

Educational Programme on Transplant Infectious Diseases

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Pediatric clinical case

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© 8 years old boy

© **Diagnosis:**

1. Acute myeloid leukemia (Dg: 15/Nov/11)
2. Allogeneic HSCT (April 13)
3. Previous to HSCT: multiple episodes of FN, probable invasive aspergillosis

JUNE 2013 (+60)



Engraftment failure

Fever (neutropenia) + cough + rhinorrhea

No findings in physical examination

Normal lung examination

Chest X-ray

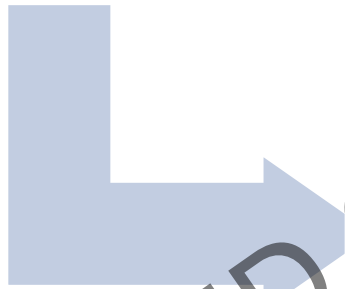
IF for respiratory viruses

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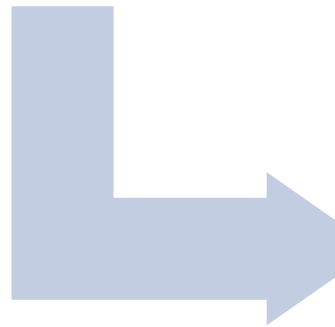


Respiratory syncytial virus

Upper respiratory
infection by
respiratory syncytial
virus



What will be do??



Infectious Diseases team

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Frequency and Clinical Outcome of Respiratory Viral Infections and Mixed Viral-bacterial Infections in Children With Cancer, Fever and Neutropenia

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TABLE 2. Respiratory Viruses Detected in 190 Episodes of Fever and Neutropenia in Children With Cancer

Respiratory Virus	Sole Viral Infection	Mixed Viral Infection	Mixed Viral-bacterial Infection	Total, n (%)
Respiratory syncytial virus	37	14	24	75 (31)
Rhinovirus	25	12	19	56 (23)
Parainfluenza	14	6	9	29 (12)
Influenza A	15	5	7	27 (11)
Bocavirus	4	12	10	26 (11)
Human metapneumovirus	4	7	3	14 (6)
Adenovirus	3	3	5	11 (5)
Coronavirus	2	1	0	3 (1)
Total	104	60	77	241 (100)

*Juan P. Torres, MD, PhD, María E. Santolaya, MD**

The Pediatric Infectious Disease Journal • Volume 31, Number 9, September 2012

TABLE 3. Clinical Presentation and Outcome of Respiratory Viral Infections, Bacterial Infections and Mixed Respiratory Viral-bacterial Infections in Children With Cancer, Fever and Neutropenia

	Respiratory Viral FN Episodes (n = 127)	Bacterial FN Episodes (n = 34)	Mixed Viral-bacterial FN Episodes (n = 63)	P
At admission				
Median age in years (p25–75%)	7 (3.5–11)	10.5 (3–13)	7 (4–11.5)	NS
CRP (mg/L) (p25–75%)	40* (15–80)	58 (26.5–128)	76* (28–147)	<0.05*
PRISM score (median)	1*	4*	1	<0.05*
Clinical outcomes				
Days of fever after admission (p25–75%)	2* (1–3)	2 (1–6.75)	3* (1–6.25)	<0.05*
Hypotension (n; %)	3*† (2%)	9* (26%)	18† (28%)	<0.05*†
PICU admission (n; %)	7*† (5%)	9* (26%)	14† (22%)	<0.05*†
Median days of stay (p25–75%)	6*† (4–9)	11.5* (7.7–17)	11† (6.5–14)	<0.05*†
Days of neutropenia after admission (p25–75%)	4 (2–7)	7 (3–13.7)	5 (3–9)	0.06
Median CRP value 48 h after admission (p25–75%)	58*† (31–124)	123* (71–178)	127† (46–193)	<0.05*†

* and †, significant P value.

PRISM indicates Pediatric Risk Mortality; NS, not significant P value.

