Pallister-Killian Syndrome (PKS): Clinical Case Report

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Pallister-Killian Syndrome is a rare dysmorphic condition characterized by specific clinical manifestations and tetrasomy 12p. This paper focuses on the general and orofacial clinical manifestations.
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INTRODUCTION

Pallister-Killian Syndrome is a cytogenetic condition which was first described in adults by Pallister et al, in 1977. In 1981, Teschler-Nicola and Killian independently described the syndrome, reporting the case of an affected child.[1-8] This is a rare syndrome with few reported cases in world literature.

Cytogenetically, the majority of cases results in autosomic tetrasomy 12p (four copies of the short arm of chromosome 12), revealed by a mosaic distribution of the supernumerary isochromosome.[1-6,8,9] Other authors mention uncommon cases presenting tetrasomy, trisomy, or disomy 12p.[7] The karyotype usually presents itself as 47, XX, +i(12p) or 47, XY, +i(12p).[1-6,8,9]

The diagnosis of Pallister-Killian Syndrome is based on phenotypical findings but can only be concluded through specific examination [*in situ* hybridization (ISH) or fluorescent *in situ* hybridization (FISH)] of fibroblasts in the skin, oral mucosa and bone medulla.[1,3-11] The syndrome's characteristic chromosomal anomalies are rarely detected in peripheral blood through conventional methods.[1,3-11]

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Prenatal diagnosis is less common but possible. When the ultrasound examination presents evidences that are coherent with Pallister-Killian Syndrome, confirmation may be obtained using blood from the umbilical cord, amniotic cells or chorionic villus.[2,6,7]

Phenotypical characteristics found in Pallister-Killian Syndrome are similar to those found in Fryns Syndrome. Thus, differential diagnosis through karyotype analysis is indispensable.[2,10]

Some authors mention that the mother's advanced age may be a predisposing etiological factor in the development of Pallister-Killian Syndrome.[2,3,7] On the other hand, one study pointed out that the affected chromosome was of paternal origin.[10] The majority of authors agree that more research is needed in order to clarify the origin of the syndrome.[2,3,5,6,10]

The main characteristics found in Pallister-Killian Syndrome are a coarse face;[1,2,4,7] prominent forehead; [1,2-4,8,10] bitemporal alopecia;[1-10] malformation and low implantation of the ears;[1,2,5-10] flat nasal bridge;[1-5,6,8,10] short nose;[1,3-7,9,10] long philtrum;[1,5,6,8-10] hypertelorism;[2-7] short neck;[1-5,7] streaks of hypo/hyperpigmented skin and hair,[1,3-10] severe mental retardation;[2-10] epilepsy;[2-7,9-11] short limbs;[2,5,7,9,10] congenital cardiac anomalies (systolic murmur, atrio-ventricular communication, coarctation of the aorta, Tetralogy of Fallot, patent ductus arteriosus, aortic stenosis, hypertrophic cardiomyopathy);[1,2,5,7,9] diaphragmatic hernia;[2,5,7,9] and visceral malformations (lungs, liver, kidneys, intestine).[1,2,4,7-9,11]

Other characteristics associated with Pallister-Killian Syndrome are: sparse eyebrows;[1,6,10] upslanting palpebral fissures;[1,6,8,9] ptosis;[1,9] ocular alterations (strabismus, retinopathy, exophthalmia);[1,6,10] anteverted nostrils;[1,2,5,6] hand finger alterations (brachydactily,[1,2,9] clynodactily,[1,2,8] syndactily;[7] polydactily,[1,2,8] hypoplastic nails[1]); foot finger alterations (broad hallux);[8] cranial alterations (brachicephaly,[8] hydrocephaly,[1] dilation of the lateral cerebral ventricles[2,6]); polythelia (supernu-

merary nipples);[5,8,9] hypotonia;[5,6,8,10] hypertonia,[9] genital malformations;[2,7,9] hyperhidrosis;[1] deafness;[1] sacral appendage;[11] and polyhydramnios.[2,6,7]

Oral alterations are rarely described. Studies indicate the presence of delayed dental eruption;[1] cupid-bow shaped mouth;[1] prominent upper lip;[1,6,9,10] prognathism;[1,9] micrognathism;[6] bifid uvula;[7,9] cleft lip and palate;[7] macroglossia;[6,9,10] macrostomia;[4,6,10] and supernumerary labial frenum.[8]

As the individual with Pallister-Killian Syndrome grows older, the phenotypical characteristics may become less evident.[4,9] There are also case reports of individuals with mild mental retardation.[4,9,10]

The aim of this paper is to report the clinical case of a patient with Pallister-Killian Syndrome and to point out general and craniofacial characteristics of this syndrome.

