Psychological and cognitive evaluation of autism in a patient with MOMO syndrome: a case report and literature review

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Abstract

MOMO is an acronym for macrosomia, obesity, macrocephaly and ocular abnormalities. The syndrome was first described in 1993, with a total of nine patients published thus far. All the cases presented intellectual disability and in one case autism was described. We present a new case of a patient with MOMO syndrome, who consulted for hallucinatory phenomena. He completed a neuropsychological, clinical and cognitive evaluation, showing a borderline intelligence quotient and fulfilled the criteria for autism spectrum disorder. This is the first neurocognitive evaluation of a patient with MOMO syndrome, supporting the use of standardized scales in order to assess the autism and other psychiatric comorbidities in patients with genetics syndromes.

Main messages

- MOMO is an acronym for macrosomia, obesity, macrocephaly and ocular abnormalities, a syndrome with an uncertain genetical basis.
- The nine reported cases present intellectual disability but in one case autism is described.
- A neuropsychological, clinical and cognitive evaluation of a patient with MOMO syndrome, who consulted for hallucinatory phenomena is presented. The patient fulfilled the criteria for autism spectrum disorder and showed a borderline intelligence quotient.
- Patients with MOMO syndrome present a psychological involvement which should always be considered.
- This report supports the psychological evaluation of patients with genetic syndromes, in order to personalize the therapy and support the patients' family.

Introduction

Overweight and obesity during childhood are highly prevalent in modern society[1,2] and children with autism are not the exception[3,4]. Most of the times, obesity is the result between genetic predisposition as a minor factor and environment as a major component, nevertheless, some obesities are most genetically influenced by a single gen as monogenic obesities (syndromic obesities) or more frequently polygenic obesities[2]. Every day, more genetic syndromes are discovered with obesity as one of their characteristic features, and some of them also have autistic-like characteristics, such as Prader-Willi syndrome[5], Bardet-Biedl syndrome[6,7] and Cohen syndrome[8,9]. Recently, a new syndrome known as MOMO has been thought to be a condition with a genetic background. MOMO is an acronym for macrosomia, obesity, macrocephaly and ocular abnormalities (Online Mendelian Inheritance in Man-OMIM 157980). It was first described in 1993 by Moretti-Ferreira et al.[10], who reported two unrelated patients with overgrowth and an association of features different from the ones previously described in this type of syndromes, suggesting a genetic etiology due to an autosomal dominant spontaneous mutation. However, the study carried out by Vu et al.[11], suggested an autosomal recessive inheritance of the syndrome. MOMO syndrome has been categorized as an overgrowth syndrome[12].

To date, there exist only nine patients reported in seven case reports[10,11,13-17]. All the cases presented intellectual disability but in one case autism was described, a neurodevelopmental disorder characterized by persistent social and communication deficits and restricted and repetitive behaviors and interests[14]. In this report, we present a new case of a patient with MOMO syndrome with a neuropsychological evaluation, including the clinical, psychological and cognitive profile. We appraise the available evidence about this topic as well.

Clinical case

A 14-year-old patient, male and white, brought by his mother, consulted a child psychiatrist because he suffered from auditory hallucinations for the past two years.

Past medical history

The patient was the second son of a non-sanguineous couple (her 46 years, him 60 years). In the family, the sister was obese with normal intelligence and she had two sons (5 years and 1 month), both with overweight but with no developmental delay. The mother of the patient took no medications and was unaware of exposition to any teratogens during her pregnancy, which was classified as normal. Prenatal ultrasounds were normal. The patient was born at term, with forceps delivery. Birth weight was 3,420 g (50^{th} centile) and length was 49 cm (50^{th} centile). He was surgically operated by aortic coarctation at 18 days of life, and now he shows a normal cardiologic exam.

