic origin characterized by excessive daytime sleepiness and cataplexy. Patients may present hypnagogic or hypnopompic hallucinations, sleep paralysis, feeding disorders, subjective feeling of memory loss, tiredness, fatigue and mood disorders. Current diagnostic criteria, established in the International Classification of Sleep Disorders[1] include the occurrence of excessive daytime sleepiness – continuous or as an irrepressible need to sleep several times a day – for at least the last three months. This must be associated to a hypocretin deficiency in the cerebrospinal fluid (CSF) (equal to or lower than 110 pg/ml) or to the occurrence of cataplexy and mean sleep latency < 8 minutes plus at least two indications of REM sleep (< 15 min) in a polysomnography study and a multiple step latency test. The prevalence is low, 0.02% in adults. Besides personal history and physical examination, this diagnosis requires an immunological study (HLA DR B1*1501, DQB1*0602, DQA1*0102), an overnight polysomnography study, a multiple step latency test and, whenever possible, measurement of the hypocretin levels in the cerebrospinal fluid. The treatment includes sleep-hygiene measures and patient-tailored pharmacological treatment.

The occurrence of hallucinations in narcolepsy requires a differential diagnosis between hallucinations inherent to the neurologic disease, those derived from the pharmacological treatment, or from a potential comorbidity with schizophre-

nia; studies have been published on the latter[2,3]. Furthermore, the clinical management may be complex, since a treatment for one of the diseases might worsen the other. Here we describe the case of a patient with such comorbidity, where the difficulties associated to differential diagnosis and therapeutic management are evidenced.

CASE DESCRIPTION

Twenty-five years old female patient admitted to hospital due to behavioral disorders, disconnection from the world, irritability, suspicion and personal untidiness.

She had been diagnosed with narcolepsy at the age of 17. The family history included the same condition in maternal grandfather. Her relatives described bizarre behavior of the mother and possible unrelated psychotic symptoms.

Psychiatric background symptoms as described by the family included peculiar personality traits (dependence, ambivalent relationships, rigidity, and excessive concern about details). Furthermore, she had presented symptoms of anorexia and bulimia from 15 to 17 years of age. However, because of her reticence, the patient never got to be examined by the mental health services, but only by primary healthcare services.

The current psychiatric condition started at the age of 23 and was characterized by delusional jealousy, suspiciousness towards her partner and environment, identity delusions (she thought her boyfriend has been impersonated by someone else), and esoteric delusions ("they are doing witchcraft on me"). Moreover, she used to speak alone and probably suffered from auditory hallucinations. The psychotic symptoms were prolonged although their consequences were fluctuating. Her personal and social performance was markedly impaired up to the point of appearing completely untidy.

At initial examination the patient was elusive and uncooperative. As the therapeutic relationship improved, she displayed delusional activity and beliefs of witchcraft, on which she based her functional deterioration with a clear morbid rationality, Capgras-like identification delusions of interpretive mechanism with variable impact, comment and command auditory hallucinations, occasional hypnagogic hallucinations, affections consistent with delusions and periods of mild hypersomnia without cataplexia with impact on concentration. She did not present harmful or self-harmful behavior or significant alterations of appetite or behavior.

Examination results from the Neurology Outpatient Clinics confirmed the diagnosis of type 1 narcolepsy (narcolepsy with cataplexia) that had been reached as she was 17 years old, on the basis of a 6-months history of symptoms of hypersomnia, isolated cataplexia episodes, hypnagogic hallucinations and sleep paralysis. The patient underwent a polysomnography study, assessment of hypocretin levels and HLA study. The polysomnography study showed 4 SOREM (sleep-onset REM), which was consistent with type 1 narcolepsy (N1). Hypocretin levels in CRF were undetectable. The patient had the HLADQB1* 602 genotype, which is typical though not specific of N1. She was prescribed sodium oxybate as recommended elsewhere[4] but failed to adhere to treatment. She was then prescribed ISRS (fluoxetine 20mg) as a REM suppressive agent and showed a good cataplexia response. Neurologic follow-up was irregular, although symptoms were described to keep stable, with moderate somnolence (scored 11 on the Epworth scale) and occasional hallucinosis. She denied having experienced recent cataplexia. Neurologic examination upon admission failed to reveal findings other than those described.

