

## PALLISTER-KILLIAN SYNDROME: RARE PHENOTYPIC FEATURES AND VARIABLE KARYOTYPES

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The Pallister-Killian Syndrome (PKS; OMIM #601803), also known as Tetrasomy 12p or Mosaic Isochromosome 12p syndrome, is a rare genetic disorder in humans. Its exact incidence is not known. The PKS is due to a partial tetrasomy of the whole, or parts of, the short arm of chromosome 12. It was first described by Philip Pallister in 1977 and further studied by Maria Teschler-Nicola and W. Killian in 1981. Prenatally, PKS can be suggested due to relatively unspecific abnormal sonographic findings such as enhanced nuchal translucency or abnormal hands or feet, as well as omphalocele. In a newborn or small child, PKS can be diagnosed with facial anomalies, streaks of hypo- or hyper-pigmentation, seizures and profound mental retardation. Characteristic for PKS is a tissue-limited mosaicism; *i.e.*, most fibroblasts have 47 chromosomes with an extra small metacentric iso-chromosome i(12)(p10), whereas the karyotype in the majority of the lymphocytes is normal (see OMIM #601803).

Even though PKS is a well-known syndrome in most recent reports [1-4], the authors are not aware of the number of previously published cases. As reviewed on the regularly updated homepage on small supernumerary marker chromosomes (sSMC) [5] on the sub-page for PKS [6], there were, up to November 2008, 103 prenatal and 129 postnatal PKS reported in the literature, including the five new prenatal cases summarized in Table 1.

Thus, of the four well-defined syndromes characterized by an sSMC, PKS is the second most frequently reported (8.4%) (this frequency is deduced from the data collected in Ref. 5), after Emanuel Syndrome (OMIM #609029) and ahead of isochromosome 18p syndrome [7] and cat eye syndrome (OMIM #115470).

More interesting is, that a variety of karyotypes have been reported in association with PKS, besides the regular ones with 47,+i(12p) and mos 47,+i(12p)/46. Unexpected cytogenetic results are sometimes detected even though the PKS phenotype is clear (Table 2) or there is no sSMC [8]. In PKS with sSMC, more complex mosaics have been reported as in cases A-D of Table 2, including complete trisomy 12 and hexasomy 12p. Three cases (E-G) in Table 2 with neocentric sSMC (12) suggest a possible small PKS critical region in 12pter to 12p13. Thus, additional case reports can be expected to further increase our clinical and cytogenetic understanding of PKS. Nonetheless, to come to an approximate assessment of the frequency of PKS in the general population, also cases with a “typical

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**Table 1.** Five new prenatally diagnosed PKS cases: tissue studied, karyotype and clinical details are listed.

| Case Number [6] | Tissue Studied | Clinical Details            | Karyotype           |
|-----------------|----------------|-----------------------------|---------------------|
| 12-Wpks-5       | chorion        | AMA; AS; hygroma colli; TOP | 47,XX,+i(12p)[50%]  |
| 12-Wpks-166     | amnion         | AMA; AS; TOP                | 47,XX,+i(12p)[100%] |
| 12-Wpks-167     | amnion         | AMA; AS; TOP                | 47,XX,+i(12p)[100%] |
| 12-Wpks-173     | amnion         | AMA; TOP                    | 47,XX,+i(12p)[67%]  |
| 12-Wpks-185     | amnion         | AMA; AS; TOP                | 47,XY,+i(12p)[50%]  |

AMA: advanced maternal age; AS: abnormal sonography; TOP: termination of pregnancy.

**Table 2.** Seven reported PKS cases with unusual karyotypes.

| Case | Case Number [6]  | Prenatal/<br>Postnatal | Karyotype   |
|------|------------------|------------------------|---|
| A    | 12-Wpks-4        | postnatal              | various mosaics of 47,XX,+i(12p)/47,XX,+del(12)(q10)/46,XX in different tissues |
| B    | 12-Wpks-47       | prenatal               | 48,XX,+i(12p),+i(12p)[16%]  |
| C    | 12-Wpks-159      | prenatal               | 47,XX,+12[20%]/47,XX,+i(12p)[80%]   |
| D    | 12-Wpks-174      | postnatal              | 47,XX,+i(12p)[29%]/47,XX,+del(12)(q10)[43%]                                     |
| E    | 12-N-pt13/1-1    | postnatal              | 47,XX,+inv dup(12)(pter?p13::p13→pter)[100%]                                    |
| F    | 12-N-pt12.3/1-1  | postnatal              | 47,XX,+inv dup(12)(pter?p12.3::p12.3→pter)[50%]                                 |
| G    | 12-N-pt11.22/1-1 | postnatal              | 47,XY,+inv dup(12)(pter?p11.22::p11.22→pter)[36%]                               |

Tetrasomy 12p<sup>7</sup> karyotype, should be reported, as the five of the present paper.

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