For his obesity, he was also seen since the age of 3-year-old by a nutritionist and then referred to endocrinologist at 4-year-old with normal laboratory tests (i.e. insulin, prolactin, cortisol, thyroid function, parathormone and electrolytes). He was seen by a child neurologist at 4-year-old by developmental delay, but later he assisted to a normal school with regular scores but difficulties in academic performance. Skull X-ray was normal, and bone age at 5-year-old (chronological) was of 3 years 6 months (< 2 SD). At the age of six, the patient consulted a psycho-pedagogical specialist, who informed an impaired emotional self-regulation, a poor impulse control, moderate difficulties in receptive and expressive language, a misuse of verbal tenses (i.e. past, present and future) and significative difficulties in visuomotor coordination (i.e. problems in oculo-manual movements and fine motor skill). The specialist also referred that the patient showed problems concerning interpretation of social situations, proverbs and fables, being able to respond correctly only to concrete situations. At this age, he consulted an ophthalmologist, being diagnosed with mild myopia.

At 12-year-old he was referred to a geneticist and Prader-Willi syndrome was suspected but later discarded with a normal methylation test. In order to look for major ocular abnormalities, the geneticist requested an optical coherence tomography, which showed a megalopapilla. It was interpreted by the ophthalmologist as a non-pathological finding. At the same age, he was derivated to child psychiatry and psychology with the diagnosis of anxiety disorder. The mother refuses drug therapy, so he was treated with psychotherapy only, discontinuing psychiatric therapy.

Current medical history

The patient consulted again a child psychiatrist at the age of 14. In this evaluation, the patient reported the presence of auditory hallucinations from two years ago, with aggressive content, associated with suicidal ideation. Patient lived hallucinations with high amounts of anxiety. A brain computerized axial tomography was performed, showing no pathological findings. It was decided to start pharmacological treatment with aripiprazole with progressively augmentation until 15 mg per day. He evolved with marked decrease in his hallucinatory phenomena and suicidal ideation during the month after starting pharmacological treatment. Nevertheless, he persisted with multiple concerns, very anxious and emotionally labile. It was decided to add fluoxetine 20 mg per day. At the moment of the consult, he had a weight of 76 kg (>>99^{th} centile, +2.81 SD), height was 152 cm (48^{th} centile), body mass index was 32.9 kg/m^2 (>>99^{th} centile) and occipitofrontal circumference was 56.7 cm (>>99^{th} centile). At the physical exam, he had macrocephaly, a round face, mild exophthalmos, normal ears, nose and mouth. He also had a central obesity with adipomastia. The hands and feet were long and slender and with joints laxity. Testis were Tanner G-3. He had a normal karyotype 46,XY and a normal Prader-Willi methylation test.

Measures

The Wechsler Intelligence Scale for Children-Third Edition (WISC-III)[18,19] was applied in order to measure the cognitive functioning. The patient had an intelligence quotient (IQ) score of 77 full scale, which places him in the range of "borderline intellectual functioning." It was observed a significant asymmetry with an overall difficulty in performance tasks (performance IQ = 65), while ver-

bal skills are in normal range (verbal IQ = 92). The MINI International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)[20,21] (which embodies the Diagnostic and Statistical Manual of Mental Disorders-IV-TR criteria for various psychiatric disorders in children and adolescents) was used to make specific psychiatric diagnoses. The patient scored high for multiple diagnosis, such as tics disorder, conduct disorder, post-traumatic stress disorder, social phobia, separation anxiety disorder and panic disorder. Finally, we applied the Autism Diagnostic Observation Schedule [22], a structured, play-like interaction with an examiner, designed to assess abnormalities in communication, reciprocal social interaction, creativity and imagination, and the presence of "restricted and repetitive behaviors." Individual target behaviors (e.g., eye contact, gestures, pointing) are coded according to operational definitions chosen to capture abnormalities typically seen in children with Autism spectrum disorder. It was administered and scored according to standardization by certified examiners[23]. In this, the patient showed much difficulty with the initiation of offering and asking for information and the integration of descriptive gestures into his verbalizations. In addition, when he spoke, he typically used mumbled and pressured speech that made him difficult to understand. With regard to reciprocal social interactions, rarely made full eye contact and did not regulate his social interactions with modulations in his facial expressions toward others. While his social response and his rapport with his psychologist were well developed, he showed little initiative to elicit social interactions. He was able to explain many of his own feelings, but he expressed limited understanding of the feelings of others and his role in social interactions with peers and family. Overall, symptoms and behaviors during this evaluation met the cut-off criteria for autism spectrum disorder.

