

POSTER PRESENTATION

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

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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 γ , IL6, IL10, IL17, TGF β , TNF α) 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

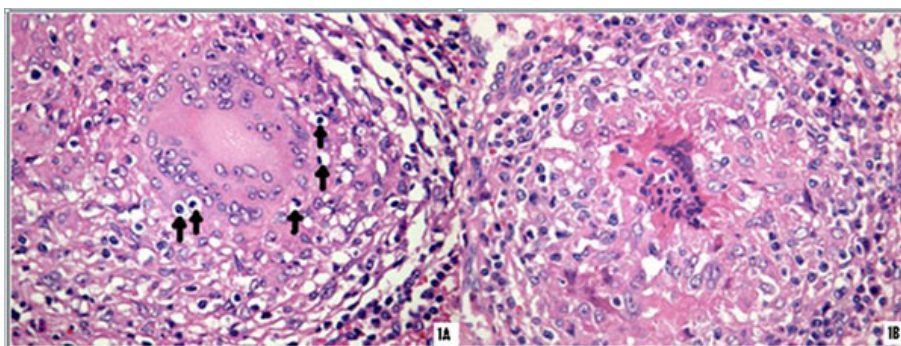


Figure 1

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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- κ B hyperactivation and influencing autophagy pathways may be involved. In CD with NOD2-SNPs, emperipolesis is exceptional and crystalline inclusions are present. (Figure 1)

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