Chemotherapy Is Not the End of the Road in Young Cancer Patients who Still Want to Become Pregnant

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In this issue of ONKOLOGIE, Hauenstein and colleagues describe a tragic case of a young patient with a non-Hodgkin's lymphoma (NHL) who died after complications from a gastro-intestinal recurrence of her NHL [1]. The authors' underlying assumption is that this tragic death could have been prevented if the patient had not refused standard chemotherapy after initial diagnosis because of a strong desire to become pregnant. Even though their 28-year old patient became pregnant only 3 months after initial surgery for a gastric NHL manifestation, she and the 19-week old fetus did not survive septic complications of the rapid NHL recurrence.

Physicians treating cancer patients are increasingly confronted with female patients who still have a strong desire to have children of their own, mostly patients with breast cancer and hematological malignancies. In industrialized countries, women tend to postpone their first pregnancy until they have established themselves in their jobs. Thus, age at first childbirth has constantly increased over the last decades. In Germany, it now lies at 26 years with a mean number of 1.37 children per woman (www.destatis.de).

In view of increased cure rates for at least some cancer types and progress in reproductive techniques, various ways of fertility protection during chemotherapy can be discussed with young patients. The advice to patients regarding the optimal method for fertility protection needs to be based on several factors, taking into account tumor characteristics (time schedule between tumor diagnosis and start of chemotherapy, kind of tumor, stage of disease, and prognosis) as well as the patient's current life circumstances such as age and availability of a partner.

Survival is probably the focus of a newly diagnosed cancer patient. Nevertheless, due to the potentially permanent consequences, the topic of fertility preservation should be early and proactively addressed by the treating physician in every cancer patient with child-bearing potential within the thorough discussion of the oncological therapy concept [2]. If this topic is an issue for the patient, more specialized counseling (i.e. reproductive medicine, psychooncology) may be required

and the patient needs to be referred – provided that the oncological situation permits.

Ideally, risk of sterility should not be a reason for tumor patients to refuse necessary chemotherapy. There is encouraging long-term outcome data for children conceived after their mothers received chemotherapy. Initially, the individual risk of chemotherapy induced amenorrhea (CIA) needs to be calculated, as described in the current DGGG guideline [3]. However, even if the risk seems rather low, particularly in very young women, fertility preservation needs to be addressed because of the potential of permanent consequences.

The planned fertility protection procedures should not interfere with the efficacy of chemotherapy, but they should be offered to any female patient between the age of 14 and at least 40 years of age. Three possible techniques of preserving fertility can be discussed: About 2 weeks are needed for ovarian stimulation and subsequent cryoconservation of oocytes or embryos after in-vitro fertilization [4]. Pregnancy rates are higher if a partner is available and in-vitro fertilization can be aimed for. For laparoscopic removal of ovarian tissue without stimulation and subsequent cryoconservation, only about 3 days are needed. The evidence for ovarian protection by GnRH analogues is still controversial [5]; if indicated, the first GnRH injection should take place at least 2 weeks before start of chemotherapy in order to allow for an initial hormone surge before cessation of ovarian function. Overall, at present, success rates of all these techniques are still limited; methodological advances may however lead to better success rates in the near future. Thus, young patients need to be adequately counseled in order to be able to make an informed choice.

In choosing the appropriate method, hormone-dependency of the cancer needs to be taken into account. In hormone-independent malignancies such as the NHL in the case report by Hauenstein et al, all fertility preservation methods would potentially be available. In hormone-dependent cancers such as the majority of breast cancers, methods potentially influencing tumor biology need to be considered with great care.

For breast cancer patients who are candidates for adjuvant chemotherapy which starts 2–3 weeks after surgery, almost all kinds of fertility protection are available. As the efficacy of GnRH therapy for ovarian protection is still controversial, such an hormonal interference has no place in early breast cancer according to current AGO guidelines (www.ago-online.de). It is not known if there is a higher risk for breast cancer recurrence after ovarian stimulation, particularly if an aromatase inhibitor is used [6]. Therefore, this option has to be discussed carefully with the individual patient. If preoperative chemotherapy is indicated, ideally there are less than 2 weeks left before starting chemotherapy and longer-lasting procedures may not be an option. Moreover, if there is any possibility of metastasis to the ovaries, ovarian stimulation or conservation of ovarian tissue for re-transplantation is not indicated.

Non-bureaucratic homogenous reimbursement of medically indicated fertility protection procedures based on stringent criteria would be desirable in order to help patients with their decision-making taking into account the psychological and time pressures at time of initial tumor diagnosis.

In conclusion, no patient should need to refuse an indicated chemotherapy in order to protect her chances for becoming pregnant after cancer therapy. Today, there are several options for fertility preservation. Early interdisciplinary counseling needs to be offered to every cancer patient with child bearing potential if pregnancy is still an issue. Oncological necessities, individual desires, and reproductive options need to be well balanced. Fertility counseling and preservation should therefore become an integral part of oncological therapy concepts if the patient still has a desire to become pregnant and the oncological situation permits. Obviously, such interdisciplinary counseling is also important for male cancer patients and children. Fortunately, the Ferti-protekt network (www.fertiprotekt.de) offers valuable information and also assistance to patients and their physicians.

Hopefully, the number of tumor patients still refusing standard chemotherapy after adequate interdisciplinary fertility preservation counseling – as the patient unfortunately did in the current case report – will decrease in the future.

References

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