Discussion

MOMO syndrome is an extremely rare syndrome with obesity, ocular abnormalities, macrocephaly and macrosomia, where the presence of intellectual/psychiatric comorbidities have been previously described. In this report, the patient has three of four cardinal features described by Morreti-Ferreira et al.[10], i.e. obesity, macrocephaly and ocular involvement, but he did not show macrosomia. Due to the frequency and the importance of the diagnosis and management of the intellectual/psychiatric features, we agree with the proposition previously noted by Di Donato et al.[17], who suggest replacing the "M" of "macrosomia," which is not always present in the previous reported patients, by "M" of "mental" (intellectual disability and/or psychiatric comorbidity). In fact, other published patients had normal or short stature and overgrowth was discussed as non-mandatory for the diagnosis[13]; instead, intellectual disability is a consistent finding in all reported patients[10,11,13-17].

In this patient, the psychiatric diagnosis was particularly difficult due to the wide range of symptoms presented. We believe that for future assessments in the context of a suspected MOMO syndrome, the first clinical hypothesis should be an autism spectrum disorder, which can encompass the difficulties identified by the patient and the family. The psychological involvement in MOMO syndrome was previously described in two patients, one of 13-year-old, with a developmental delay observed during childhood and intellectual disability, associated with "schizoid behavior" and irritability[10], and an older patient of 29-year-old with intellectual disability and autism[14]. Also, in the case reported by Wallerstein and Sugalski[15], the patient, as in the presented case, showed a developmental delay, a trait frequently observed in autism spectrum disorders[24]. The authors pointed out that the patient showed great anxiety because his extreme sensitivity to environmental noises, which, in addition to cognitive delays, may constitute part of the disorder[15].

The Autism Diagnostic Observation Schedule evaluation met the cut-off criteria for autism described for the first time by Giunco et al.[14]. The symptoms described in that report were lack of reciprocal social interaction, impairment in the use of eye-to-eye gaze, restricted interest and activities, aggressiveness, repetitive and stereotyped behavior, absence of verbal communication and inflexible adherence to routines. In this sense, the application of psychological batteries for evaluate autism as Autism Diagnostic Observation Schedule is recommended, because other test to study the Axis I disorders, such as the MINI-KIDS, might not be able to capture these changes when they are subtly.

There are some similar genetic obesity syndromes that may have similar clinical features, so they should be considered in the differential diagnosis such as Prader-Willi[5], which was discarded by a methylation test, as well as other genetic syndromes, e.g. MOMES syndrome[25] (mental retardation, obesity, mandibular prognathism, eye and skin abnormalities), because the patient did not have skin anomalies.

Conclusions

The clinical findings described in this report may indicate that we are in front of the tenth patient diagnosed with MOMO syndrome and the second one associated with autism. These results need to be seen in the context of his complex genetic and medical presentation with MOMO syndrome and accompanying difficulties, and, considering that the evidence of the condition is very scarce. Some new clinical features such as hallucinatory phenomena and aortic coarctation are uncharacteristic of the syndrome and should be considerate as part of the syndrome if they are seen it in future patients.

This is the first neurocognitive evaluation of a patient with a MOMO syndrome, supporting the use of standardized scales to the appraisal of autism and other psychiatric comorbidities in patients with genetics syndromes. The psychological involvement should be always evaluated in these patients and the use of psychological batteries could be useful to obtain a better management for the patients and their families, with the goal to improve and personalize their treatments.

Notes

Roles and contributions of authorship

CP, MG, ES, DT, MV: conceptualization, methodology, investigation, resources, writing (original draft preparation), writing (review and editing), visualization, supervision. MA: methodology, investigation, writing (original draft preparation), writing (review and editing), visualization, supervision, project administration.

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Competing interests

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Ethical aspects

The Journal is aware that the investigation has the patient's informed consent to be published.

From the editor

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