Leucemia Aguda: como Segunda Enfermedad Maligna 29 años de experiencia en el Htal Garrahan

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Objetivos

- ✓ Distribución de LA como SMN
- ✓ Latencia de las SMN
- ✓ Analizar la evolución de las SMN
- ✓ Evaluar el rol de los tratamientos administrados

Leucemias ingresadas al HPG

Agosto1987 - Agosto 2016

LEUCEMIAS AGUDAS

Total= 2477

LLA	LMA
Total=1878	Total=599

7-LLA 87 Total=99	1-LLA 90 Total=403	4-LMA 90 Total=96	1-LMA 95 Total=75
1-LLA 96 Total=487	ALLIC-02 Total=522	4-LMA 99 Total=196	1-LMA 08 Total= 232

Protocolos actuales

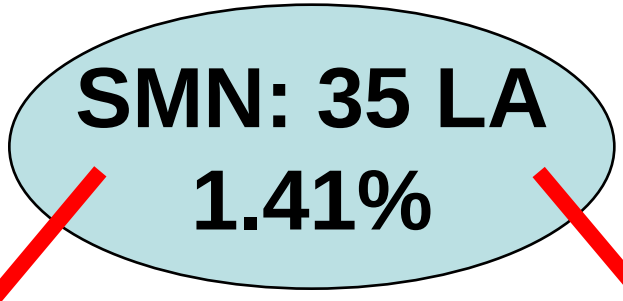
ALLIC 2010

TOTAL: 367

LMA 08

TOTAL: 232

Distribución de SMN



LMA: 27
4.5%

LLA: 6
0.3%

LALA: 2

Latencia y tto de SMN

Latencia media: 31 (rango: 5 - 110) meses

Tratamiento:

- ✓ los 35 pacientes recibieron tratamiento
- ✓ Quimioterapia 35
- ✓ Tmo 4

Evolución de SMN

N= 35

- ✓ Remisión Completa (RC) 26 (76,2%)
- ✓ Muertes tempranas 4 (9,5%)
- ✓ Respuesta parcial 3 (9,5%)
- ✓ Progresión de enfermedad 2 (4,8%)

- ✓ Muertes en RC 5 (10%)
- ✓ Remision Completa a la actualidad 21 (60%)

Media de seguimiento: 55,3 (rango: 14-221) meses

Primera enfermedad

N= 35

- ✓ Leucemias agudas 15
- ✓ Retinoblastoma 9
- ✓ Linfomas 2
- ✓ Tumores solidos 9

- Las leucemias agudas son la enfermedad oncológica más frecuente en pediatria, seguida de los tumores de sistema nervioso central y los linfomas.

- Se diagnostican un promedio de 482 LA por año 40% (ROHA)

- El 78% son LLA y el 20% LMA

- La LA como SMN es una entidad infrecuente en pediatría, que oscila entre el 2 y el 7%

- La SMN mas frecuente es LMA

Segunda enfermedad maligna

La aparición de una segunda enfermedad maligna (SMN) depende de:

- factores genéticos
- del tipo de tratamiento oncológico recibido,
- de exposiciones medioambientales y del estilo de vida.

Leucemia secundaria

- La LMA secundaria ocurre en pacientes tratados previamente con agentes alquilantes: *ciclofosfosfamida, ifosfamida, melfalán, clorambucilo,busulfán, nitrosureas (carmustina, lomustina, fotemustina, etc), hidracinas y derivados de tiazinas (dacarbazina, procarbazina, temozolamida)*

- o con inhibidores de la topoisomerasa II, como el *etopósido y el tenipósido*, y su riesgo es dosis dependiente.

Latencia:

- Los alquilantes: la latencia media de aparición de la enfermedad es de 4 a 6 años

- Los inhibidores de la topoisomerasa II: de 2 a 4 años

- Por encima de los 10 a 15 años, el riesgo disminuye francamente.

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Research Article

Cancer Epidemiology, Biomarkers & Prevention

Subsequent Malignant Neoplasms in a Population-Based Cohort of Pediatric Cancer Patients: A Focus on the First 5 Years

Jason D. Pole[1,2], Lan Ying Gu[3], Victoria Kirsh[2,3], Mark L. Greenberg[1,4,5], and Paul C. Nathan[4]

Abstract

Background: The purpose was to describe the development of subsequent malignant neoplasms (SMN) among a population-based cohort of pediatric cancer patients, with a focus on SMNs that occurred within the first 5 years from diagnosis.

