SPONTANEOUS PREGNANCIES IN FEMALE SURVIVORS OF CHILDHOOD HEMATOLOGICAL MALIGNANCIES POST ALLOGENEIC HAEMOPOIETIC STEM CELL TRANSPLANTATION

Lee S, Zacharin M, Tiedemann K, Royal Children's Hospital & Murdoch Children's Research Institute, Melbourne, Australia

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Background

Improved survival
➔ Fertility in HSCT survivors important as part of holistic care

Survivors of childhood malignancies who received alkylating agents
➔ ⇩ likelihood of siring/conceiving vs. siblings [1]

Pituitary irradiation of 1 to 30Gy ➔⇧ Risk of infertility [2]

Of 500 transplant centers in 2002-2007
➔ 14 pregnancies in a mixed cohort of female HSCT survivors of hematological malignancy [3]

10 / 92 female survivors of childhood/adolescent HSCT achieved pregnancy (38% had non-malignant diagnoses) [4]

1) Chow EJ, Stratton KL, Leisenring WM et al. Lancet Oncol. 2016 May;17(5):567-76.
2) Barton SE, Najita JS, Ginsburg ES et al. Lancet Oncol. 2013 Aug;14(9):873-81.
3) Loren AW, Chow E, Jacobsohn DA et al. Biol Blood Marrow Transplant. 2011 Feb;17(2):157-66
4) Vatanen A, Wilhelmsson M, Borgström B et al. Eur J Endocrinol. 2013 Dec 27;170(2):211-8.

Aim

To identify spontaneous fertility outcome in a cohort of childhood onset HSCT survivors

Methods

Retrospective review of all female allogeneic HSCT survivors

- HSCT at =/<18 years for hematological malignancies at RCH
- HSCT between 1985 – 2011
- Identify spontaneous pregnancy resulting in live-birth(s)
- Data from 1) current hematologists/endocrinologists, 2) medical records, 3) Self completed questionnaires
- Exclusion: 1) Pre-pubertal, 2) Sexually inactive
- Stratification:
  Total body irradiation (TBI) - Group 1 & Chemotherapy alone - Group 2
- Descriptive statistics for data analysis

Results

- 155 allogeneic HSCT survivors transplanted for hematological malignancies
- 55 females survivors identified, 18 excluded (refer to Table)
- 37 female survivors included, 24 (TBI) & 13 (non-TBI)
  - ALL/NHL - 23 (62.2%%), AML - 8 (21.6%), MDS - 4 (10.8%), CML - 2 (5.4%)
  - 67.6% responded to questionnaires
- Median age at HSCT for those with spontaneous pregnancy
  - 15.5 yr (TBI) & 11.3 yr (non-TBI)
- Median age at pregnancy: 28.5 yr (TBI) & 22.8yr (non-TBI)
- Mean duration from HSCT to 1st pregnancy: 12 yr (TBI) & 14yr (non-TBI)

Reasons for exclusion	No. excluded
<18 years	
• Pre-pubertal	3
• Post-pubertal	
• Not in relationship as stated in questionnaires/ medical notes	5
• Severe intellectual disability and not in relationship as stated in questionnaires	1
• No documentation in clinic notes being sexually active, but did not respond to questionnaires	2
• Died at age of 17	1
≥18 years and stated as not sexually active in the questionnaires	6

Pregnancy resulting in live birth
Group 1 – Female HSCT survivors with TBI (3 of 24 ➔ 12.5%)
Group 2 – Female HSCT survivors without TBI (3 of 13 ➔ 23.1%)

Group 1 – With TBI

Patient	Age at transplant	Diagnosis of malignancy	Cyclophosphamide (gram/m²)	Total irradiation dose	Menarche before HSCT	Gonadal failure post-HSCT	Age at pregnancy	No. of live-birth(s)
1	15.6 years	CML (CP 1)	6.1	TBI 12 Gy	Yes	Yes	28.5 years	2 (Twins)
2	13.9 years	Relapsed ALL	6.2	TBI 12 Gy CRT 18 Gy	No	Yes	22.5 years	1
3	15.5 years	Relapsed ALL	9	TBI 12 Gy CRT 12Gy	Yes	Yes	~30 years	1

Group 2 – Without TBI

Patient	Age at transplant	Diagnosis of malignancy	Cyclophosphamide (gram/m²)	Dose of other Alkylating agent	Menarche before HSCT	Gonadal failure post-HSCT	Age at pregnancy	No. of live-birth(s)
4	5.7 years	CML (Ph +)	5.1	Busulfan 16 mg/kg	No	Yes	22.8 years	1
5	11.7 years	MDS with monosomy 7	3.5	Busulfan 16mg/kg	Yes	Yes	30.2 years	1
6	11.3 years	AML -> relapsed biphenotypic leukemia	2	Melphalan 160mg/m²	No	Yes (4 yr post HSCT)	18.4 years	2

- 1st study of sexually active female allogeneic HSCT survivors transplanted at ≤ 18 years for hematological malignancies, reporting successful spontaneous pregnancy resulting in live-birth(s).
- Higher proportion of female childhood HSCT survivors having spontaneous pregnancies than previously reported
- Findings important for physicians caring for HSCT adults, to optimize planning for contraception, pre-conception cardiac assessment & to assist family planning