EDITORIAL

Preservation of Fertility in Female Cancer Patients

From Experiment to Everyday Clinical Practice

Thomas Strowitzki

In this volume of Deutsches Ärzteblatt, a group from the University Department of Gynecology at Erlangen report Germany's first case of the reimplantation of cryopreserved ovarian tissue. This marks a step forward in efforts to preserve fertility for patients undergoing cancer treatments. Strategies to preserve fertility in cancer patients are much needed. The numbers of long-term cancer survivors especially in childhood, adolescence, and early adulthood are rising constantly. The five-year survival rate for Hodgkin's lymphoma in childhood, for example, is over 90%, and almost 80% for acute lymphoblastic leukemia (1). In the year 2010, one in every 715 adults will have a history of childhood cancer (2). These good long-term prospects open the possibility of life choices, of which the choice to have a family is one. This is however compromised by the fact that the cytotoxic damage to the gonads resulting in infertility is a predictable consequence of oncological treatment, whether chemotherapy or radiotherapy.

Fertility preservation at an experimental stage

Only recently have techniques for fertility preservation in women been developed, but most remain purely experimental. This is often due to the long time interval which often separates cytotoxic therapy and the desire to being a family, and the fact that at a moment of life threatening illness the question of fertility may not be considered. This was not the case in Erlangen, however. Tissue removal and retransplantation were separated by two years during which time the course of the disease could be evaluated.

The preservation of sperm in men is a simple procedure and available without delay. The situation in women is more complex. Three distinct types of treatment are now recognized: pharmacological protection, assisted reproductive techniques, and surgical measures involving the removal and cryopreservation of ovarian tissue for later reimplantation. Medical treatment with GnRH agonists can be instituted without delay and has few side effects, but its efficacy remains controversial (3). Artificial fertilization methods are standard, but require hormonal stimulation, a delay, and a stable relationship. Only tissue removal and later reimplantation is free of these constraints. Tissue recovery and cryopreservation are already carried out on a wide scale in Germany.

The Erlangen group has now for the first time gone a step further and reimplanted ovarian tissue in a patient with anal carcinoma. At the very least, the successful restoration of hormonal functioning has been demonstrated. The first successful reimplantation was described in 2000 by the New York based group led by Kutluk Oktay (4), the first live birth in 2004 by Jacques Donnez's group in Brussels (5). Worldwide, more than six pregnancies have been reported following reimplantation. The leading groups oversee the cryopreservation of several hundred ovarian tissue samples.

Advantages of cryopreservation

What makes cryopreservation so attractive in comparison with other techniques? It can be begun without delay before the onset of chemotherapy; It is independent of a stable relationship. This is all the more important as many patients become ill at a very young age. And the techniques of tissue recovery, cryopreservation and reimplantation can now be seen as established. As was the case in Erlangen, small tissue pieces are for the most part reimplanted peritoneally, either in a residual ovarian fossa or in a peritoneal pocket. However, current research is investigating the removal and cryopreservation of a whole ovary (6). Concern is frequently raised about the possibility of unwanted reimplantation of tumor tissue or tumor cells, particularly where there is lymphatic disease. Evidence on this question is lacking. In the few studies looking at ovarian tissue, no evidence was found to support this concern (7, 8). The Erlangen patient was well selected, since her tumor was solid, non-systemic, and not hormone dependent.

An alternative for young women not in a stable relationship might be the removal of oocytes for long-term cryopreservation. A disadvantage of this approach is the need for hormonal stimulation. And even in the hands of the leading group in Italy, more than 100 oocytes would be needed on average to achieve one pregnancy (9). For the time being, therefore, this is not a practicable alternative.

Nationwide network under construction

It must be the goal, following these promising reports of ovarian reimplantation, to achieve a universal service offering fertility-preserving treatment, to meet the needs of tomorrow's patients. Uniquely in Europe this has

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been made possible in Germany by the Network Fertiprotekt, coordinated by the Departments of Gynecological Endocrinology and Reproductive Medicine of the Universities of Heidelberg and Bonn, with participants from 100 centers across Germany. The last meeting was held recently in Erlangen. Further details can be found on the homepage www.fertiprotekt.de.

In the euphoria of success, it should not be forgotten that the success rates for all methods remain very limited. Nevertheless, it is only these methods at this time which can place patients in a position to benefit from possible medical progress in the coming years.

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