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CLINICAL BRIEF

An Indian Boy with Additional Features in Pallister-Killian Syndrome

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Abstract Pallister-Killian syndrome (PKS; OMIM: # 601803) is a rare sporadic genetic disorder characterized by pigmentary skin changes, distinctive dysmorphology, developmental delay, and mosaicism for tetrasomy of chromosome 12p. The authors report a case of PKS in a 2-y-old boy. He had pigmentary skin changes, characteristic facial features, developmental delay and hearing loss. He had sacral and post-auricular pits in addition, which has not yet been reported. A diagnosis of PKS was suspected on the basis of the patient's clinical features. Skin fibroblast culture was done which showed mosaic tetrasomy of isochromosome 12p consistent with Pallister-Killian syndrome. This case highlights the importance of dysmorphology as a diagnostic tool for recognition and accurate genetic counseling in genetic syndromes.

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Introduction

Pallister-Killian syndrome (PKS) is a rare genetic syndrome characterized by mental retardation, seizures, streaks of hypo- or hyperpigmentation and dysmorphic features. Hallmark of this aneuploidy syndrome is tissue limited mosaicism for isochromosome 12p[i12p].Here the authors report a case of PKS with additional manifestations of sacral sinus and postauricular pits.

Case Report

A 2-y-old boy presented with developmental delay and dysmorphic features. He was the single child born to non-consanguineous parents with an uneventful antenatal and post-natal period. Cesarian - Section was done in view of non-progression of labour. Birth weight was 3.75 kg. There was a history of child being operated for left inguinal hernia.

Head circumference was 47.5 cm (25th–50th percentile); height: 86 cm (10th–50th percentile); weight: 13.2 kg (50th–90th percentile for age)(IAP recommendations). He had coarse facial appearance, sparse hair on temporal sides of scalp, frontal bossing, epicanthal folds, low set ears with folded helix, broad thick lips, high arched palate with presence of median furrow, ptosis and macrostomia (Fig. 1a and b). Skin examination showed linear hypo and hyperpigmented

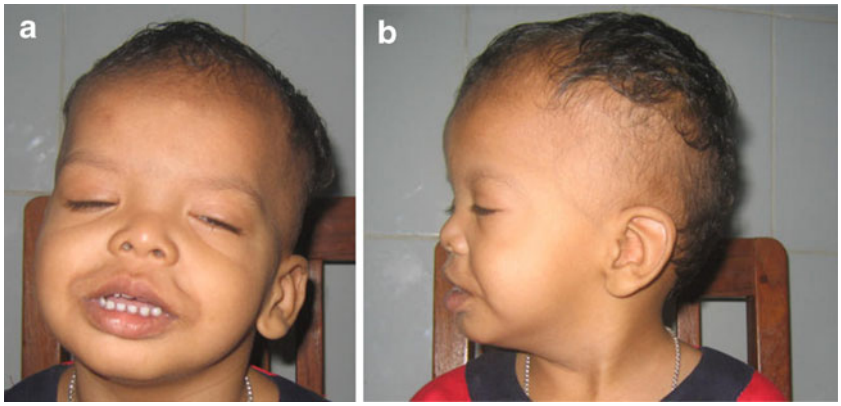

Fig. 1 **a** Photograph showing overall coarse face and distinct facial dysmorphism. **b** Lateral profile of face

patches on groin and legs along Blaschko's lines, thick skin over dorsae of hands, velvety hyperpigmentation on knuckles and minimally over the cubital fossae and axillae. He also had post-auricular and sacral pits. On the Griffith's Mental Developmental scales his developmental age was equivalent to 9.2 mo and on the Modified Checklist for autism in Toddlers (MCHAT) he scored five of the six 'critical items' and was at high risk for autism. He was also detected to have bilateral sensori-neural hearing loss and was provided with hearing aids in both ears.

MRI brain done at 1 y of age was normal. The clinical features pointed to a mosaic pigmentary disorder namely PKS. A chromosome analysis for blood and skin fibroblasts was therefore asked for.

Cytogenetic analysis was performed on Giemsa-Trypsin Leishman (GTL)-banded chromosomes from both peripheral blood and skin fibroblasts of the hyperpigmented and hypopigmented areas. The results of the cytogenetic analysis were confirmed by fluorescent *in situ* hybridization study (FISH). All these procedures were performed using standard protocols.

Results

Peripheral blood karyotype was 46, XY. Culture of hyperpigmented skin showed 47,XY,+i(12)(p10)[5]/46,XY[15] and hypopigmented skin showed 47,XY,+i(12)(p10)[8]/46,XY [12] (Fig. 2). Fluorescent *in situ* hybridization (FISH) analysis showed four copies of the locus on chromosome 12p (Abott-Vysis).

