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RESEARCH ARTICLE

RING CHROMOSOME 20 SYNDROME WITH NON-CONVULSIVE EPILEPTIC STATUS PHENOTYPE.

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ABSTRACT

The ring chromosome was described by Atkins in 1972, this chromosomal arrangement has an estimated frequency of 1 in 25,000-60,000 births, generally it is de novo with 1% being heritable. The clinical picture of this genetic condition is characterized mainly by the presence of refractory epilepsy, intellectual disability, and behavioral disorders. The age of onset is between 2 to 4 years of age and is generally not associated with a phenotype or particular dimorphism at birth.The presence of a triad consisting of treatment-resistant frontal lobe epilepsy, recurrent non-convulsive status epilepticus, and classic EEG manifestations has been described. A clinical case of a patient with drug-resistant seizures with a diagnosis of ring chromosome 20 is presented, with a normal magnetic resonance and an electroencephalographic pattern characterized by long-duration shocks with slow waves, with frontal spikes, as well as recurrent electroclinical activity and frontal predominance, even with the use of high doses of anticonvulsants that began at 4 years of age with a diagnosis of regressive syndrome. Currently, the patient is 14 years old, with low weight and height for his age, grade III malnutrition, failure to thrive, moderate mental retardation and the presence of seizures 3 to 4 per month, despite the use of 3 anticonvulsants.

INTRODUCTION

The ring chromosome was described by Atkins in 1972 (1), this chromosomal arrangement has an estimated frequency of 1 in 25,000-60,000 births (2) (3).This rearrangement is generally de novo with 1% being heritable; (4)the clinical picture of this genetic condition is characterized mainly by the presence of refractory epilepsy, intellectual disability, and behavioral disorders. The age of onset is between 2 to 4 years of age and is generally not associated with a phenotype or particular dimorphism at birth. Seizures initially manifest as brief absence seizures and may later evolve into non-convulsive states epilepticus (NCSE) accompanied by confusion and even drowsiness, nocturnal frontal neurological activity has also been described (5)(6).The presence of mosaicism is generally found in 1-100% in lymphocytes, with respect to clinical manifestations they do not seem to be related to the severity of the phenotype (7).The presence of a triad consisting of treatment-resistant frontal lobe epilepsy, recurrent non-convulsive status epilepticus, and classic EEG manifestations has been described, which are reported as electrical activity in the frontal lobe, slow waves of prolonged duration. and elevated voltage with frontal unilateral or bilateral spikes, front temporal theta waves that are not influenced in the ocular opening, characteristically these can be less pointed than those compared to Lennox-Gestaut syndrome (8)(9)(10).

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Presentation of the case: It is a 4-year-old male, the son of apparently healthy non-consanguineous parents, the purpose is the product of the first pregnancy, regular prenatal control; a 4-year-old brother with a history of language disorder, attention deficit, and hyperactivity. She was born at 38 weeks' gestation by chance delivery, with an Apgar score of 8/9, birth weight of 3,100 grams(p.25), size 49 centimeters (p50); head circumference 35 centimeters (p.50). During the first 3 years of life, no alterations in psychomotor development were observed and developmental milestones were normal. His condition began at 4 years of age when the diagnosis of regressive syndrome was integrated; At this age, it begins with an absence seizure of 5 to 7 events per day of variable duration. Initial treatment was with carbamazepine, clonazepam, and valproic acid at high doses for age and weight, with partial control of events. In the comprehensive interdisciplinary approach, moderate intellectual disability is diagnosed, accompanied by unspecified anxiety disorder managed with risperidone and physical rehabilitation and special education. On physical examination, normocephalic skull, within normal percentiles for age, normolinear phenotype, normal cardiopulmonary, with integral and functional limbs. Magnetic resonance imaging with normal anatomical parameters, EEG shows a sharp and slow wave point irritative focus located in the frontal region with secondary generalization. In the follow-up by electroencephalography, interictal activity was reported in the left temporal region, generalized epileptiform activity in

the form of polypots, an event of generalized ictal electrical activity, and severe subcortical dysfunction. The GTG band karyotype at standard resolution 450-500 bands reported: mos45, XY, r (20) (p13q13.3) [14] / 46,46XY [33] which is interpreted as a karyotype of a male individual with three lines Cellular (mosaic): a cell line with monosomy of chromosome 20 in 3 cells, another cell line with a ring on chromosome 20 observed in 14 cells and another normal preponderant cell line with 33 metaphases studied.

Currently, the 14-year-old patient is ectomorphic, cardiopulmonary without compromise, weight 30.1 kilograms, percentile <1, score Z -5.05, height 148.5 in percentile <1, score Z -2.91, BMI 13.6 in percentile <1, score Z -4.64, hypoactive , hypersalivation, hypotrophic extremities, pubic tanner 2. He continues in management with the 3 anticonvulsants described above, with evolution of the clinical picture manifesting with 3-4 epileptic seizures per month accompanied by moderate mental retardation and significant failure to thrive.

DISCUSSION

We present a patient with drug-resistant seizures with a diagnosis of ring chromosome 20, with a normal magnetic resonance and an electroencephalographic pattern characterized by long-duration shocks with slow waves, with frontal spikes, as well as recurrent and predominantly frontal electroclinical activity, even with the use of high doses of anticonvulsants, as presented in the case; (8) Another important characteristic is the delay that occurs at 3 years of age and that is considered the average age range in this disease, with normal neurodevelopment up to this age. (11) (10) Ring chromosome 20 syndrome is one of the seizure syndromes associated with chromosomal disorders, which include: 1p36 deletion syndrome, Wolf-Hirschhorn syndrome, chromosome 14 syndrome and Angelman syndrome to name a few.(12). These syndromes can represent 2-3% of all epilepsy cases, the onset can be subtle as reported in some cases, presenting delay in speech development, but without alterations in developmental milestones within the first years of life as it appeared in our case, in turn presenting without dysmorphism and with a progressive encephalopathic pattern with evidence of bifrontal onset up to generalized epileptic activity and settling as intractable epilepsy. (9) On chromosome 20q13.3 they contain the CHRNA4 and KCNQ2 genes, the former encoding the alpha 4 subunit of neuronal acetylcholine receptors, while the latter encoding voltage-dependent potassium channels; In the latter case, some authors consider that it may be the cause of the clinical manifestations, even suggesting defining it as an epileptic channelopathy. (13) (14)Other epileptic syndromes related to these genes (KCNQ2 y CHRNA4), Benign familial neonatal seizures are found, which are characterized by a normal initial clinical examination and remission of seizures is found in the first month of life requiring anticonvulsant management. (15)

Conclusion

In our case, there were many of the electroclinical manifestations previously described in the international literature, which is why we consider the report of the present case important due to the low prevalence worldwide, so we must be suspicious of this pathology, especially in patients with absence crisis non-epileptic women with normal neurodevelopment at approximately 3 years of age, giving the patient a prognosis and the health professional a diagnostic probability.The authors declare that they have no conflicts of interest in this study.

Glossary of abbreviations

ABBREVIATION	MEANING
NCSE	Non-convulsive States Epilepticus
EEG	Electroencephalogram
BMI	Body Mass Index

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