The laboratory tests performed as a part of the admission protocol, brain CAT and EEG were completely normal. The patient was additionally administered the MMPI-2-RF, which yielded valid and interpretable results. She showed high scores in impaired thinking (paranoid delusions, hallucinations and delusional thinking) (THD), persecutory delusions (RC6), abnormal experiences (RC8) and revised psychoticism (PSYC-r).

Because of the presence of a neurological disease, the differential diagnosis included the possibility of psychological symptoms secondary to narcolepsy. Possible hallucinatory symptoms associated to narcolepsy could account for subsequent delusional interpretations. However, the nature of her auditory hallucinations (comment and command) suggested a psychiatric comorbidity. The possibility that psychotic symptoms were due to the anti-narcolepsy treatment was also evaluated. However, the fact that she completely failed to adhere to the treatment prescribed by the Neurology Service (except for fluoxetine) since the moment of diagnosis, as reported by the family and admitted by the patient herself, ruled out such possibility. Moreover, the characteristics of her psychotic symptoms together with severe functional deterioration pointed out to a procedural condition, consistent with paranoid schizophrenia.

The patient was started on antipsychotic treatment with 3 mg/day risperidone. Additionally, after in-hospital examination, the Neurology Service maintained the prescription of 20 mg/day fluoxetine. After a good initial response with attenuation of productive symptoms, risperidone had to be discontinued due to prolactin elevation and associated

bilateral galactorrhea, and was replaced by aripiprazole increasing doses up to 20 mg/day. A slow though adequate response was obtained, with attenuation of sensorial-perceptive symptoms and their impact, while the patient gained some distancing and critical ability towards her delusions. Finally, suitable interventions in her environment were carried out, providing information on her comorbid diagnostic and support for managing the situation, as well as close coordination with the Neurology Service.

DISCUSSION

The co-occurrence of narcolepsy and psychosis is a rare clinical entity, more frequently appearing in teenagers than in adults. For decades, such an association has been of interest to several authors, who highlighted the relationship between both entities, as well as the difficulties associated to their treatment and proposed hypothesis on this comorbidity[2,3,5,6,7]. The coexistence of both diseases has poor clinical and therapeutic prognosis[3]. The relationship between narcolepsy and psychosis can be established in three different ways: sensorial-perceptive symptoms like hypnagogic and hypnopompic hallucinations; psychotic symptoms as adverse effects of the narcolepsy treatment (modafinil, psychstimulatory drugs, sodium oxybate and other); or comorbidity of schizophrenia and narcolepsy. Using antipsychotic drugs that do not induce strong sedation has been recommended[2,3].

In the present case, once ruled out the iatrogenic etiology and despite the occurrence of sensorial-perceptive symptoms typical of narcolepsy, the occurrence of schizophrenia symptoms[8] (long-existing structured harm or identity delusions with impact, comment and command auditory hallucinations and overt biographical rupture) lead us to diagnose this comorbidity.

Regarding the etiopathogenesis, this comorbidity has been found to be associated to the presence of antigen HLA DQB1*06:02. Elevated antigens DRB3*03 and DPA1*02:01[7,9] have also been found. The presence of such antigens has been associated to higher severity of psychotic disorders, even without narcolepsy[10]. This comorbidity on the other hand, has been associated with the presence of anti-NMDA antibodies in absence of encephalitis symptoms[11], although other authors failed to find anti-NMDA antibodies in patients with type 1 narcolepsy with or without psychosis[12]. The role of orexin deficiency in eating disorders and schizophrenia is still under study[13,14,15]. Finally, a mutation of the myelin oligodendrocyte glycoprotein (MOG) gene was detected in a large family, who suffered from narcolepsy. Mutations in the myelin oligodendrocyte glycoprotein have also been associated with susceptibility to other complex neuropsychiatric disorders[16].

CONCLUSIONS

The presented case evidenced the difficulties associated to both diagnosis and therapeutic management of narcolepsy and psychosis comorbidity. Adequate coordination between specialists is essential to improve these patients' prognosis.

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