X Chromosome Imprinting in Turner Syndrome

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ABSTRACT

The objective of this study was to assess indirectly the existence of X imprinting and its potential role in a number of clinical characteristics of Turner syndrome patients. Highly polymorphic X linked microsatellite markers were used to determine the origin of the single X chromosome in 13 patients with Turner syndrome. Ten (77%) patients retained the maternal X chromosome (Xm), while only three patients (23%) retained the paternal X chromosome (Xp). Fisher exact statistical test was used for the association of X chromosome origin with the clinical phenotype. No significant difference was found between the two groups of patients regarding the following phenotype characteristics: lymphoedema at birth, short neck, low posterior hairline, eye anomalies (ptosis, epicanthal folds, hypertelorism, strabismus), multiple pigmented naevi, cardiac and renal anomalies. Absence of association between the X chromosome origin and Turner phenotype was confirmed by a meta-analysis combining five studies, including this one. It was only neck webbing that showed a trend of association with Xm.

Key words: Turner syndrome, X chromosome, imprinting, chromosome origin, phenotype, PCR.

INTRODUCTION

Turner syndrome (TS) phenotype is remarkably variable, even in those patients with supposedly non-mosaic karyotype. The reasons for 45, X karyotype association with variable phenotype features are unknown. A possible explanation is that the TS phenotype may be related to the parental origin of the retained X chromosome (Chu et al., 1994). Undeniably, there is evidence on imprinted X loci affecting somatic, psychological and social traits (Chu et al., 1994, Skuse et al., 1997; Iwasa and Pomiankowski, 1999; Donelly et al., 2000; Skuse, 2005).

The present study examines a series of 13 live born individuals with TS, which is a significant number for Serbian population. The aim was to assess indirectly the existence of X imprinting and its potential role in the expression of certain clinical features.

We were able to study 13 individuals and their families, who were examined at the Department of Endocrinology, University Children’s Hospital, and the Department of Genetics, Institute of Mental Health Belgrade, Serbia. Clinical evaluation included anamnestic data and a detailed physical examination.

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The following anatomic and physiologic findings were assessed according to the criteria modified by Ogata and Matsuo (1995):

a) the presence of lymphoedema at birth, webbed neck and short neck;

b) cardiac anomalies (coarctation of aorta);

c) renal anomalies;

d) other phenotypic traits (ptosis, hypertelorism, epicanthal folds, strabismus, multiple pigmented naevi, four finger line).

**MATERIALS AND METHODS**

Chromosome analysis was performed for each proband and both parents, where available, by using trypsin G banded chromosome preparations from peripheral lymphocyte cultures; 30 metaphases for each individual were scored.

Polymerase chain reaction (PCR) was carried out on the DNA extracted from peripheral blood samples of affected children and both parents by standard salt procedure (Miller et al., 1988). Microsatellite markers DYS I and DYS II, giving PCR products of 177 to 185 bp and 214 to 228 bp respectively, located at the 5′ terminus of the dystrophin gene (Xp21), were used in order to determine the X chromosome origin. Primer sequences and reaction conditions were as recommended by the PCR protocol (Feener et al., 1991). PCR products were separated on 10% non-denaturing polyacrylamide gel, and visualized by ethidium bromide staining.

Differences in expression of phenotypic characteristics between groups of X<sup>p</sup> and X<sup>m</sup> patients were analyzed by Fisher exact probability test.

In addition, our intention was also to combine the results of the present study with other researchers’ results regarding a possible association between cardiac abnormalities, neck webbing and parental origin of the X chromosome. Meta-analysis (Comprehensive meta analysis version 2.0) was carried out using five studies (including this study).

**RESULTS**

All probands were diagnosed as non-mosaic for sex chromosome monosomy, at cytogenetic level. We were able to determine unambiguously the parental source of the single X chromosome in 12 probands. In one case blood sample was available only from the mother. In 10 of 13 our probands (77%), the X chromosome was of maternal origin (X<sup>m</sup>), while in only 3 patients (23%) it was of paternal origin (X<sup>p</sup>) (Fig. 1).

The association between the X chromosome origin and

![Figure 1](image-url)