Rett Syndrome in a Peruvian patient: A case report

Síndrome de Rett em um paciente peruano: Um relato de caso

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ABSTRACT
Rett syndrome is of genetic origin, caused by a mutation of dominant characteristic in the MeCP2 gene, which studies with psychomotor alterations in children. In this sense, this article aims to report the case of a Peruvian patient with the late diagnosis of the disease. The patient started the clinical characteristics of the disease at one year and two months, but the diagnosis, with a genetic study that identified the mutation, was only made at 3 years. During this period her diagnoses were: absence epilepsy and microcephaly. These misconceptions favored the accentuation of biopsychomotor delays. Currently, at the age of 4, the patient is being treated with a multidisciplinary approach, but as there are serious sequelae, there are delays in development and results take time to appear. Therefore, this work shows the difficulty of diagnosis, the need for a multidisciplinary approach in treatment and that there is a need for more studies to learn more about this syndrome and thus be able to provide a better safeguard of the lives of the patients.

Keywords: Child, Genetics, Rett Syndrome.
Given the epidemiology of the disease, there is a lack of data regarding the incidence of Rett syndrome. Data published in different studies point to a worldwide prevalence between 1:10,000 and 1:15,000 girls.\textsuperscript{4} However, the incidence in South American countries is still inaccurate, which points to a possible lack of investigation or underreporting.

The disease, which is subdivided into IV stages named by Hagberg & Witt-Engerström, has a predictable course, and its characteristic clinical pattern is accompanied by a period of regression, followed by recovery or even stabilization.\textsuperscript{5-7}

Stage I or early deceleration stage begins between six and 18 months and is characterized by deceleration of cranial perimeter growth. Stage II or rapidly destructive: begins between one and three years of age lasting weeks or months. There is a rapid psychomotor regression in terms of voluntary hand function, postural control, withdrawal reflexes and routine activities such as combing the hair or brushing the teeth.\textsuperscript{8-10} Furthermore, the presence of autistic behavior is seen.\textsuperscript{11} They also begin to develop respiratory irregularities that range from apnea and hyperventilation to obstructive apnea or waltz.\textsuperscript{12} Finally, the first epileptic seizures are common to the stage. Stage III, called pseudo-stationary, lasts between three and 10 years, and there may be an improvement in behavior, social and communicative skills.\textsuperscript{8} Stage IV or late stage of motor deterioration begins around 10 years of age and it is possible to observe severe physical disability, reduced mobility in the face of increased behavioral rigidity, choreoatetosis, decreased oral motor capacity leading to difficulties in swallowing. At this stage, it is common to have cases of malnutrition and gastrointestinal dysfunction.\textsuperscript{13-17}

The diagnosis of Rett syndrome is clinical based on the criteria proposed by the Rett Syndrome Diagnostic Criteria Work Group or those defined by DSM-IV-R.\textsuperscript{18-20} The disease is incurable; however, palliative treatments can promote improved functional, sensory and motor skills. Women's survival spans at least six decades, and deaths are commonly classified as sudden and unexpected.\textsuperscript{21,22}

Due to the scarce studies and uncertainty about the real incidence of the disease, we present this case report on a Peruvian patient in order to better understand the clinical and epidemiological aspects of Rett syndrome.

2 CASE REPORT

M.D.L, female, 4 years old, native and from Huancayo-Peru. Born after 39 weeks, emergency cesarean section by oligoamnion and fetal distress. Birth weight 2600g, height 40 cm, cephalic
perimeter 35cm and apgar 6/9. She presented cyanosis at birth, with crying present and no need for hospital admission. Up to 1 year and 1 month presented normal growth age and development, although the mother refers lentification in the development of the daughter from 3 months of age. The mother reports that the child started grabbing objects at 5 months of age, sustained the head at 6 months, crawled and babbled words at 8 months, but never showed control of the sphincters.

Later, at 1 year and 2 months it started with episodes of measured fever of 38 to 40 degrees, associated with watery and bulky diarrhea, adynamia and hyporexia, being in all 10 occurrences in 1 year and 8 months. Since the onset of this condition, the patient presented lower limb plegia, associated with aphasia and partial loss of upper limb functionality. In addition, the mother states that her daughter, on presenting this functional loss, presented periods of greater irritability, hyporexia, lethargy, not reacting to stimuli and with stereotyped movements (taking her hand in the mouth frequently, an uncommon habit before the onset of the condition). In addition to fever and diarrhea, there are reports of recurrent throat infections, with improvement in the use of antibiotics. As for accidents, the child suffered a fall at the age of 1 year on the stairs at home, but without head trauma. Blood transfusions and operations are denied.

In 2015, the mother sought out a pediatrician in her home town who requested Skull Magnetic Resonance, which showed a hydrocephaly and an electroencephalogram that concluded areas with brief slow-wave discharges, which led to the diagnosis of absence epilepsy. However, it presented normal laboratory tests. With this, he began drug treatment with 250mg Valproic Acid of 12/12 hours. Due to her daughter's situation, the mother decided to start physiotherapy treatment, without medical orientation, since her daughter used to be a normal child before the onset of the condition and had become 100% dependent on care.