Methods: The cohort was identified from POGONIS, an active provincial registry. Cohort members were Ontario residents ages 0 to 14.9 years at primary diagnosis between January 1985 and December 2008. SMNs that developed <18 years were captured by POGONIS, whereas SMNs diagnosed later were identified through linkage. Cumulative incidence and standardized incidence ratios (SIR) were calculated, and proportional hazards models were estimated to examine factors associated with SMN development.

Results: A total of 7,920 patients were eligible. 2.4% (188/7,920) developed 197 SMNs. Mean follow-up time was 10.7 years (SD = 7.6 years; range, 0.0–26.4 years) with mean time to SMN of 8.5 years (SD = 6.3 years; range, 0.0–24.9 years). The SIR for the development of a SMN was 9.9 [95% confidence interval (CI), 8.6–11.4]. 40.6% of SMNs (80/197) developed within 5 years. Early SMNs were more likely to be leukemia and lymphoma. Factors associated with early SMN were primary diagnosis of a bone tumor (OR, 4.88; 95% CI, 1.52–15.60), exposure to radiotherapy (OR, 1.82; 95% CI, 1.02–3.22), and the highest dose of epipodophyllotoxin (OR, 3.74; 95% CI, 1.88–7.42).

Conclusions: Over 40% of SMNs diagnosed in childhood cancer patients occurred in the first 5 years after diagnosis, suggesting a need for early and ongoing surveillance.

Impact: The early development of certain SMNs reinforces the need for early and continued surveillance at all stages for pediatric cancer patients. *Cancer Epidemiol Biomarkers Prev; 24(10); 1585–92. ©2015 AACR.*

Introduction

Over the last 30 years, survival among children diagnosed with cancer has risen dramatically, from 5-year survival rates below 60% in 1975 to rates exceeding 80% today (1). Consequently, the size of the childhood cancer survivor population has expanded. It is estimated that there are over 400,000 survivors (0.11% of the population) in the United States, of whom 24% have survived more than 30 years (2). Although better risk stratification at diagnosis has made it possible to reduce treatment intensity for a proportion of childhood cancers, much of the improvement in survival has been achieved by intensifying therapy for high-risk patients using combinations of surgery, chemotherapy, radiotherapy, and hematopoietic stem cell transplantation (3). In particular, chemotherapy survival as a result of intensified treatment place childhood cancer survivors at risk for long-term adverse outcomes.

Childhood cancer survivors have been shown to have elevated risks for the development of diverse chronic physical health conditions (collectively known as "late effects"; refs. 5–7). Among the most consequential late effect is the development of subsequent malignant neoplasms (SMN), which can cause serious morbidity and premature mortality. Although several cohort studies exist that examine the development of SMNs among pediatric cancer patients, most only consider SMNs that develop 5 years or more from the primary diagnosis. This exclusion criterion can lead to an underestimate of the true incidence of SMN development in this population.

The Childhood Cancer Survivor Study (CCSS), a large North

Conclusiones

- Conocer los efectos tardíos a largo plazo y vigilancia permanente
- La SMN es un evento infrecuente en pediatría
- La SMN más frecuente es la LMA
- De las 35 LA como SMN todas habían recibido inhibidores de Topo II y/o agentes alquilantes en su primer tratamiento
- En las SMN hematológicas, un segundo tratamiento puede ofrecer resultados semejantes a los de las enfermedades hematológicas *de novo*

Conclusiones

- El desarrollo de SMN refuerza la necesidad de una vigilancia temprana y continua en todas las etapas para los pacientes de cáncer pediátrico. *Cáncer Epidemiol Biomarkers Prev; 24 (10); 1585-1592. © 2015 AACR* .

- Promoción de la salud, estilo de vida saludable:

  - evitar tabaquismo, disminuir la ingesta de alcohol.

  - realizar ejercicio físico en forma regular

  - minimizar la exposición al sol

  - mantener una adecuada salud bucal

¡Muchas Gracias!