ISFP – Newsletter

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Assessment of folliculogenesis in ovarian tissue from young patients with Turner syndrome using a murine xenograft model

Peek R, et al. *Fertil Steril,* 2023; doi: 10.1016/j.fertnstert.2023.04.008

Evaluation of ovarian reserve in young females with non-iatrogenic ovarian insufficiency to establish criteria for ovarian tissue cryopreservation

Zajicek M et al. *Reprod Biomed Online,* 2023; doi: 10.1016/j.rbmo.2023.03.004

Background:

Turner syndrome (TS) is a genetic disorder affecting approximately 1 in 2,500 newborn females, characterized by partial or complete loss of one of the X chromosomes. It causes impaired folliculogenesis, leading to infertility and premature ovarian insufficiency (POI) (1). Due to accelerated rates of germ cell apoptosis, affected individuals could benefit from early fertility preservation options (2, 3), such as oocyte cryopreservation and/or ovarian tissue cryopreservation (OTC), the latter being the only way to preserve fertility in prepubertal patients (4). However, considering the low follicle density levels in these patients, it is crucial to conduct a full evaluation of the ovarian reserve before proceeding to OTC.

Summary of the articles:

Assessment of folliculogenesis in ovarian tissue from young patients with Turner syndrome using a murine xenograft model:

In this study, researchers used a murine xenograft model to assess whether frozen-thawed primordial ovarian follicles from TS patients could progress to later stages. Ovarian tissue samples from 18 patients with mosaic TS and 13 age-matched controls were cryopreserved and subsequently transplanted into immunodeficient mice. Patients were divided into prepubertal and peri-/postpubertal groups. Follicle density and expression of proliferating cell nuclear antigen (PCNA) and anti-Müllerian hormone (AMH) were analyzed before and after transplantation (5 months).

Prior to transplantation, follicle density in TS tissues was significantly lower than in healthy controls and yielded a higher proportion of abnormal follicles. However, after transplantation, there was a significant drop in the proportion of abnormal follicles in TS tissues. Moreover, secondary and antral follicles were observed in grafts from Turner patients, indicating possible folliculogenesis and follicle growth after transplantation. Expression of PCNA and AMH in follicles from patients with TS increased significantly during grafting, pointing to regular follicle development.

Rapid follicle loss occurs around puberty in TS patients. After transplantation, the peri-/postpubertal group showed a greater drop in follicle density than the prepubertal group. These results confirm that it is vital to offer OTC to TS patients before puberty, as the younger the subject at cryopreservation, the greater the chances of finding follicles after transplantation.

Overall, the study suggests that OTC and subsequent transplantation may be a feasible option to preserve fertility in TS patients, as long as the patient is still prepubertal.

Evaluation of ovarian reserve in young females with non-iatrogenic ovarian insufficiency to establish criteria for ovarian tissue cryopreservation:

This retrospective study involved a cohort of 37 young females diagnosed with non-iatrogenic ovarian insufficiency, and included mainly patients with TS (27 patients). Researchers assessed the ovarian reserve using various methods, including serum AMH values, antral follicle count (AFC), and basal follicle-stimulating hormone (FSH) levels before OTC. The procedure was only offered if one of the three parameters was positive according to the following criteria: AMH >0.16 ng/ml, detection of at least one antral follicle by transabdominal ultrasound, and FSH ≤20 mIU/ml.

Fourteen patients exhibited at least one positive parameter and underwent OTC. Follicles were observed in ovarian biopsies from 11 of them (79%) with one or more positive parameters, and in all subjects (100%) with two or three positive parameters.

This study highlights the importance of evaluating the ovarian reserve in young females with POI prior to considering OTC.

Conclusions:

- In patients with TS, OTC should be offered only in the presence of at least one positive parameter of the three evaluated (serum AMH, AFC and FSH levels) in order to minimize the risk of needlessly reimplanting ovarian tissue containing very few follicles. These criteria could serve as valuable guidelines for clinicians trying to determine which patients would benefit most from this fertility preservation approach.

- Because of the rapid decline in the follicle pool in young patients with TS, fertility preservation should be considered at the earliest age possible (preferably before 12 years of age), in order to preserve as many follicles as possible.

- The xenografting study supports the notion that OTC is a realistic fertility preservation option in patients with TS, as it shows that small follicles from TS patients undergo folliculogenesis, despite the presence of aneuploid ovarian cells.

References:

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4. Chen L, Dong Z, Chen X. Fertility preservation in pediatric healthcare: a review. Front Endocrinol (Lausanne). 2023;14:1147898.

*Please note: This newsletter reflects the views of the author and not the ISFP.