*Juan P. Torres, MD, PhD, María E. Santolaya, MD**

Table 2. Risk Factors of Respiratory Syncytial Virus–Associated Complications in Hematopoietic Stem Cell Transplantation Patients

Progression to LRTID

- Lymphopenia $<0.2 \times 10^9/L$
- Older age
- Mismatched/unrelated donor
- Allogeneic HSCT <1 mo
- Neutropenia $<500/\mu L$
- No therapy with aerosolized ribavirin + IVIG

Mortality

- Preengraftment
- Lymphopenia $<0.2 \times 10^9/L$
- Allogeneic HSCT <1 mo
- Severe immunodeficiency
- Older age (>65 y)

Abbreviations: HSCT, hematopoietic stem cell transplantation; IVIG, intravenous immunoglobulin; LRTID, lower respiratory tract infectious disease.

RSV infection mortality in HSCT recipients



© High risk immunocompromised patients:

Preengraftment HSCT (mortality > 80% without therapy)

Pediatr Infect Dis J 2007;26: 1089–1093

J Pediatr. 2003;143: 532–540.

J Pediatr Hematol Oncol • Volume 29, Number 4, April 2007

¿ Which is the best therapy for this child?



- A. Oral Ribavirin
- B. Inhaled Ribavirin
- C. IVIG
- D. Palivizumab
- E. No specific therapy is indicated

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Upper respiratory
infection by
respiratory syncytial
virus

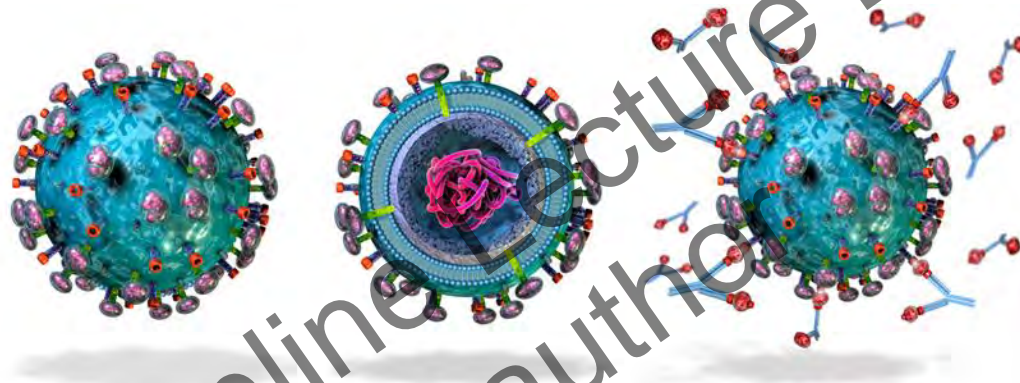


Immunocompromised patient
HSCT / engraftment failure

PALIVIZUMAB 15 mg/k IV

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PALIVIZUMAB



- © IgG₁ Humanized, murine, monoclonal antibody, that bind RSV glycoprotein F, inhibiting the entry of the virus to the host cell

PALIVIZUMAB (Prophylaxis)



- © **High risk for severe RSV disease:** prematurity, chronic pulmonary disease, congenital heart disease, **immunocompromised host**
- © Prophylaxis in children < 2 years of age with high risk of severe disease: Safe and effective, ↓ morbi-mortality: FDA, AAP, EMA
- © Standard of care in high risk patients

PALIVIZUMAB / IMMUNOCOMPROMISED PATIENTS



© High risk immunocompromised patients:

Preengraftment HSCT (mortality > 80% without therapy)

