Management of gonads in adults with androgen insensitivity: an international survey

E. Maris (1), LHJ Looijenga (2), M. Cools (1)

1. Department of Pediatrics, UZ Gent and Ghent University, Ghent, Belgium. 2. Laboratory for Experimental Patho-Oncology, Department of Pathology, Josephine Nefkens, Erasmus Medical Center Rotterdam, the Netherlands

**Background**

Individuals with androgen insensitivity syndrome (AIS) have an increased risk for developing a germ cell cancer (GCC). The risk is highest during childhood; therefore, gonads are commonly preserved until after puberty in women with CAIS and men with PAIS to allow for spontaneous gonadal development. Preservation of gonads thereafter is controversial given that little is known about GCC development in adulthood and given the lack of tools for conservative follow-up of gonads in situ. This question is particularly relevant as many adult AIS women decline gonadectomy.

**Aims and objectives**

We wanted to gain insight in attitudes towards gonadectomy in various DSD centers around the world and estimate the proportion of AIS adults who have retained gonads, reasons for declining gonadectomy and frequency of GCC occurrence. We hypothesize that many adult women with CAIS, especially in lower-income countries have retained gonads without ever developing a GCC.

**Methods**

We performed an international survey among health care professionals working in DSD centers around the world, retrieved through the I-DSD Registry. Respondents were invited to participate in this survey by email or by an announcement and flyer distributed at the ESPE 2014 meeting. The questionnaire was sent by e-mail.

**Results and Discussion**

In CAIS, 16/22 centers routinely propose gonadectomy before (4/22) or at the end (12/22; 145/188 patients (77%)) of puberty. 23/188 (12.2%) of CAIS individuals have retained gonads, either because gonadectomy was not proposed, or because patients refused this procedure (13/23). Reasons for declining are being anxious about surgery and its complications and worries about long-term effects of hormone replacement therapy, timing of surgery and not having processed the diagnosis. One invasive and one in situ neoplasia were reported in two patients who had both received routine gonadectomy at the end of puberty, suggesting a tumor risk of 1.2%.

Decision and timing of gonadectomy in PAIS is highly variable; overall, only 8/38 (21.0%) of PAIS males in this survey still have one or both gonads (62.5% scrotal testes, 12.5% inguinal testes, 25% no information about testes position). No (invasive) GCC were mentioned, not in the patients with retained gonads, nor in the gonadectomized group.

The fact that only two tumors occurred in 2/226 individuals (0.8%), mainly adults, is reassuring. Since premenarcheal changes and CIS have previously been shown to occur in 15 - 44%, this questions at least in AIS the hypothesis that all CIS progresses towards invasiveness over time, or alternatively, that there is an important tendency to overdiagnose CIS in AIS.

**Conclusion**

Differences in attitudes towards gonadectomy exist in centers caring for AIS individuals. Affected persons are concerned about surgery and generally accept gonadectomy at the end of puberty. The occurrence of (an invasive) GCC seems rare in AIS adults, questioning the need for routine gonadectomy in this population. Expert histological review is necessary to optimize diagnostic accuracy and to avoid overdiagnosis. Gaining further knowledge about the eventual progression of (pre)neoplastic changes towards invasiveness in AIS and in different ethnic populations, specifically will help to improve counseling and patient-oriented management.