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Pallister-Killian Syndrome: The Importance of Clinical Findings

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Abstract

Pallister-Killian Syndrome is a rare genetic disease caused by mosaicism for tetrasomy of chromosome 12. It is characterized by dysmorphic phenotype and multiple organs malformation. This syndrome also includes developmental disabilities such as intellectual and motor disability, muscle hypotonia and it is often related with seizures. Here below we present the case of a patient diagnosed in early neonatal period, highlighting the importance of clinical findings which define this syndrome.

Keywords: Mosaicism • Chromosomes • Human • Tetrasomy • Phenotype • Developmental disabilities

Introduction

Pallister-Killian Syndrome is an uncommon genetic affection which incidence is approximately 1/25,000 patients [1]. It is caused by the presence of mosaic tetrasomy of short arm of chromosome 12 (12p) [2,3]. Its genetic inheritance remains unknown, being notified cases for the most part sporadic onset. This disease is a multisystem disorder characterized by a dysmorphic phenotype which includes rounded forehead, broad nasal bridge and short nose, hypertelorism, wide mouth with thin upper lip and long tongue, and low-set ears. It is distinguished by sparse hair (principally temporal alopecia), pigmentation and multiple organic disorders such as diaphragmatic herniation, heart, renal, genital or palate abnormalities. Some cases may also include skeletal deformities: supernumerary fingers or rhizomelic limbs. This syndrome also includes hypotonia in early childhood, developmental delay, intellectual disabilities, seizures, hearing impairment and sight issues [2,4-6].

Case Presentation

We report a case of a female 36 weeks gestation preterm who was diagnosed in early neonatal period. It was the second gestation of a non-consanguineous parents. This fact might be important because it reduced the possibility of recessive inheritance diseases. The pregnancy was controlled. It presented polyhydramnios which cause remained unknown after a complete test. Routine sonography showed a 15.9 mm left pyelocaliceal ectasia, a small renal pelvis dilation which remained alike until birth. There were no other abnormalities seen. It was a cesarean birth with 8/9 Apgar score. At the operating room she immediately initiated acute respiratory distress, so she was admitted to the Neonatal Unit. From the moment she was born, it stood out the presence of a dysmorphic phenotype with a wide forehead, frontotemporal alopecia, broad and depressed nasal bridge, ascending crosswise small palpebral edges, hypertelorism, downwards mouth corners and rhizomelic upper limbs (Figure 1).

Figure 1. Phenotype features seen in a Pallister-Killian syndrome patient.

On the first physical examination she presents generalize hypotonia, which will gradually disappear, persisting axial hypotonia. On account of this findings, we carried out a complete metabolic test which included amino acids and organic acids analysis and a karyotype. The results where normal and de chromosome formula was 46XX.

The first day of life she came through with an episode of abnormal movement lying in limbs hyperextension and oxygen desaturation which lasted few seconds, and no stimulus was needed to go down. In that moment, a digital scalp awake electroencephalogram was carried out which showed an immature pattern for the patient's gestational age. The study was completed with a cranial ultrasound and an evoked response audiometry which result was negative for both ears. Furthermore, we asked for an abdominal ultrasonography which verified fifteen millimeters left pyelocaliceal ectasia already seen during pregnancy. It also showed eight millimeters right pyelocaliceal ectasia. We began single dose amoxicillin 20 mg/kg/day as preventive treatment. A cardiac sonography did not reveal any structural disease, but it was remaining a little patent foramen oval. She kept in stable condition for the next days, but 96 hours later she began a series of paroxysmal episodes consisting of limbs hyperextension and internal hand rotation, sucking and hyper salivation, upward gaze and oxygen desaturation which will not go down spontaneously [7,8].

Due to suspicion of seizures and the impossibility to get a vascular access for intravenous treatment, intramuscular midazolam was used to end the episodes. In the absence of cerebral function monitor in our intensive care unit, we decided to transfer the patient to a tertiary hospital. She stayed there for 48 hours. Cerebral function was monitored showing a continuous background

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pattern with sleep-wake cycle. No seizures were recorded. Two days later, the patient came back to our Neonatal Unit with Levetiracetam treatment for seizures. She was discharge seven days after without showing any new event. Owing to the patient's peculiar phenotype, Genetic assessment was conduct. Geneticist runs an CGH-array test due to clinical suspicion of Pallister-Killian Syndrome. This test detected the presence of increase genetic dose (up to four times) in 12p13.33-p11.1 chromosomic region (about 33.8 Mb size). This variation was present in about the 60% of the total analyzed cells. After these results, the tetrasomy of 12p was confirmed.

At the age of 3 months old a complete auditory test which included a brainstem evoked response audiometry was performed. The results showed a severe neurosensorial hearing impairment involving both sides, but the right one was more damaged [9]. Since that moment she is carrying hearing aids in both ears.

Nowadays, our patient is being followed up by a multidisciplinary team in our hospital. Neurologically, she has psychomotor developmental delay with axial hypotonia and upper limbs hypertonia. We kept Levetiracetam seizures treatment until she was 11 months old. It was suspended due to the absence of seizures and normal electroencephalogram. There have not been cardiac structural abnormalities detected, except for mild mitral valve insufficiency. Bilateral hydro-nephrosis remain steady after several renal ultrasonography tests and she has not presented any urinary infection episode. The ophthalmologist has detected a visual acuity decrease with normal nerve impulse transmission. She bears glasses to improve her visual development. She also carries hearing aids which have helped her in her language and socialization development [3,10].

Conclusion

Pallister-Killian Syndrome is a non-common genetic disease for which clinical suspicion is the key for running the most suitable tests. This fact is due to the presence of a mosaicism for the tetrasomy of the short arm of chromosome 12 (12p). This means that the different body tissues present a combination of abnormal and normal cells in distinct percentages. It hinders the possibility of finding the chromosome disorder in a conventional karyotype, just as it was described in the case report. The difficulty in finding the disorders in routine test, hence the importance of clinical findings to run the most suitable test. So, in the presence of a dysmorphic phenotype which include rounded forehead, wide nasal bridge, hypertelorism, thin upper lip, low-set ears an alopecia, among others, hypotonia or early onset seizures, more specific tests such as CGH-arrays or, even a skin biopsy to analyze the fibroblasts which include the chromosomal abnormality, are needed. It should be pointed out that the number of cells in a specific tissue with tetrasomy 12p is not useful to predict the scale of mental disability, due to other tissues may not have the same percentage of cells affected, such it could be the brain. This syndrome includes such many different affections; therefore, our patient is getting a close and multidisciplinary follow up which includes psychomotor development and all the related pathologies.

Ethical Aspects

The pictures and information dissemination has been written authorized by the mother.

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