CASE REPORT

The patient, I.L.B.N., Caucasian, male, 4 years old, sought treatment at GEAPE (Special Patients Study and Treatment Group), Department of Orthodontics and Pediatric Dentistry, Faculty of Dentistry, University of São Paulo.

He is the first-born son of a young couple with no blood relationship. The child's Mother had had prenatal examinations since the first month of pregnancy. During pregnancy, she had recurrent urinary infections and on the fifth month, polyhydramnios was detected.

The child was born by cesarean section, normal term, 8.752 lb in weight, 16.93in height, and with an Apgar score of 7-9. Within 19 hours of life, he had hematemesis and melena, suggesting the possibility of an intestinal perforation. With 33 hours of life, he underwent explorative laparotomy, where the doctors observed laceration of the gastric mucosa and performed rafia suture. On the fifth day of life, an abdominal ultrasound revealed hydronephrosis on the left side. The patient also developed hypoglycemic crises and neonatal jaundice.

The boy presented hypotonia since birth. When he was six months old, he started having tonic-clonic convulsions and he has been taking anticonvulsive medication since then.

At seven months of age, the patient was referred for genetic evaluation. On that occasion, he presented the following anomalies: ponderal-statural deficit, a dolichocephalic cranium aspect, peculiar facies, prominent and large forehead, bitemporal narrowing, sparse hair and eyebrows, upslanting palpebral fissures, small eyes, vertical nystagmus, partially cloudy left cornea, divergent left strabismus, flat nasal bridge, small nose with anteverted nostrils, convex nasal philtrum, prominent cheeks, retrognatia, thick and high-arched palate without clefts, ears with posterior implantation, short neck, hypoplastic nipples, abdominal distension, diastasis of abdominal muscles, umbilical hernia, palpable left kidney in left flank, bilateral hydrocele, sacral appendage, rhizomelic upper limb shortening, bilateral brachydactyly, and moderate cervical and axial hypotonia.

Cranial ultrasonography revealed discrete prominence of lateral cranial ventricles; urinary tract ultrasonography revealed hydronephrosis suggestive of ureteropelvic junction (UPJ) stenosis. The echocardiogram was normal.

Since the clinical findings were compatible with Pallister-Killian Syndrome, chromosomal analysis of a peripheral blood sample and an oral mucosa sample were requested. A cytogenetic molecular study using fluorescent *in situ* hybridization (FISH) was also conducted. Isochromosome 12p was detected in the peripheral blood sample. Karyotype: 47, XY, +i(12p). In the oral mucosa sample, 64.5% of interphasic nuclei

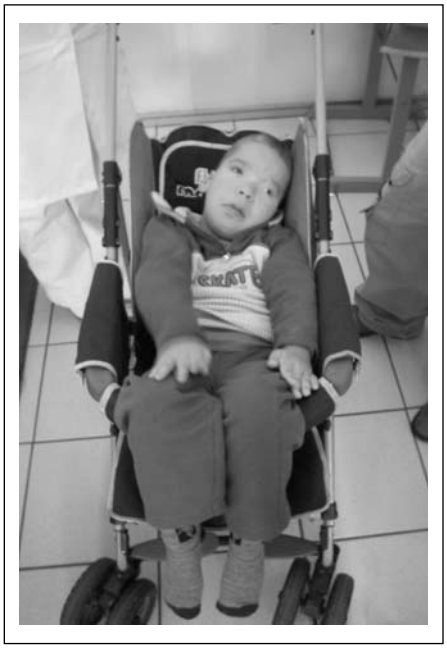

Figure 1. Postural characteristics

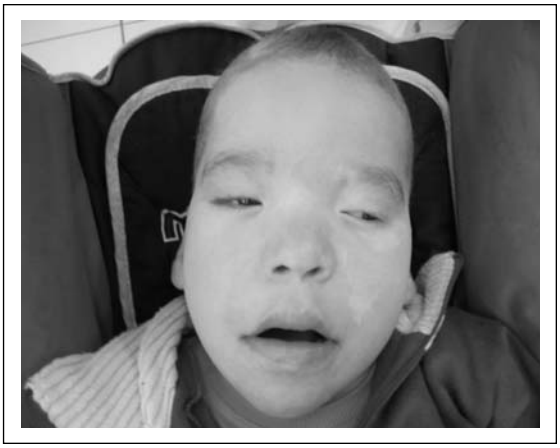

Figure 2. Fenotype of PKS.

