VIA MEDICA

CLINICAL VIGNETTE

Ginekologia Polska
2024, vol. 95, no. 6, 506–507

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/gpl.97811

Five consecutive spontaneous pregnancies in a patient after high-dose chemotherapy and peripheral blood stem cell transplantation

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INTRODUCTION

The use of high-dose chemotherapy with autologous bone marrow or peripheral blood stem cell transplantation (PBSCT) has increasingly gained acceptance for malignant lymphomas with a high risk of relapse. Ovarian toxicity is a well-recognized potential side effect of the cytotoxic drugs used in most pretransplant conditioning protocols. Spontaneous pregnancies in patients treated with high-dose chemotherapy and autologous stem cell transplants due to malignant lymphomas are extremely rare [1]. We report a case of full reversal of fertility following PBSCT due to aggressive non-Hodgkin's lymphoma.

CASE STUDY

A 25-year-old nulliparous woman was diagnosed with stage IV diffuse large cell lymphoma. The patient underwent high-dose chemotherapy with RCHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) and ICE (ifosphamide, cyclophosphamide and etoposide) protocols. Subsequently, the patient was treated with CED (cytoxan, etoposide and dexametasone) to mobilize stem cells. Consolidation of remission was achieved using BEAM (cytarabine, etoposide and melphalan). Peripheral blood stem cell transplantation was performed. The patient presented to our clinic several months after transplantation with amenorrhea, hot flashes, and vaginal dryness. Her follicle-stimulating hormone (FSH) level was 53 IU/L. The patient was placed on estradiol 50 µg/day and dydrogesterone 20 mg for 10 days per month. The patient conceived on replacement therapy about a year and a half after her PBSCT. The pregnancy course was uneventful and at 37 weeks of gestation a healthy baby girl was delivered vaginally. Following delivery, during the breast-feeding period, the patient was placed on oral contraception with desogestrel. Following breast-feeding period, the patient resigned from oral contraception, her menstrual cycles became regular, and the hormonal profile returned to the fertile range. Three months later she spontaneously conceived. The patient became spontaneously pregnant five times. All pregnancies proceeded without complications, and deliveries occurred naturally. Healthy children were born. There was no recurrence of the underlying disease. The patient did not require further oncological treatment.

DISCUSSION

Loss of fertility is a common result of treatment affecting quality of life in cancer survivors. Patient's age, type of cytotoxic agents and their cumulative doses are the most important factors that determine the likelihood of gonadal failure, which might lead to amenorrhoea in many cases resulting in concerns about climacteric symptoms and an increased risk of osteopenia/osteoporosis [2].

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Received: 12.10.2023 Accepted: 17.12.2023 Early publication date: 9.02.2024

Chemotherapy with alkylating agents may produce a reduction in primordial follicles, which causes temporary or permanent ovarian function loss. This may manifest as acute ovarian insufficiency during treatment, shortly thereafter or later as premature-early menopause. Five groups of alkylating agents are the first line of chemotherapy. They have the most potent gonadotoxic effect, especially if they are used in combination. Some of such agents are cyclophosphamide, ifosfamide and melphalan, busulfan and chlorambucil, and these are the agents with a higher risk. Cisplatin and carboplatin, with low cumulative doses, and adriamycin, are of intermediate risk. Treatment protocols with bleomycin, actinomycin D, vincristine, methotrexate and fluorouracil, without alkylating agents, are of low risk [3].

Literature is limited to population-based studies comparing pregnancy or birth rates after cancer against unexposed women, or smaller studies using markers of the ovarian reserve as a proxy of infertility among female survivors of cancer [4]. There are no prognostic factors for the return of fertility after stem cell transplantation. Crude birth rate estimated in the biggest study analyzing pregnancy outcome in patients after stem cell transplantation performed in 229 European transplant centers (total number of patients = 37 362) was 0.6% [1]. A retrospective analysis was conducted by Carter regarding the impairment and fertility restoration in 619 women (patients and female partners of male patients who underwent stem cell transplantation) [5]. Pregnancy was reported by 5.5% of patients. 85% of pregnancies ended in live birth. There was no statistically significant increase in the frequency of miscarriages and premature births in these patients compared to general population.

CONCLUSIONS

This is the first report of fertility return after treatment of aggressive non-Hodgkin's disease with high-dose chemotherapy and PBSCT. Although the treatment induced menopause, it was reversed, and the patient conceived five times spontaneously. Patients undergoing conditioned autologous stem cell transplantation should be counseled about the possibility of return of normal ovarian function and pregnancy occurrence after transient menopausal changes.

Article information and declarations

Ethics statement

This manuscriot was prepared in accordance with ethical standards of The Helsinki Declaration.

Author contributions

All authors contributed to preparation of this manuscript. MNK, MG, JKB, ERW participated in patient's management, the literature search, first and final draft preparation.

Funding

None.

Acknowledgments

None.

Conflict of interest

Authors declare no conflicts of interest

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