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Relationship of Phenotypic Characteristics with Growth, Gonadal Pathology and Tumor Risk in Patients with 45,X/46,XY Mosaicism

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Introduction: The 45,X/46,XY mosaicism represents a wide spectrum of phenotypes, from phenotypically normal females to males and varying degrees of genital ambiguity. Growth seems to be impaired in these patients. Patients with this mosaicism have increased risk of gonadoblastoma and germ cell neoplasia *in situ* (GCNIS). Risk of germ cell neoplasia in terms of the clinical phenotype is conflicting. Some studies reported high risk in patients with female phenotype, on the contrary, others showed the highest risk in patients with ambiguous genitalia.

Objective: To evaluate the growth data, gonadal functions and tumour risk in children with 45,X/46,XY mosaicism

Design: We reviewed retrospectively the records of 45 patients with 45,X/46,XY mosaicism or variants presented to our Unit from 1989 to 2019. Patients were divided into 3 groups as those with female external genitalia, ambiguous genitalia, or male external genitalia with respect to phenotypic characteristics at diagnosis.

Results:

- The age at diagnosis ranged from 0.03 to 17.5 years.
- Twenty-eight patients had genital anomaly, 14 patients had female external genitalia and 3 patients had normal male genitalia.
- Patients showed normal height under 2 years of age. Mean height standard deviation score (HSDS) of 19 patients diagnosed before 2 years of age was -0.9±0.6 and -2.6±1.5 in 26 patients diagnosed after 2 years of age.
- Ten patients diagnosed before 2 years of age showed growth deceleration after 2 years of age (HSDS decreasing from -0.6±0.7 to -1.4 ±0.9).
- Twenty-one patients reached adult height (AH). Growth hormone (GH) treatment was initiated in 10 patients. Although AHSDS of GH treated patients was significantly greater than their mean HSDS before GH therapy (p=0.013), it was not significantly different from AHSDS of the untreated group.
- Seventeen (37.8%) patients exhibited phenotypical features of Turner syndrome other than short stature.
- Two patients with genital anomaly had gonadoblastoma and germ cell neoplasia *in situ* in their bilateral abdominal dysgenetic testes. One patient with female external genitalia had gonadoblastoma in bilateral streak gonad.

Conclusions: GH therapy seems to improve AH of patients. Both patients with genital anomaly and female external genitalia have increased risk of germ cell tumors.

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