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JOURNAL ARTICLE

Testicular pathology in 46,XY dysgenetic male pseudohermaphroditism: an approach to pathogenesis of testis cancer

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Eleven children with dysgenic male pseudohermaphroditism (DMP) and 18 boys with isolated penile hypospadias, all with 46,XY karyotype, were studied. Testicular dysgenesis was associated with significantly lower testosterone response to human chorionic gonadotropin (0.9 +/- 0.2 ng/mL) than it was in hypospadias (3.3 +/- 0.1 ng/mL), and with significantly higher mean serum follicle-stimulating hormone (FSH) levels (8.4 +/- 2.3 IU/L vs 1.5 +/- 0.3 IU/L). Gonadoblastoma, a tumor that arises from the sex cords, was found in more than 1/4 of patients with DMP, whereas testicular carcinoma in situ (CIS) cells were present in all of these patients. Forty-two percent to 98% of CIS cells revealed an aneuploid pattern of nuclear DNA, indicating that most of them are neoplastic cells. In patients with hypospadias, CIS was not seen, and no other abnormalities were detected. In children with DMP, the percentage of tubules populated with germ cells was significantly lower than it was in those with hypospadias (48.3% +/- 10.6% vs 92.4% +/- 4.0%). The total number of germ cells (CIS cells + spermatogonia) did not differ significantly between the 2 groups, but the number of spermatogonia was significantly reduced in children with DMP (0.08 +/- 0.05 vs 3.65 +/- 0.2), suggesting impaired differentiation of gonocytes to spermatogonia. The following significant correlations were present with DMP: 1) the higher the seminiferous tubule cross-section area, the higher the number of CIS cells (r = 0.78); and 2) the higher the serum gonadotropin levels, the higher were tubular diameter (r = 0.93 for FSH and r = 0.75 for luteinizing hormone [LH]), area (r = 0.79 for FSH and r = 0.82 for LH), percentage of tubules populated with germ cells (r = 0.86 for FSH and r = 0.81 for LH), and number of CIS cells (r = 0.87 for FSH and r = 0.79 for LH). The results indicate that in intersex children with 46,XY karyotype, CIS occurs in dysgenetic testes in all cases and is frequently associated with gonadoblastoma. Impaired organogenesis of sex cords, relative inhibition of testosterone secretion, and the associated increased secretion of gonadotropins may create a milieu that induces or is favorable for the formation or maintenance of neoplastic lesions in dysgenetic testes early in childhood.

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