Mood disorder in a patient with Smith-Magenis syndrome: A case report

Giuseppe Bersani, Daniele Russo, Lucilla Limpido & Daniela Marconi

Department of Psychiatric Sciences and Psychological Medicine, "La Sapienza" University of Rome, Italy

Correspondence to: Prof. Giuseppe Bersani
III Clinica Psichiatrica, Università "La Sapienza"
Viale dell'Università 30, 00185 Rome, Italy
PHONE: +39-0649914591
FAX: +39-064454765
EMAIL: giuseppe.bersani@uniroma1.it

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Abstract

Smith-Magenis syndrome (SMS) is a microdeletion syndrome characterized by physical and neurobehavioural features. This report describes the case of a 27 year old female affected by SMS associated with a diagnosis, according to DSM-IV criteria, of Mood Disorder N.O.S. and Intermittent Explosive Disorder. To our knowledge, the association of SMS with mood shifts has never been reported. Considering the genetic alterations that characterizes the SMS, further investigations on the region of the chromosome 17p11.2 could help produce more information on the role of melatonin in the genesis of mood disorder.

CASE REPORT

Introduction

Smith-Magenis syndrome (SMS) is a genetic disease associated with an interstitial microdeletion aberration at chromosome 17p11.2, with an incidence approximately of 1 per 25 000 individuals.

The clinical phenotype includes minor craniofacial anomalies (brachycephaly, broad square-shaped face, flattened mid-face, unusually shaped ears, broad nasal bridge, prognathism, prominent forehead, palatoschisis), short stature, brachydactyly, infantile hypotonia, mental and language retardation. Other clinical signs include a hoarse and deep voice, congenital cardiopatic defects, renal anomalies, laryngeal anomalies, ophthalmic anomalies, scoliosis, peripheral neuropathy [11,16,21]. Serious sleep disturbances are constantly recurring too [8,12,22], as well as behavioural problems, such as self-injurious behaviours, hyperactivity, attention deficit and psychomotor agitation [10,15,20] (Table 1). These symptoms seem at least partially correlated with the inversion of the circadian rhythm of melatonin [7,8]. In fact, the cytogenetic examinations in the chromosome 17p11 revealed a deletion of a region of roughly 5 MB, that codifies for a protein involved in the check of N-acetyltransferase metabolism, an enzyme that regulates the production of melatonin [2,7,15,18].

A rich documentation in the literature shows the high frequency of modifications of melatonin secretion in mood disorders [6,14,17,23,24]. The case of the examined patient suggests a relationship between the neuroendocrine anomaly of the SMS and mood-related to behavioural symptoms.

Case report

A 27 year old female patient enters the psychiatric clinic accompanied by her mother and reports of a symptomatology characterized by mood symptoms, with frequent and sudden dysphoric shifts, lack of impulse control with physical and verbal hetero-direct aggressiveness and vaguely persecutory behaviours. The mood variations occur every day with short periods of expansiveness linked with hilarity, interwoven with moments of real depression, sadness and crying.

The explosive aggressiveness arises shortly and once regressed leaves in the patient a weak feeling of what happened.

The diagnosis, according to DSM-IV, is Mood Disorder N.O.S. and Intermittent Explosive Disorder.

The mother also refers the patients shows sleep difficulties in the evening, with frequent night awakenings, difficulty in falling asleep again and a tendency to short sleeps during the afternoon.

From the anamnesis, it is evident that since the first years of life the patient has shown a mild mental retardation, that seems to have generated difficulties in socializa-

