Screening for Microdeletions in the AZF Region of the Y Chromosome in Patients with Disorders of Sex Development due to 45,X/46,XY Chromosome Abnormalities

Nishi, M.Y.; Santos, P.T. L.; Costa, E.M.F.; Mendonca, B.B.; Domenice, S.

The etiology of the disorders of sex development (DSD) in patients with 45,X/46,XY karyotype and variants is not yet completely understood. The presence of Yq microdeletions in men with azoospermia or severe oligospermia are frequent, but recently these deletions have also been identified in subjects with Klinefelter syndrome (KS) and with 45,X/46,XY mosaicism. It has been hypothesized that deletions of the Azoospermia factor region (AZFa, AZFb and AZFc sub-regions), located at Yq, might predispose to Y loss. Deletions of AZFc, which includes the DAZ genes, are a common cause of spermatogenic failure. To screen Yq microdeletions in Brazilian patients with DSD due to 45,X/46,XY chromosomal abnormalities. Twenty-seven subjects with 45,X/46,XY or with 45,X/46,X,idic(Y) karyotypes were selected, 16 with mixed gonadal dysgenesis (MGD) and 11 with Turner syndrome (TS). DYZ3 (centromere) and seven loci covering AZF regions were screened using PCR in DNA from blood. The loci DYS280 and UTY are located in AZFa; DYS216, DYS231 and DYS224 in AZFb; DAZ and PPP1R12BP1 in AZFc regions. Yq microdeletions were detected in 6 (22%) patients: 3 with MGD and 3 with TS. Regarding MGD patients, in one it spans at least 6 Mb (DYS216 to PPP1R12BP1), in the second 4.5 Mb (DYS231 to PPP1R12BP1), and in the third one as so as in the 3 patients with TS they span at least 3 Mb (DAZ to PPP1R12BP1). he Yq deletions identified in DNA of these patients involve the AZFb and AZFc regions. The longest deletions of Yq, containing AZFb and AZFc regions, were identified in two MGD patients with male phenotype. The AZFc region was deleted in all 6 patients. Likely, the deletions of AZFc region are the most common identified in patients with idiopathic infertility due to oligozoospermia or complete absence of germ cells as in KS. In 45,X/46,XY patients, there are a few reports identifying deletions in AZFb beyond in the AZFc region as in the present study (1,2). Alvarez-Nava et al.(3) studying gonadal tissues from 45,X/46,XY patients, identified a higher incidence of Yq microdeletions in dysgenetic gonads than in blood. Extensive studies are needed to establish the exact association between specific Yq microdeletions and the various degrees of gonadal dysgenesis in patients with DSD due to 45,X/46,XY chromosome abnormalities and to confirm the role of this mechanism for the formation of 45,X cell lines in TS and in MGD patients.