© No randomized, double blind, placebo controlled trial

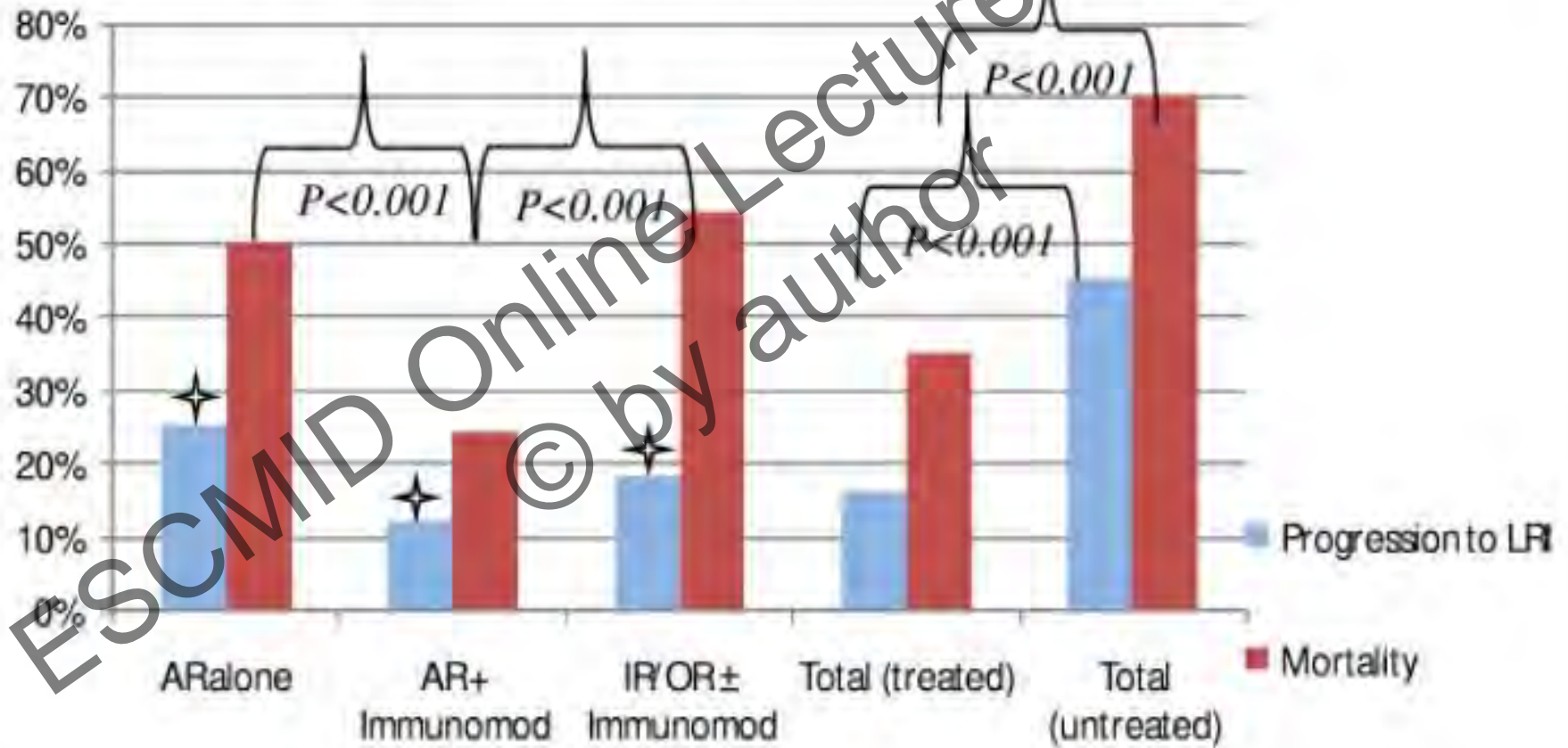
© Extrapolated from another risk groups

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Figure: Summary of outcome data by type of regimen received



✦ For progression to LRI: AR alone vs AR plus immunomodulators or IR or OR with or without immunomodulators; $P=0.13$

PALIVIZUMAB / INMUNOCOMPROMISED PATIENTS



- © 11 children: Ribavirin + PVZ IV (survival: 91%)
- © Good tolerance (therapy)
- © ↓ time of viral shedding
- © Early use (URTI)
- © Considered cost/effectiveness

What happened to the child?



After Palivizumab therapy

- No more fever
- Decrease cough and rhinorrhea
- VRS negative
- No LRTID
- Natural evolution or palivizumab effect???

