Poster Number: P1-P140

Sertoli cell function after chemotherapy in boys with hematologic malignancies

Romina P. Grinspon[1], María Arozarena[2], Silvina Prada[2], Graciela Bargman[3], María Sanzone[1], Marjorie Morales Bazurto[1], Marcela Gutierrez[2], Patricia Bedecarrás[1], Ana Kannemann[4], Silvia Gottlieb[1], Ariel J. Berenstein[1], María Gabriela Ropelato[1], Ignacio Bergadá[1], Luis A. Aversa[2], Rodolfo A. Rey[1]*

1 Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE), CONICET – FEI – División de Endocrinología, Hospital de Niños Ricardo Gutiérrez. 2 Unidad de Hematología, Hospital de Niños Ricardo Gutiérrez. 3 División de Endocrinología, Hospital Pedro de Elizalde. 4 División de Hemato Oncología, Hospital Pedro de Elizalde. Buenos Aires. Argentina

Background

Evidence exists on the deleterious effect that chemotherapy and radiotherapy have on germ cells, and some attention has been driven to the effects on Leydig and Sertoli cells of the adult gonads, but information is virtually non-existent on the effects of oncologic treatment on testicular somatic cell components during childhood and adolescence.

Aim of the Study

To determine whether the oncologic treatments used in prepubertal and pubertal boys with ALL (acute lymphocytic leukaemia), AML (acute myeloid leukaemia) or NHL (non-Hodgkin lymphoma), the set of most frequent paediatric cancers, affect the endocrine function of the somatic component of the developing testis

Methods

Design: Retrospective, analytical, observational study at Ricardo Gutiérrez and Pedro de Elizalde Children's Hospitals, Buenos Aires, Argentina.

Main outcome measure: Serum concentration of AMH (EIA AMH/MIS®, Beckman-Coulter Co).

Secondary outcome measures: Serum LH, FSH and testosterone.

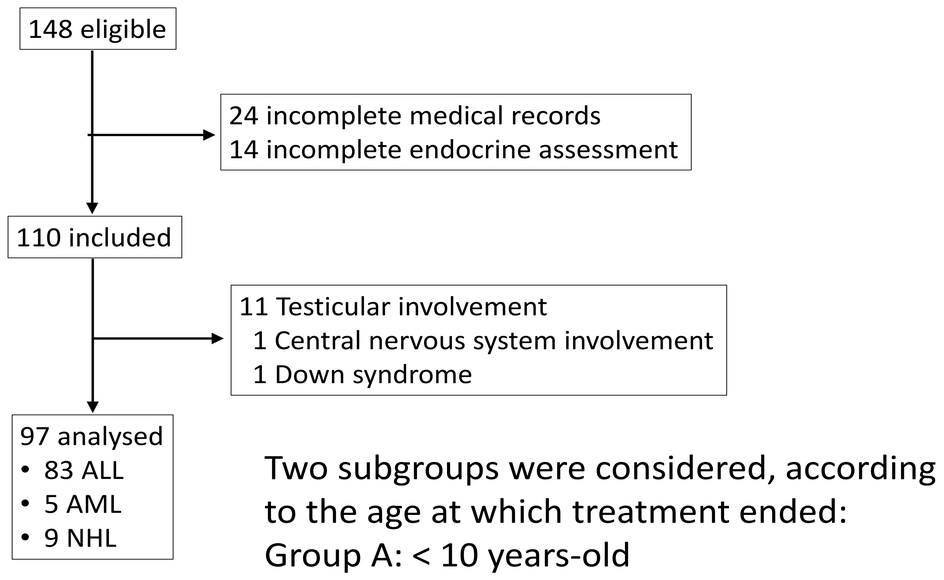
For comparison, serum hormone levels from a normal population of 179 apparently normal prepubertal boys were used.

Inclusion criteria: Males aged 1-18 years referred with the diagnoses of ALL, AML or NHL from the Units of Haematology to the Divisions of Endocrinology for the assessment of gonadal function (2002 and 2015).

Exclusion criteria: Conditions affecting the gonadal axis, as malignancy involving the central nervous system or the testes, trisomy 21 or in any other condition known to affect the hypothalamic-pituitary-testicular axis.

Results

Fig. 1 Hormone serum levels in cryptorchid boys



Two subgroups were considered, according to the age at which treatment ended:
Group A: < 10 years-old
Group B: ≥ 10 years-old

Table 1. Characteristics of the whole study sample.

