

Clinical spectrum of 45,X/46,XY mosaicism and variants in children

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OBJECTIVES

The 45,X/46,XY karyotype and its variants are also known as mixed gonadal dysgenesis (MGD). Patients present with varying phenotypes including Turner syndrome females to phenotypic males with or without genital ambiguity. There are challenges in management due to this diversity. The aim of this study was to describe the clinical spectrum of 45,X/46,XY mosaicism and variants diagnosed in childhood.

METHODS

A retrospective review of patients diagnosed with mixed gonadal dysgenesis who were followed up at a single tertiary center between January 1997 and July 2014. Review of 20 patients (7 males, 13 females) with the following karyotypes: 45,X/46,XY (n=7) 45,X/46,X,der(Y) (n = 12) 46,X,der(X);t(X;Y) (n=1) Reviewed for: birth history, presenting symptoms, events leading to diagnosis, anthropometric measures, growth patterns, presence of Turner syndrome like features, phenotypic appearance of the external and external genitalia (graded and scored)[1], sex determination and sex of rearing, pubertal changes, gonadectomy and histopathologic characteristics of removed or biopsied gonads.

RESULTS

1. Age at diagnosis: The mean age at diagnosis was 5.0 years (range 0.1-15.1). There were no cases of prenatal diagnosis.
2. Presenting symptoms: The diagnostic presentation was genital ambiguity, short stature and delayed puberty. Genital ambiguity was present in 86% of 45,X/46,XY patients and in 33% of 45,X/46,X,der(Y) patients ($p=0.09$).
3. Gonadectomy and gonadoblastoma: All patients with 45,X/46,XY karyotype (n=7) and 75% of 45,X/46,X,der(Y) karyotype who showed ambiguous genitalia (n=4) or signs of virilization (n=1) underwent gonadectomy. Gonadoblastoma was detected in intraabdominal gonads of 3 phenotypically female patients, 2 of which were diagnosed at later ages of 9.5 and 13.7 years respectively.
4. Sex of rearing, external and internal masculinization scores: Thirteen patients were reared as females while 7 were reared as males. External masculinization scores with maximal 12 points were evaluated (males 9.2 vs. females 1.2, $p<0.001$).
5. Turner characteristics present in 16 patients (80%): cardiac anomalies (n=3, 20%), kidney anomalies (n=4, 31%)
6. Growth and growth hormone: The percentage of patients with height z-scores less than the third percentile increased from 42% at diagnosis to 68% by the time of initiation of growth hormone (GH) treatments ($p=0.005$). Sixteen patients received GH and showed significant increases in height z-scores ($p<0.001$). Ten patients achieved final adult height with a median height z-score of -1.07 ± 0.89 .

CONCLUSIONS

This study describes the clinical characteristics of 45,X/46,XY mosaicism with attention to sex determination, growth, puberty, and gonadal histology. The clinical spectrum of the 45,X/46,XY karyotype is diverse and patients require individualized care. Turner syndrome like characteristics should be considered requiring thorough evaluation and management. Further studies are required for optimization of clinical practices regarding this diverse group of patients.

References

1. Ahmed SF, Hughes IA. The role of a clinical score in the assessment of ambiguous genitalia. BJU International 2000; 85: 120-124