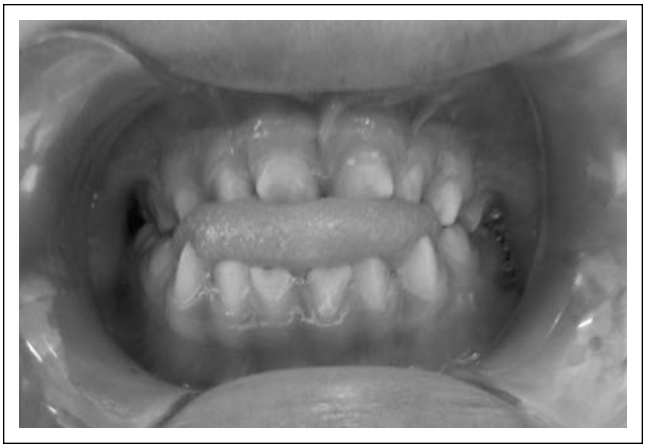

Figure 3. Intra-oral aspect

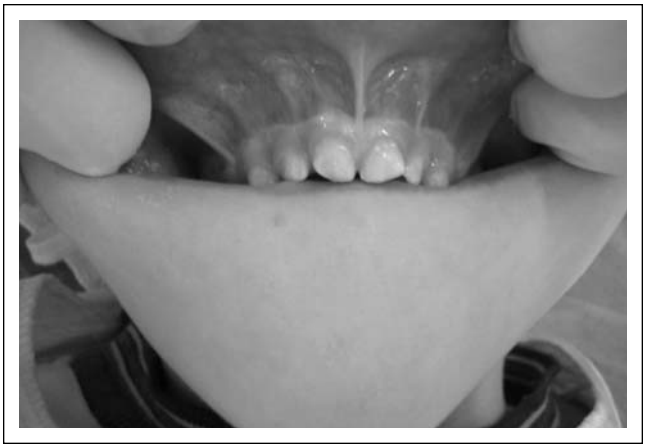

Figure 4. Presence of suprenumerary labial frenum

with 3 signals were detected. These examinations confirmed the diagnosis of Pallister-Killian Syndrome or tetrasomy of the short arm of chromosome 12p.

During the dental exam, when the patient was 4 years old, he presented severe neuropsychomotor development delay: he was unable to support his own head, unable to sit down without support, and he did not crawl or stand up (figure 1). Also, he did not present language development and had no sphincter control. He was fed semi-solid baby food in a bottle or with a spoon since he did not know how to chew properly. The boy goes to a special school, where he receives early developmental stimulation and speech therapy.

The general alterations observed were: tonic-clonic convulsions (controlled with Trileptal® and Depakene®), generalized hypotonia, motor arrhythmia, umbilical scar from the hernia surgery, scar in the left flank from the renal surgery, hypoplastic left nipple, shortening of the left leg, short neck and streaks of hypopigmentation on the arms, legs and back.

The craniofacial alterations observed were: prominent and large forehead, temporal narrowing, low implantation of the ears, bitemporal alopecia, sparse eyebrows, hypopigmented areas on the hair, eyebrows and eyelashes, ocular hypertelorism, visual deficit (5 and 6 degrees of myopia/nearsightedness), vertical nystagmus, upslanting palpebral fissures, short and bulbous nose, flat nasal bridge, anteverted nostrils, and long philtrum (figure 2).

Oral examination revealed: prominent upper lip (in the shape of a cupid bow), hypotonia of tongue and labial muscles, high-arched palate, supernumerary labial frenae, macrostomia, prognathism, anterior open bite, complete primary dentition, generalized enamel hypoplasia, cavities on the buccal surfaces of the maxillary central incisors due to loss of enamel structure, and thick and abundant bacterial plaque (figures 3 and 4).