	Group	Whole sample (n=97)	ALL (n=83)	AML (n=5)	NHL(n=9)
n	A	58	51	4	3
	B	39	32	1	6
Age at diagnosis, yr	A	3.9 (1.1-7.1)	3.7 (1.8-7.1)	3.4 (1.1-5.0)	6.4 (4.7-6.9)
	B	12.1 (8.1-16.6)	12.0 (8.1-16.6)	9.4	12.5 (8.2-15.4)
Age at end of chemotherapy, yr	A	6.1 (2.6-9.3)	6.0 (3.8-9.3)	5.8 (2.6-8.2)	7.2 (5.2-8.7)
	B	13.5 (10.3-18.6)	14.0 (10.3-18.6)	11.6	12.8 (10.6-17.4)
Elapsed time, end of chemotherapy-first endocrine assessment, yr	A	1.9 (0.1-12.9)	1.6 (0.1-12.9)	2.5 (1.8-5.3)	1.1 (1.1-8.6)
	B	0.8 (0.1-11.0)	0.8 (0.1-6.9)	3.9	1.5 (0.2-10.4)
Elapsed time, end of chemotherapy-last endocrine assessment, yr	A	4.3 (0.1-12.9)	4.0 (0.1-12.9)	3.2 (1.9-9.8)	5.5 (4.8-12.7)
	B	2.5 (0.1-12.0)	2.4 (0.1-6.9)	3.9	3.5 (0.2-12.0)

End of chemotherapy < 10 years of age | **End of chemotherapy > 10 years of age**

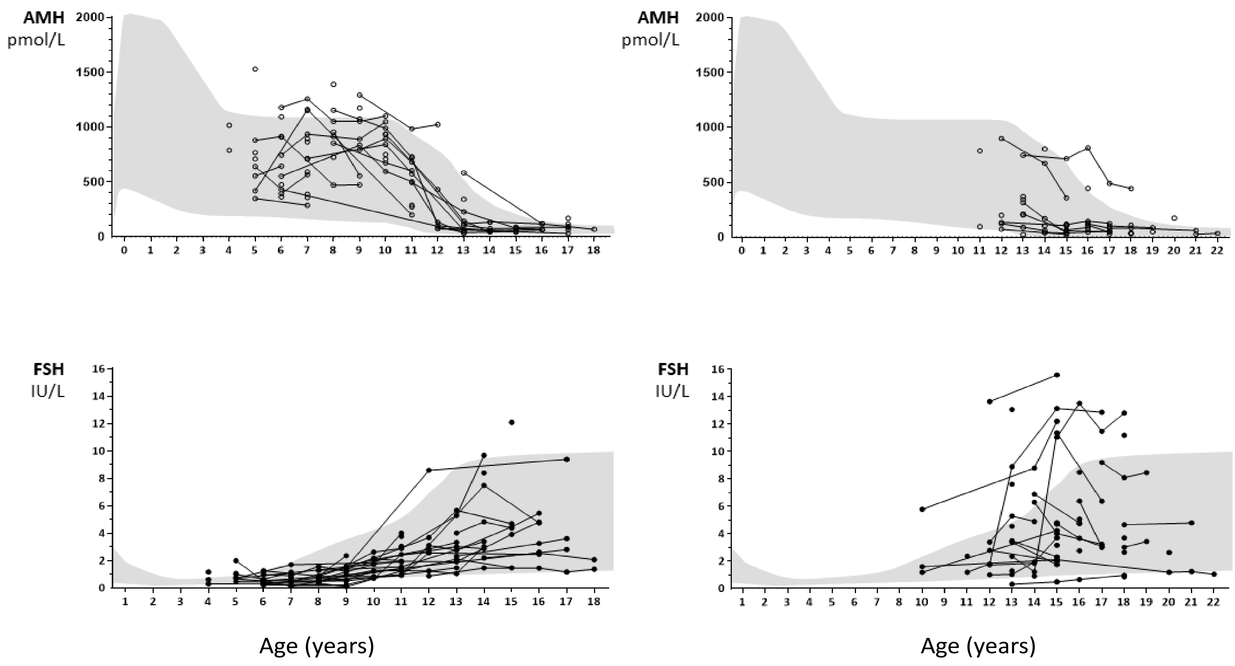


Fig 2. Progression with age of absolute serum levels of AMH and FSH

Serum AMH was never < 2 SDS for up to 12 years of follow-up.
FSH was elevated (>2 SDS) in: 8 patients (13.8%) of group A and 11 patients (28.2%) of group B

End of chemotherapy < 10 years of age | **End of chemotherapy > 10 years of age**