HOME MESSAGES



- ⊙ The most important issue is PREVENTION
- ⊙ Suspected respiratory virus infection
- ⊙ Early diagnosis/early therapy
- ⊙ Palivizumab could be considered as one of the drugs available for RSV treatment in HSCT patients.
- ⊙ Newer therapies on the horizon

Gracias
Thanks
Obrigada



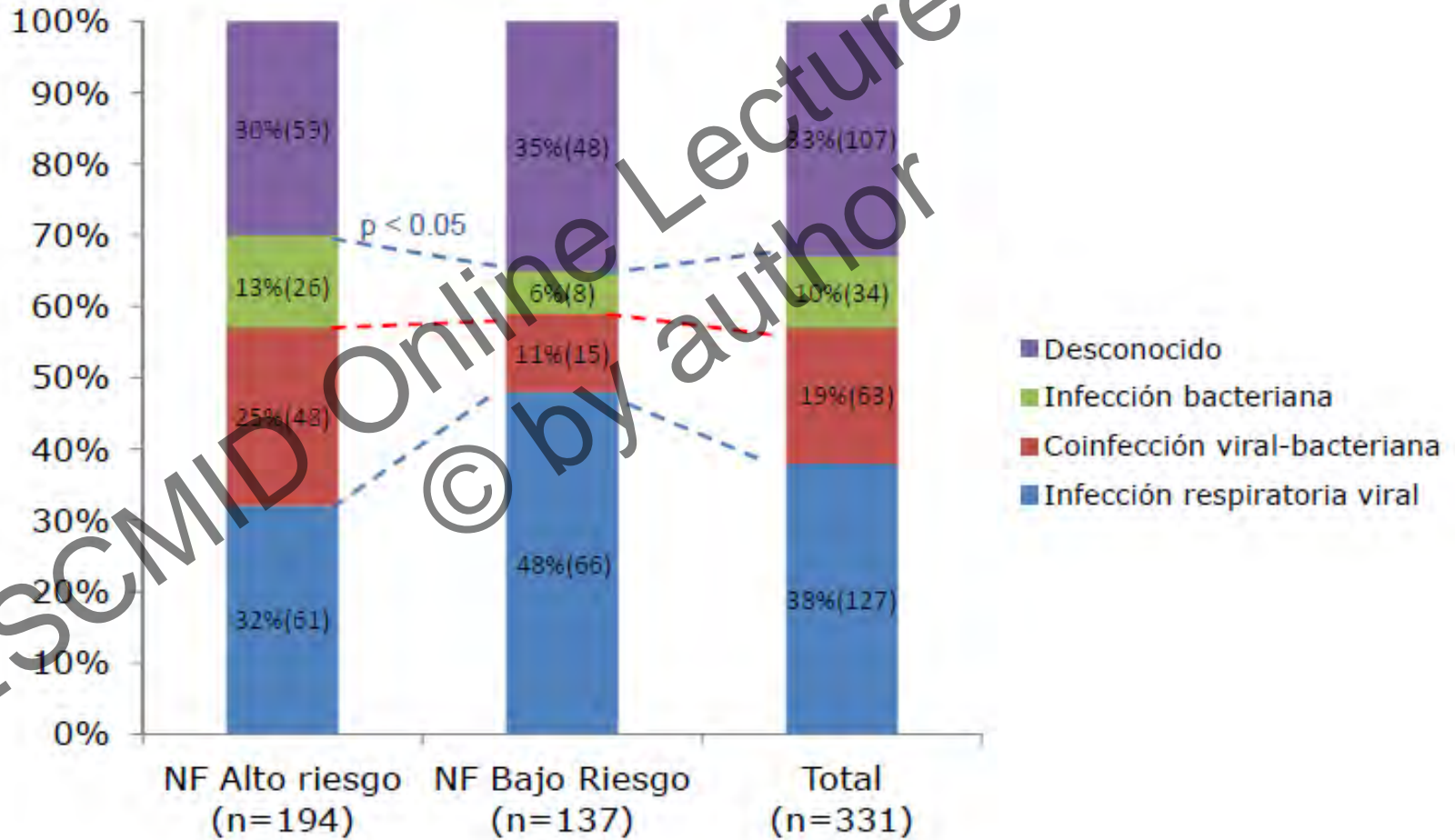
¿ What is the most likely etiology?



- A. Adenovirus
- B. Influenza
- C. *Streptococcus pneumoniae*
- D. Respiratory syncytial virus
- E. *Mycoplasma pneumoniae*



Respiratory viral detection in children with cancer, fever and neutropenia



A review of palivizumab and emerging therapies for respiratory syncytial virus

for RSV. Palivizumab is usually not started until lower tract disease occurs which may impair maximum effectiveness [75]

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