sex-mismatched after stem cell transplant: a case report

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Introduction :

More than 90% of cases of primary ovarian insufficiency (POI) are idiopathic, but they can be attributed to chromosomal abnormalities, autoimmune or iatrogenic causes. POI associated with stem cell transplantation is generally awarded to total body irradiation and chemotherapeutic agents. This treatment, also called "conditioning", is performed in the days preceding the transplant. The particularity of this observation is that it describes a change in cell line in our patient following bone marrow transplant from her HLA matched brother This led to a diagnostic confusion at first with disorders of sexual development patient.

Case report :

A 15-year old girl was referred to our department of endocrinology in 2017 with secondary amenorrhea. She was diagnosed with lymphoblastic Leukemia at the age of 13. She received chemotherapy and total body irradiation(TBI) after which she had bone marrow transplantation. Patient had menarche at 12 years and 9 months, she had regular menstruations for 5 months. Breast development was automatically since the age of 10 years and physical examination showed normal female genitalia, Tanner stage 3. The hormonal profile showed elevated FSH and LH, low estrogen, and normal prolactin and testosteron(table1) .The diagnosis of POI was confirmed than . Pelvic ultrasound showed a pubertal uterus and two small ovaries without follicles. She had a grouth retardation in bone age (14 years). Chromosomal analysis was 46, XY. The genotype of the patient had changed after the allogeneic stem cell transplant from her brother. However, chromosomal analysis on skin fibroblasts showed a normal female genotype identic to the karyotype convenient before the transplantation.

FSH mIU/mL	LH IU/mL	Prolactine ng/ml	Testosterone ng/ml	Estrogen Pg/ml	TSH mIU/L	AMH ng/ml
84,6	**41,4**	10,6	0,5	**12,3**	2,32	<0,02

Table 1: hormonal exploration

Discussion :

- Ovarian follicles constitute a principal target for chemotherapeutic agents. The damage is secondary to the apoptosis of primordial follicle and blood vessel damage [1]
- Treatment by Alkylating Agents (busulfan and cyclophosphamide), similar to what our patient has received, is associated to POI in about 100% of cases [2][3]
- Comparing auto and allo-SCT, this last is responsible for a more severe immunosuppressive effect of the conditioning regimens to avoid graft rejection. That's why it is associated with a more severe derangement of the immune system than auto-SCT .
- It is noted that pubertal or adult female' ovary function would be more affected by chemotherapy than pre-pubertal girls[4]
- Our patient has a high probability of developing POI: underlying diseases (ALL), sex, pubertal phase, Alkylating agents, total body irradiation and allo-SCT.
- The particularity of this observation is the change of the karyotype to a male karyotype after CST from her full HLA matched brother. This led to a diagnostic confusion at first with disorders of sexual development patient. the geneticist's opinion was to confirm the possibility of karyotype change in a gender-mismatched SCT (xy). We complete by a karyotype on skin fibroblasts, it was 46 XX. Her karyotype is so changed to a karyotype of donor origin (her brother). Only the karyotype of hemocyte was 46 XY.
- Two similar cases were reported in literature, the first was presented with secondary amenorrhea and the second with primary amenorrhea(table 2).

	Case 1 (2016)	Case 2 (2015)	Case3 (2017)
Age year	18	17	15
Motif	primary amenorrhea	secondary amenorrhea	Secndary amenorrhea
Underlying disease	ALL Allo-SCT : Brother, 12 years CT : 12 years	ALL Allo-SCT : Brother, 15 years CT: 10 years + TBI	ALL Allo-SCT : Brother, 15 years
physical examination	height 172 cm; female genitalia A2P2S3M0	menarche at 11 years, regular cycles 4 years	Menarche at 13 years , regular cycles 5 months
Laboratory examination	FSH= 73 U/ml; LH= 30 U/ml E2= 23 pg/ml	FSH, LH , E2	FSH=84,6 LH=41,4 E2=12,3
Perineal and pelvic ultrasound	Small uterus ovaries not visualized	Small uterus and ovaries	Small uterus and ovaries
Karyotype before SCT	46XX	46 XX	46XX
Karyotype after SCT	46 XY	46 XY	46XY

Table 1: caracteristics of three cases of sex mismatched after cell transplant

Conclusion

Ovarian failure is common after allo-stem cell transplant (SCT). It is usually secondary to POI due to chemotherapy. Sex-mismatched after SCT does not affect fertility. Only the karyotype of hemocyte is 46 XY, but other somatic cells and germ cells are 46 XX as somatic and germ cells originated during the embryonic stage.

Références:
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