Discussion

The index patient presents with characteristic features of Pallister-Killian syndrome with sacral and post-auricular pits. It is a mosaic tetrasomy disorder where clinical

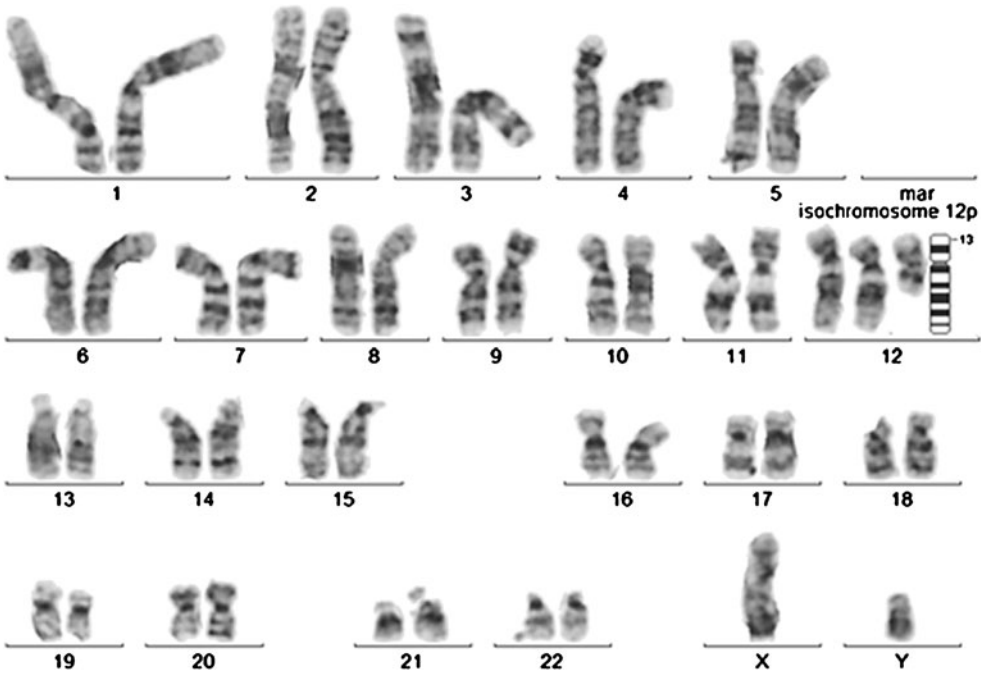

Fig. 2 Karyotype from skin fibroblasts of the patient showing tetrasomy 12p (with partial ideogram)

diagnosis plays an important role and the tissues other than blood, such as skin are required for chromosome analysis. Fibroblast culture and FISH using chromosome 12–specific DNA probes have been used successfully to detect i (12p) in the index case. Reynolds et al. reported 11 patients ranging from a 22-wk-gestation fetus to a 45-y-old man with tetrasomy 12p mosaicism [1]. Isochromosome 12p was detected in lymphocytes in only one of the cases. Recently microarray based comparative genomic hybridization (aCGH) in blood has been used to detect this syndrome [2]. Buccal smear preparations by interphase FISH have also been reported to be a competent and noninvasive method for detecting i(12p) and confirming the diagnosis of PKS [3].The proportion of tetrasomic cells in lymphocytes and fibroblasts does not correlate with the severity of the phenotype. Although in the present case there were no episodes of seizures and MRI brain showed no abnormality, severe neurological manifestations have been described with PKS [4]. The index patient has additional manifestations of sacral pit and postauricular pits expanding the phenotypic spectrum of the syndrome. Similar other case reports have been published where anorectal anomalies and diaphragmatic hernia are additional features [5].

The iso- chromosome 12p in the present case was seen in both hypo and hyperpigmented areas. Anomalous pigmentation should be carefully evaluated to exclude chromosomal mosaicism thus verifying the correlation between the skin fibroblast karyotype and the pigmentary abnormalities [6]. PKS is one of the four most common well-defined syndromes characterized by sSMC (supernumerary small marker chromosomes), others being Emanuel Syndrome (OMIM #609029), isochromosome 18p syndrome and cat eye syndrome(OMIM #115470) [7].

Conclusions

This case highlights the fact that conventional cytogenetic techniques may fail to diagnose mosaic aneuploidy syndromes such as PKS. Fibroblast culture forms an important alternative diagnostic method where aCGH is not readily available to detect the cytogenetic abnormality. Clinical recognition of the dysmorphic syndrome helped the authors to choose the right tissue for karyotyping. This helped in providing the parents, information about the long term outcome and requirement of follow up. Genetic counseling was provided to reassure the sporadic nature, low recurrence risk and availability of prenatal diagnosis to the family.

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Conflict of Interest None.

Role of Funding Source None

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