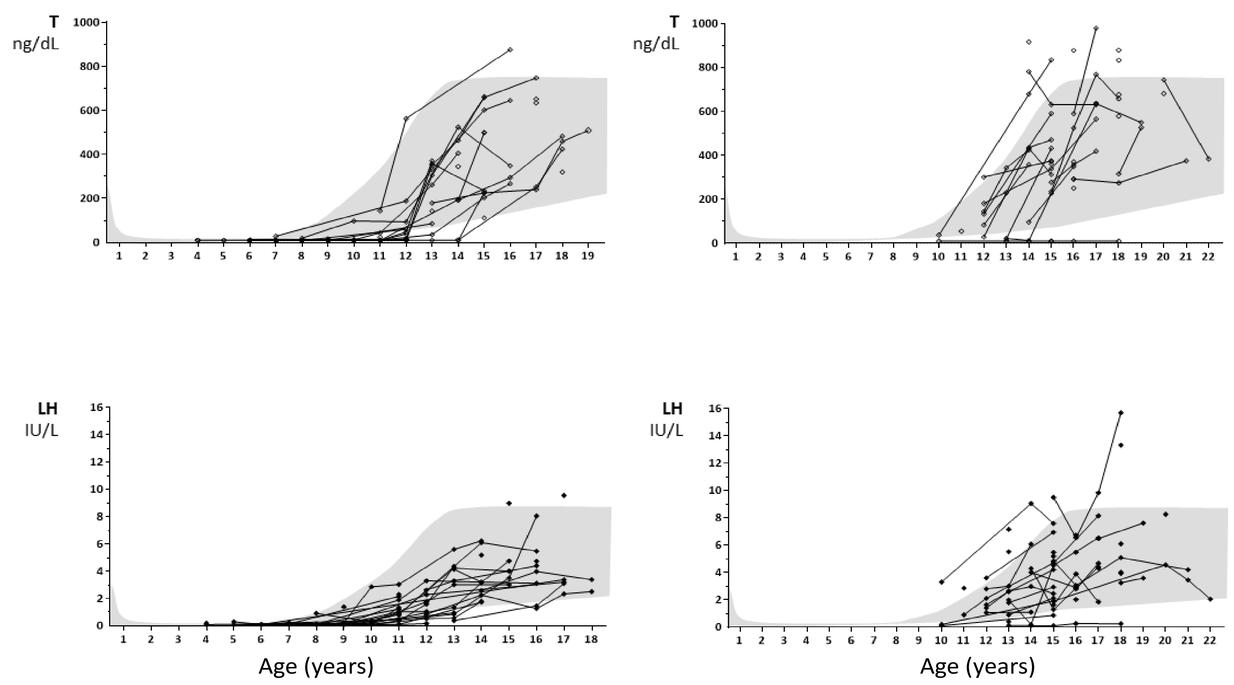


Fig 3. Progression with age of absolute serum levels of Testosterone (T) and LH

Serum testosterone remained below the reference range in only one pubertal patient of group B.
LH was elevated (> 2 SDS) in: 4 patients (6.9%) of group A and 10 patients (25.6%) of group B

End of chemotherapy < 10 years of age | **End of chemotherapy > 10 years of age**

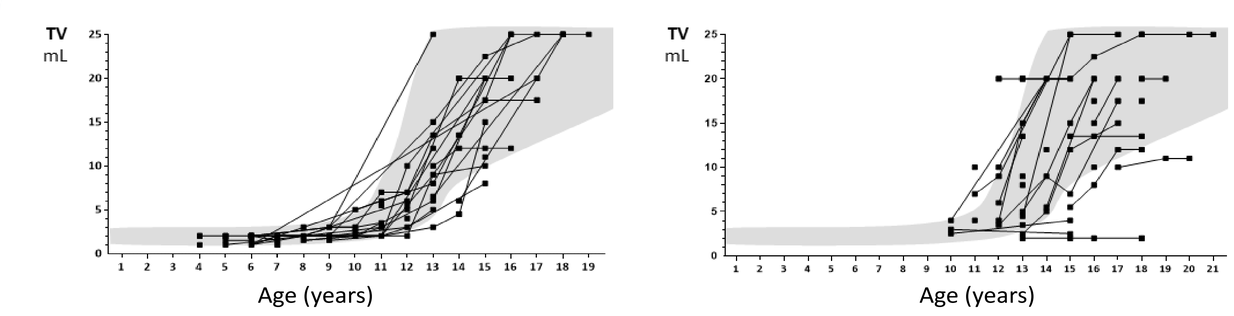


Fig 4. Progression with age of mean testicular volume (TV)

Testicular volume remained below the expected value in one patient at age 15 years. In another case, testicular volume was initially low but recovered as pubertal development progressed.
Testicular volume remained below the expected value in 5 cases.

Conclusions

The regimens used in the treatment of patients with ALL, AML or NHL in the last two decades seem not to provoke an overt damage of testicular somatic components, as revealed by normal levels of AMH and testosterone. However, a mild primary testicular dysfunction may be observed, usually compensated by slightly elevated gonadotropin secretion by the pituitary, which generally does not require hormone replacement therapy.