

POSTER PRESENTATION

Open Access

# Emperipolesis and cell death in NOD2-related Blau Syndrome and Crohn's disease

Carl El Janssen<sup>1\*</sup>, Carlos D Rose<sup>2</sup>, Antonio Naranjo<sup>3</sup>, Brigitte Bader-Meunier<sup>4</sup>, Rolando Cimaz<sup>5</sup>, Miroslav Harjacek<sup>6</sup>, Pierre Quartier<sup>4</sup>, Rebecca TenCate<sup>7</sup>, Caroline Thomee<sup>8</sup>, Isabelle Cleynen<sup>1</sup>, Tammy M Martin<sup>9</sup>, Gert De Hertogh<sup>1</sup>, Tania Roskams<sup>1</sup>, Valeer J Desmet<sup>1</sup>, Carine H Wouters<sup>1</sup>

From 18th Pediatric Rheumatology European Society (PReS) Congress Bruges, Belgium. 14-18 September 2011

## Background

Blau Syndrome (BS), a rare autoinflammatory disease characterized by non-caseating granulomas, is caused by gain-of-function mutations in NOD2. Crohn's disease (CD) is associated with intestinal granulomas, and SNPs in NOD2. Emperipolesis, the 'inside round about wandering' of lymphocytes within other cells is a typical feature of Rosai-Dorfman disease, and seen occasionally in malignancies. Cell survival and cell death are possible outcomes for both the engulfed and engulfing cells.

## Aim

To investigate emperipolesis and cell death in BS and CD granulomas.

## Methods

Morphological and immunohistochemical study of granulomas was undertaken in 8 BS and 7 pediatric CD biopsies, using H&E and immunohistochemistry for leukocyte markers (CD68, CD4, CD8, CD20), cytokines (IFN $\gamma$ , IL6, IL10, IL17, TGF $\beta$ , TNF $\alpha$ ) and death-proteins (Bcl2, Fas, FasL, activated caspase 3).

## Results

All BS biopsies showed polycyclic granulomas with large lymphocytic coronas and extensive emperipolesis of lymphocytes within multinucleated giant cells (MGCs). This was associated with macrovesicular/microvesicular degeneration of lymphocytes inside MGCs (Fig1a), and MGC death (Fig1b). Emperipolesis selectively involved

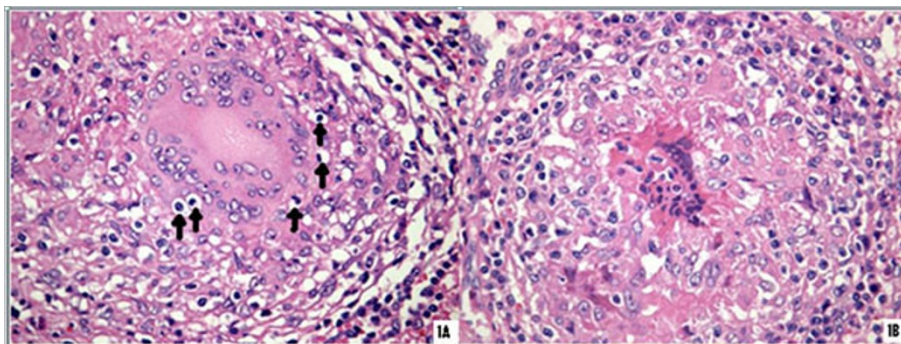


Figure 1

\* Correspondence: Carljanssen39@hotmail.com

<sup>1</sup>Leuven University Hospital, Belgium

Full list of author information is available at the end of the article

CD4+ T cells. In addition, vesicles and degenerative remnants inside MGCs stained strongly for IL-6 and IL-17. A moderate expression of Bcl2 was present, Fas and FasL expression were seen in emperipoletic lymphocytes and MGCs but caspase 3 was virtually absent. In contrast, CD biopsies demonstrated simple isolated granulomas with subtle lymphocytic coronas; emperipolesis was sporadically found in a few biopsies, and was associated with crystalline inclusions, but not with MGC death.

## Conclusion

Emperipolesis of CD4+lymphocytes is an important feature of BS and is associated with MGC death. NOD2 mutations causing NF- $\kappa$ B hyperactivation and influencing autophagy pathways may be involved. In CD with NOD2-SNPs, emperipolesis is exceptional and crystalline inclusions are present. (Figure 1)

## Author details

<sup>1</sup>Leuven University Hospital, Belgium. <sup>2</sup>DuPont Children's Hospital, Wilmington, US. <sup>3</sup>Hospital Universitario de Gran Canaria, Spain. <sup>4</sup>Hôpital Necker, Paris, France. <sup>5</sup>AOU Meyer and University of Florence, Italy. <sup>6</sup>University Hospital Zagreb, Croatia. <sup>7</sup>Leiden University Medical Center, The Netherlands. <sup>8</sup>Centre Hospitalier Luxembourg. <sup>9</sup>Casey Eye Institute, Portland, Oregon.

Published: 14 September 2011

doi:10.1186/1546-0096-9-S1-P293

**Cite this article as:** Janssen *et al.*: Emperipolesis and cell death in NOD2-related Blau Syndrome and Crohn's disease. *Pediatric Rheumatology* 2011 **9**(Suppl 1):P293.

**Submit your next manuscript to BioMed Central  
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
www.biomedcentral.com/submit

