

Tumor Risk in Disorders of Sex Development

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Abstract

Certain patients with disorders of sex development (DSD), who bear Y chromosome material in their karyotype, are at increased risk for the development of type II germ cell tumors (GCT), which arise from early fetal germ cells. DSD gonads frequently harbor immature germ cells which express early fetal germ cell markers. Some of them (e.g. OCT3/4 and NANOG) seem to be of pathogenetic relevance in GCT development providing cells with the ability of pluripotency, proliferation and apoptosis suppression. Also TSPY (testis-specific protein Y-encoded), the main candidate for the so-called gonadoblastoma locus on Y chromosome, is overexpressed in germ cells of DSD patients and possibly contributes to their survival and proliferation. Nowadays, the use of immunohistochemical methods is highly relevant in identifying DSD gonads at risk. The risk for GCT development varies. While the prevalence of GCT is 15% in patients with partial androgen insensitivity, it may reach more than 30% in patients with gonadal dysgenesis. Patients with complete androgen insensitivity and ovotesticular DSD develop malignancies in 0.8% and 2.6% of cases, respectively. However, these data may be biased for various reasons. To better estimate the risk in individual groups of DSD, further investigations on large patient series are needed.

Key Words

Disorders of sex development _ Germ cell tumors _ Pathogenesis _ Risk

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