Implications of chromosomal mosaicism and X-inactivation on a familial Xp22.3 deletion in a mother with Turner’s syndrome mild phenotype and daughter with MIDAS

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MMB, female, born with 40 weeks gestation, weight 2.880g with normal length. During the prenatal period a left cleft lip and palate, confirmed at birth, was identified associated to IUGR. At birth, a diagnosis of MIDAS (Microphthalmia, Dermal Aplasia and Sclerocornea) syndrome was proposed. Clinical follow-up revealed a global developmental delay, corpus callosum agenesis, normal right eye; small left eye with absent left lens and an abnormal optical nerve. The facial “reddish” linear skin lesions observed at birth resumed as “white linear strikes” in her left facial region. A G-band karyotype identified a terminal Xp deletion comprising pter-p22.3 in her lymphocytes. Her mother revealed a mos 45,X[30]/46,X,del(X)(pter-p22.3)[70] karyotype. Physical examination of the patient’s mother showed a healthy woman with small stature (145cm - p<5), nevi, cubitus valgus, absent Madelung or Kosowicz sign, and a left inversion of lines A and T in her left hand dermatoglyphic pattern. A CGH-array (genome build hg 18) of the proband revealed an interstitial Xp deletion comprising p22.3p22.2 region [arr.Xp22.33-p22.2(2679225-13632604)x1]. X-inactivation studies using the HUMARA region that contains the CAG insert and subsequent HpaII digestion revealed informative patterns: (a) in the undigested DNA of the mother with a mosaic karyotype, the HUMARA region of the normal X chromosome was preferentially amplified when compared to her daughter’s DNA where similar amplifications were observed; (b) mother and daughter shared the CAG insert characteristic of the deleted X chromosome; (b) mother and daughter showed an extreme skewed pattern, with preferential inactivation of the deleted X-chromosome. Our report describes the second family in the literature with this clinical, cytogenetic and non-random X-inactivation pattern.

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