Turner syndrome: analysis of changes in the age at diagnosis and phenotypic and genotypic description of 174 patients

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Background : Turner syndrome, characterized by complete or partial absence of second sexual chromosome, is responsible for phenotype of variable severity. It may involve intrauterine and postnatal growth retardation, dysmorphic signs, neonatal lymphedema, gonadal dysgenesis, and ENT, visceral or metabolic malformation .

Objectives : The main objective of this work is to describe the evolution of the age at diagnosis of this syndrome over time. We also performed a phenotypic and genotypic description of these patients and sought a possible evolution of this description over time.

Material

- **Monocentric descriptive observational epidemiological study of a serie of cases.**

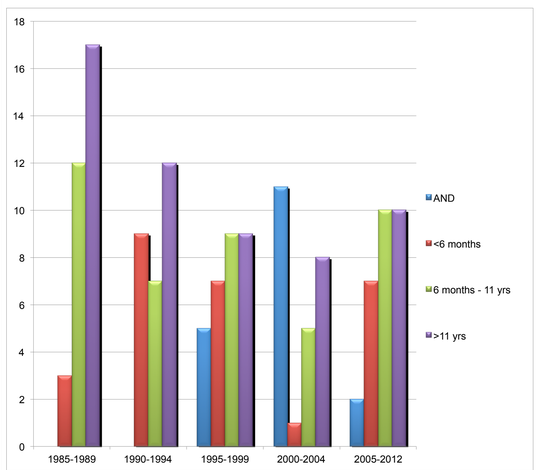
- **Patients included: All female subjects followed since 1969 in the center of reference of Nancy (France) for which time of diagnosis was known and karyotype available.**

= 174 patientes

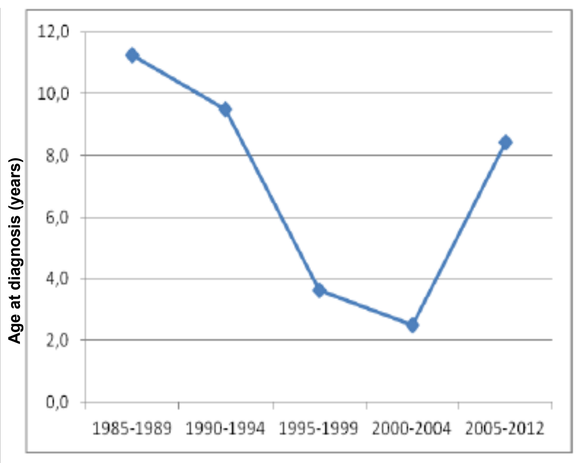
Methods

- Crossing the Turner data base of the service with PMSI files of the consultation
- Collecting the date of diagnosis, karyotypes and phenotypic data in the letters, medical records and the laboratory
- **Ranking karyotypes in 5 groups**

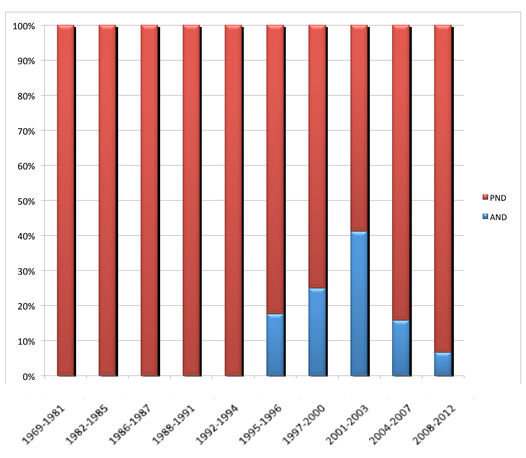
-1st cluster : 45,X
-2nd cluster : 45,X/46,XX ; 45,X/46,XY ; 46,XisoYq
-3rd cluster : 46,XisoXq ;45,X/46,XisoXq
-4th cluster : 45,X+fragment ; 45,X/46,X+fragment
-5th cluster : other karyotypes



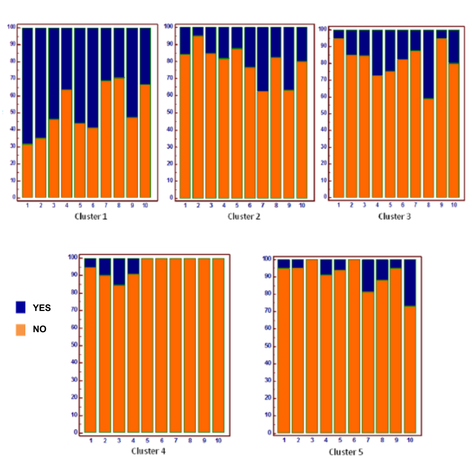
Proportion of age groups at diagnosis according to ranges of years



Evolution of the median age at diagnosis



Changes in the proportion of antenatal diagnoses (AND) over time



Evolution of each cluster karyotype based on years of diagnosis (deciles)

Results - discussion

- **The median age at diagnosis was 100 months (0-150 months). 10,3% of patients were diagnosed in antenatal period, 24,1% before 6 months, 29,9% between 1 and 11 years and 35,6% after 11 years. There is a statistically significant inverse correlation between age at diagnosis and time since 1985 (p = 0,0290). The median age at diagnosis decreased until 2000, but then increased back : 2,5 years between 2000 and 2004, versus 8,3 years between 2005 and 2012. 48,9% of all the patients had a 45, X homogeneous karyotype but the proportion of monosomy X decreased significantly over time (p = 0,016) benefitting mosaic forms with expression less pronounced in post natal.** Stochholm is the only one who studied the evolution of age at diagnosis in Turner syndrome. It has shown, like us, in a Danish population, a decrease over time.
- **Antenatal diagnosis appeared in 1995, they increased until 2003 and then declined over the past decade.** To our knowledge, there is no data in the literature to discuss the recent decrease in the number of patients alive with prenatal Turner diagnostic. This is certainly involved in the re-increase in the median age at diagnosis observed since 2005. We assume that the increase in medical termination of pregnancy in cases of prenatal Turner karyotype explains this phenomenon.
- **48.9% (85/174) of patients had a 45, X homogeneous formula but the proportion of monosomy X decreases significantly over time (p = 0.016) while the mosaics proportion increases. We have shown that the phenotype is more severe in case of monosomy X.**

Conclusions

Our work helped to highlight a notable recent epidemiological evolution of Turner syndrome in our center.
The distribution of karyotypes has changed with an increase in the prevalence of mosaics.
The number of live cases diagnosed in antenatal period decreased.
Although the median age at diagnosis has decreased overall since 1985, there is, in the last ten years, a re-increase of the age at diagnosis, which is , in our opinion, related to the increase in medical abortions of 45, X formula, usually diagnosed earlier.
Our conclusion should encourage all health professionals involved to be more vigilant and systematic in case of short stature or delayed puberty in a girl as therapeutic issues are the same regardless of the karyotype found.

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