Bone Marrow Transplantation (2012) 47, 313–314

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LETTER TO THE EDITOR

Fertility preservation in young patients before allogeneic haematopoietic SCT

Bone Marrow Transplantation (2012) **47,** 313–314; doi:10.1038/bmt.2011.235; published online 28 November 2011

In a recent paper, Borgmann-Staudt *et al.*[1] reported very interesting data on the fertility status of patients who had received (preparative regimens for) an allogeneic haematopoietic SCT (HSCT) at an early age. Impaired fertility was observed 3–12 years after the treatment, in 69% of male patients and in an even more staggering 83% of female patients.

As the long-term survival rate of patients receiving HSCT increases, quality of life issues, including the possibility to parent children, deservedly gain ever more attention. We therefore fully endorse the authors' appeal for fertility preservation in this patient group, and appreciate their efforts to raise awareness of this issue in the medical community. We would like to take the opportunity to emphasise that the options for fertility preservation for this group are restricted. To illustrate this notion we would like to supplement their paper with a brief discussion of the available options.

For male patients, fertility preservation is relatively easy, provided that their HSCT starts after puberty, that is the onset of semen production. Semen cryopreservation is a readily available option that can be offered in practically every fertility centre and can be performed with no or hardly any delay in the treatment. For pre-pubertal boys, unfortunately, there are to date no options. The cryopreservation of spermatogonial stem cells with the aim of retransplanting them after cure resulting in the initiation of spermatogenesis, is currently being investigated.[2]

For female patients the situation is more complicated. Considering the young age of most patients, emergency *in vitro* fertilisation followed by cryopreservation of the generated embryos will in the majority of cases not be an option, as this requires a stable relationship with a male partner. The cryopreservation (by means of vitrification) of oocytes is the next logical alternative. This option is suitable for post-pubertal girls and requires hormonal ovarian hyperstimulation to increase the number of mature oocytes that can be obtained.[3] Depending on the number of oocytes one wishes to obtain, one or more cycles of hyperstimulation may be required. As a consequence, treatment will have to be postponed for at least 14 days or up to several months. It should be determined for each patient individually what period of postponement of the treatment is acceptable. In pre-pubertal girls, or in those cases where delay of the treatment is not advisable, immature oocytes may be obtained and vitrified. These oocytes have to be matured *in vitro*, before they can be used for fertilisation at a later stage of life. To the best of our knowledge, there is currently no clinical experience with this complicated chain of procedures.

The final option is the cryopreservation of ovarian tissue before HSCT. This procedure is suitable for both pre- and post-pubertal girls. Orthoptic reimplantation of ovarian tissue has so far led to the birth of 15 healthy babies.[4] Seven of them were born from patients who underwent HSCT in the past,[5,6] providing proof of concept for this treatment. A major drawback of autotransplanting ovarian tissue, however, is the distinct possibility (especially in the case of diffuse tumours such as leukaemia) that the ovarian graft may harbour malignant cells. After transplantation this might result in the reintroduction of the malignancy.[3,7] Rosendahl *et al.*[7] have actually shown that leukaemic cells were present in ovarian tissue from patients with ALL, CML and AML, as determined by PCR. On the basis of their results, the authors advised not to autotransplant ovarian tissue in patients with leukaemia, until the malignant potential of residual cancer cells in the ovary is properly assessed. Another option is to grow and mature primordial follicles to pre-antral stages in pieces of ovarian tissue and then to pre-ovulatory follicles *in vitro*. Although this is not possible yet, it might become a good alternative when metastases cannot be excluded in ovarian tissue.

In addition to the abovementioned concerns, the issue of fertility preservation in children is complex because parental decisions may not always reflect the patients' wishes later in life.[3]

In conclusion, the choice for the appropriate fertility preservation option is a complex decision, especially for female patients. It will be the responsibility of the physician to properly counsel the patients and their parents on the (dis)advantages of the available options and accompany them in making the most appropriate decision.

Conflict of interest

The authors declare no conflict of interest.

L Bastings, JR Westphal, CCM Beerendonk, DDM Braat and R Peek
Department of Obstetrics and Gynaecology, University Medical Centre St Radboud, Nijmegen, The Netherlands
E-mail: R.Peek@obgyn.umcn.nl

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