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P28. Rare Copy Number Variants (CNVs) in the Genome of Chinese Female Adolescents with Turner Syndrome

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Context:Turner syndrome (TS) is a congenital disease caused by complete or partial loss of one X chromosome. Low bone mineral status is a major phenotype associated with TS, although the underlying mechanism is unclear. We have previously reportedthat TS patients with a 45,X/46XY karyotype do not have a more severe male phenotype,compared to patients with 45,X,45,X/46,XX without Y karyotype. Undetected low percentage mosaicism might be a possible explanation. Examination of genomic copy number variations (CNVs) might be a more objective method to specifically reveal structural variation, duplication or deletion of sections of the genome.

Objective: This study aimed to investigate potential genetic mutations in TSthrough CNV examination performed by array based comparative genomic hybridization (a-CGH) analysis.

Methods:Whole blood genomic DNA of 17 TS patients and 15 healthy volunteer women was extracted, CNVs identified and compared by a-CGH.The abnormal CNV of one identified gene (CARD11) was verifiedby quantitative PCR. T and B lymphocyte cell populations in the peripheral blood of TS patients and controls were assessed by flow cytometry.

Patients:Seventeen TS patients and fifteen healthy volunteer girlswere recruited at the Departments of PediatricEndocrinology and Gynecology Endocrinology, Guangzhou Women and Children'sMedical Center. None of the participants suffered from any other disease known to be associated with abnormal bone mineral statusor had been treated with growth hormone (GH).

Intervention:The girls (aged >13 years) with primary amenorrhea had been treated by hormone replacement therapy (HRT), started as continuous low-dose conjugated estrogen therapy, which is continued cyclically from the second year.

Main Outcome Measures: Standard karyotyping, bone mineral status,CNV analysis, peripheral blood T cell population analysis.

Results: Three rare CNVs, located individually at 7p22.3, 7p22.2 and Xp22.33, where six genes (TTYH3, AMZZ1, GNA12, BC038729, CARD11 and SHOX) are identified, were found in TS patients. Quantitative PCR confirmed the CNV of CARD11 in the genome of TS patients.Peripheral blood regulatory T cell numbers were reduced in TS patients.

Conclusions: The CARD11 gene has beenshown to be associated with immune defects;dysregulation of the gene dosage of CARD11 may contribute to lowered immune and bone mineral status in TS patients.

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