Table 1. More frequent somatic features reported in Smith-Magenis syndrome

%	Somatic features
>75% of individuals	• Brachycephaly • Midface hypoplasia • Prognathism • Broad, square-shaped face • Braod nasal bridge • Deep-set, close-spaced eyes • Short broad hands • Dental anomalies • Middle ear and laryngeal anomalies • Hoarse and deep voice • Mental and language retardation • Speech delay • Laryngeal anomalies • Infantile hypotonia • Sleep disturbance • Inverted circadian rhythm of melatonin • Stereotypic behaviors • Self-injurious behaviors • Hyporeflexia • Hyperactivity • Attention deficit • Peripheral neuropathy • Oral sensorimotor dysfunction (early childhood) • Psychomotor agitation
50%-75% of individuals	• REM sleep abnormalities • Hearing loss • Ophthalmic anomalies • Ocular abnormalities • Peripheral neuropathy • Hoarse and deep voice • Scoliosis • Mild ventriculomegaly of brain • Congenital cardiopatic defects • Tracheobronchial problems • Velopharyngeal insufficiency • Short stature • Hypercholesterolemia/hypertriglyceridemia
25-50% of individuals	• Cadiac defects • Disorder of thyroid • Seizures • Immune function abnormalities
<25% of individuals	• Retinal detachment • Renal anomalies • Forearm abnormalities • Laryngeal anomalies

tion and learning (the patient achieved the middle school certificate with the support of an assistant teacher).

A clear motor uncoordination determines awkwardness in the posture during the motion, faulting of skill-dexterity and inability in the language.

Mild craniofacial anomalies are evident (large face, large root nose, round forehead) as well as brachydactyly, short stature, shrill voice and muscular hypotony (Table 2).

The instrumental investigations (brain CT, MRI, EEG) effected in childhood did not show noteworthy anomalies. Since she was six years old, the patient was cared by a child hospital division. The clinical referral reports behaviour, language and social interaction disturbances and dyspraxia. From the first contacts with the clinical institution, the patient was assigned to group psychotherapy sessions and family therapy. The therapeutic relationship lasted nine years. In 2003 the mental health department of the hospital performed a W.A.I.S. test, that reported an I.Q. of 67, which is a value corresponding to a mild intellective deficit. In other examinations (Spinnler and Stroop test) the patient showed problems in mental focusing.

Over the last three years, the patient has been on psychopharmacological treatment with Quetiapine, Oxcarbazepine and Clonazepam, which has resulted in partial benefit in her mood and aggressiveness.

The patient still shows frequent mood variations, but of minor intensity, as well as episodes of aggressiveness against her relatives and sleep disturbances.

During a recent visit at another general Hospital in Rome, aiming at a further neuropsychological evaluation, the diagnosis of Smith-Magenis Syndrome was confirmed, on the basis of cytogenetic investigation that highlighted the microdeletion in the chromosome 17. The same examination performed on the patient's parents did not find out any similar anomaly.

Table 2. Psychiatric symptoms and somatic features that characterize this clinical case

Psychiatric symptoms
• Depression
• Intermittent Explosive Disorder
• Hetero-direct aggressiveness (physical and verbal)
• Sleep disturbance
• Dysphoric shift
• Lack of impulse control
• Self-injurious behaviors
• Mood liability (Expansiveness, depression, sadness and crying)
• Mental retardation
• Attention deficit
Somatic features
• Motor Uncoordination
• Large face
• Large root nose
• Round forehead
• Brachydactyla
• Short stature
• Shrill voice
• Muscular hypotony
• Dyspraxia
• Language and social interation disturbances

Discussion

As previously described, the SMS is characterized by both somatic alterations and neuropsychiatry symptoms. Sleep and behaviour disturbances, hyperactivity, attention deficit and psychomotor agitation are reported in about 70% of the patients [11,16,21].

Cases reporting mood shifts and thinking disturbances (guilty feeling, lack of self esteem and persecutory behaviours) in subjects affected by the SMS were not described in medical literature.

The prevalence of mood disorders could currently be underestimated in subjects affected by the SMS, since a rich documentation in literature suggests an implication of melatonin secretion anomalies and mood disorders [1,9,13,19].

In fact, melatonin is a hormone secreted in nocturnal hours, whose production is correlated to the duration of the dark period, and behavioural and somatic phenomena, like sleep, somatic temperature, general activity and modifications of metabolic functions during all the day are influenced by the circadian secretion of melatonin. Moreover, melatonin contributes to regulating the secretion of many other hormones, as CRH, ACTH and cortisol, even implicated in the pathogenesis of depression [3,4,5].

In conclusion, this clinical case encourages new studies aimed at improving the knowledge of the relations between the SMS and mood disorders. Moreover, considering the genetic alteration that characterizes the SMS, further investigations on the region of the chromosome 17p11.2 could help produce better information on the role of melatonin in the genesis of mood disorders.

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