During 6 months of treatment the child had progressed, but during a trip to Lima the girl presented an absence crisis (SIC) and returned to the initial stage of the picture. Thus, the mother chose to interrupt the use of Valproic Acid and take her to other doctors because she believed that the diagnosis was wrong, which made her look for traumatologists, pediatricians, nuclear doctors and neurologists, in addition to maintaining the physical therapies (psychomotor and language. Nevertheless, the child did not take any more medications and presented a worsening in the picture.

After 1 year and 6 months, in 2017, the mother decided to go to the children's hospital of reference in Lima, being assisted by a pediatric neurologist. She was asked to undergo a karyotyping examination, which showed a possible mosaicism of chromosome 21, a new electroencephalogram, which concluded a focal cortico-spinal and cortical paroxysmal dysfunction in the parieto-occipital region, potentially epileptogenic, and a new skull MNR, which showed no alterations, maintaining
the diagnosis of epilepsy of absence and the then use of the previous medication prescribed. This genotypic alteration did not justify the condition.

In view of this, the patient did not present any improvement and in returns to the same doctor in 2018, the patient remained with plegia and paresis of limbs, being reestablished the treatment with Valproic Acid in the same dosage, without new reported crises. In this sense, in order to elucidate the diagnosis, the physician then requested a new electromyography of the lower limbs, which showed no alteration, even if she presented hypotonia and hypotrophy of the limbs at physical examination. With this, the pediatric neurologist decided to refer to a geneticist and investigate chromosomopathies that did not appear in normal karyotyping.

In this new test requested in March 2019, the result was released in September of the same year with alteration in the MCP2 gene of the X chromosome, which closed the diagnosis of Rett syndrome, justifying the whole picture. It is worth mentioning that there was no family history for genetic mutations, the parents were not users of any kind of drugs and there is only a report of a second cousin of the girl who only wandered around at 5 years of age without any pathology attributed to him.

Currently, the patient is still undergoing treatment with valproic acid and performing the therapies: language, multi-sensory and psychomotricity. Moreover, she did not present any more episodes of fever and presents a slight improvement of the picture, however, the irritability and stereotyped movements remained.

On physical examination: bradirreagent pupils, hypotrophic, hypotonic musculature with strength absent in lower limbs, but plastic hypertonia. In the upper limbs the force was 4/5, despite hypotrophic and normotonic musculature. Reflexes: babinski present, cutaneous-abdominal at T10-T12 absent, patellar and hyperreflexed Achilles. BMI: 17.26 Kg/m².

3 DISCUSSION

The syndrome described by Andreas Rett is related to mutations in the MECP2 gene, where recent studies indicate that about 80% of patients with the classic SR form have mutations in this gene. The MeCP2 protein, produced by the gene, is considered to act as a global transcription repressor. Since this protein has some different action sites, it is believed that the different mutations found in the gene would be responsible for the different phenotypes observed in SR carriers.\textsuperscript{1,3}

Although previous studies have stated that girls are normal at birth and show normal development up to six or eighteen months of age, it is now known that in most if not all cases there is actually a delay in motor development with muscle hypotonia and crawling impairment, which
are the early signs of the disease. These alterations, reported by the patient’s mother when she was one year and one month old, such as: head support at 6 months, crawling at 8 months, babbling of words at 8 months, and grabbing objects at 5 months, in addition to the inability to control sphincter.

Classically, SR is divided into 4 main stages. The first stage, called early stagnation, begins between 6 and 18 months and is characterized by a halt in development, deceleration of growth, decreased social interaction with consequent isolation. During this period, the patient presented lower limb plegia, associated with aphasia and partial loss of upper limb functionality.

As regards the second stage - between one and three years old. It is marked by rapid psychomotor regression, with the presence of unmotivated cries and changes in mood and irritability that were perceived after the loss of functionality developed by her, and the appearance of stereotyped hand movements, presented by the patient holding her hand in her mouth, with subsequent loss of its practical function. Respiratory dysfunctions that caused several respiratory infections in the reported individual, obtaining an improvement in this condition by means of antibiotic therapy. Convulsive crises, presented by the patient as crises of absence (CIS) and which caused a regression in the evolution that had been obtained with physiotherapy treatment.

4 FINAL CONSIDERATIONS

This case report shows the difficulty of diagnosis and underreporting that this disease has presented, which corroborates the fact that prevalence and incidence rates do not express what actually happens in this disease. In addition, this work has made it possible to demonstrate the differential diagnoses that this disease may have and even a typical clinical picture.

Therefore, it is concluded that there is a need for more studies on this syndrome and the promotion of more research in order to treat patients with suspicion and/or with the right diagnosis earlier, with the purpose of reducing future sequelae and increasing the quality of life.
REFERENCES