The patient's dental treatment included: Glass ionomer restorations of the cavities on the buccal surfaces of the maxillary central incisor, sealing of the fissures and sulcus of the lower second molars, dental prophylaxis, and fluoride varnish application (figure 5-6). After evaluating the patient's dietary diary, counseling was done, emphasizing the need for adequate oral hygiene. The patient will be revaluated every four months in order to observe any oral alterations that may develop in the future.

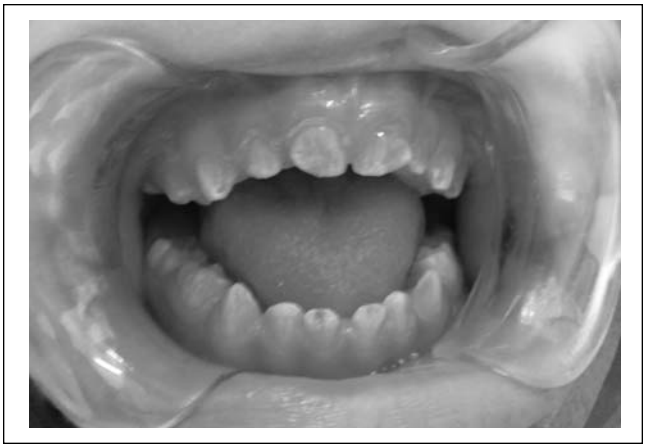

Figure 5. High plaque score index

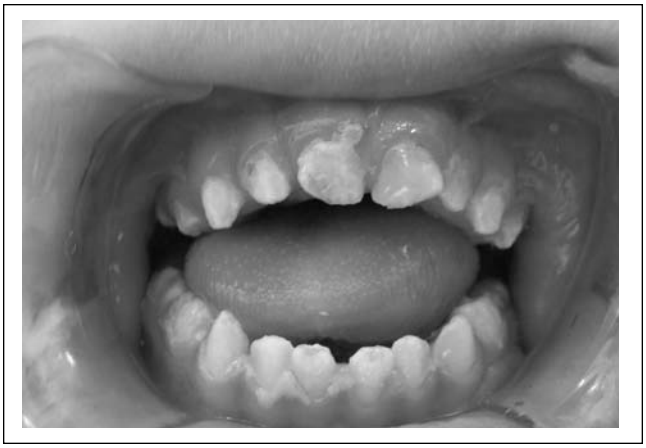

Figure 6. Fuoride varnish application

DISCUSSION

Although studies suggest that maternal age may predispose the child to the occurrence of Pallister-Killian Syndrome,[2,3,7] in this case, the patient's parents were both young. Cytogenetic examination of the patient revealed tetrasomy 12p, confirming the phenotypical findings.[1,3-11]

The main characteristics of Pallister-Killian Syndrome, described in the majority of studies, were observed in this case. These characteristics are: prominent and large forehead,[1-4,8,10] bitemporal alopecia,[1-7,9,10] low implantation of the ears,[1,2,5-10] flat nasal bridge,[1-6,8,10] short nose,[1-3,7] long philtrum,[1-6,8] short nose,[1-5,7] streaks of hyper/hypopigmented skin,[1,3-10] severe mental retardation[2,-10] epilepsy,[2-7,9-11] ocular hypertelorism,[2-7] short limbs,[2,5,7,9,10] and visceral malformation (umbilical hernia, renal stenosis).[1,2,4,7-9,11]

Other characteristics such as visual alterations,[1,6,10] upslanting palpebral fissures,[1,6,8,9] sparse eyebrows,[1,6,10] prominent upper lip,[1,6,9,10] hypotonia,[5,6,8,10] supernumerary labial frenum,[8] macrostomia,[4,6,10] and prognathism[1,9] were also found.

However, supernumerary nipples,[5,8,9] malformation of the hands[1,2,7-9] and feet,[8] congenital cardiac alterations,[1,2,5,7,9] and delayed dental eruption[1] were not observed in this case.

The patient's diet, as analyzed through a dietary diary, was very cariogenic consisting mainly of carbohydrates (bread, crackers, cookies, flour diluted in milk, rice, pasta, jam, and sweetened juices).

Due to the neuropsycomotor impairment of patients with PKS, oral health care measures, by both the dentist and the caregivers, must be justified.

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