Journal of Andrology, Vol. 24, No. 2, March/April 2003

Neoplastic Potential of Germ Cells in Relation to Disturbances of Gonadal Organogenesis and Changes in Karyotype

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The study consisted of 46 intersexual patients who underwent gonadectomy at the age of 3 months to 19 years because of gonadal dysgenesis (GD; 40 cases) or true hermaphroditism (bisexual gonads; 6 cases). In patients with GD, the incidence of the 46,XY karyotype was 67.5%, whereas the remaining patients exhibited numerical and structural aberrations of sex chromosomes (NSASs), and all patients with bisexual gonads revealed NSAS. Seminoma was diagnosed in 1 patient with the 46,XY karyotype and pure GD (streak gonads). Intratubular carcinoma in situ (CIS) appeared as an exclusive lesion in 61.5% of 13 patients with mixed GD, in 54% of 11 patients with partial GD (bilateral testes), in 16.7% of 6 patients with bisexual gonads, and in none of 13 patients with pure GD. CIS also appeared in tubules in the vicinity of sex cord-derived tumors (gonadoblastoma nests and unclassified mixed germ cell-sex cord-stromal tumor; MGCSCST) and within the tumors. In 3 patients, gonadoblastoma replaced the whole bilateral gonads and is referred to as gonadoblastoma-only GD. The incidence of neoplastic lesions (mostly bilateral) was 90.9% in patients with partial GD, 76.9% (mostly unilateral) in patients with mixed GD, 23.1% (unilateral) in patients with pure GD, and 16.7% (unilateral) in patients with bisexual gonads. Disregarding types of disturbances of gonadal organogenesis, the incidence of lesions was 71.4% in 28 patients with the 46,XY karyotype and 35.3% in 17 patients with NSAS. We conclude, first, that NSAS is not a prerequisite for the appearance of GD and GD is more frequently associated with the 46,XY karyotype. Second, the spectrum of germ cell neoplastic lesions in GD is wider than reported. Besides germ cell carcinoma, CIS, and gonadoblastoma nests, the spectrum also includes a tumor of gonadoblastoma-only in cases of GD and MGCSCST. Third, the incidence of neoplastic lesions is related more to the severity of the disturbances of gonadal organogenesis than it is to aberrations in sex chromosomes. Fourth, less disturbed testicular organogenesis predisposes these patients more toward germ cell neoplastic lesions, which suggests that the testicular environment of a dysgenetic gonad plays an important role in germ cell neoplasia initiation, maintenance, or both.

Key words: Testicular carcinoma in situ, gonadoblastoma, mixed germ–cell sex cord stromal tumor, gonadal dysgenesis, sex chromosomes.

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