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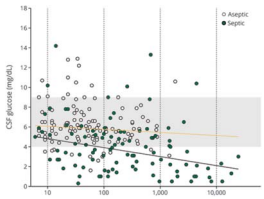
Abstracts

Articles appearing in the January 2018 issue

Pleocytosis is not fully responsible for low CSF glucose in meningitis



Objective The mechanism of hypoglycorrhachia—low CSF glucose—in meningitis remains unknown. We sought to evaluate the relative contribution of CSF inflammation vs microorganisms (bacteria and fungi) in lowering CSF glucose.

Methods We retrospectively categorized CSF profiles into microbial and aseptic meningitis and analyzed CSF leukocyte count, glucose, and protein concentrations. We assessed the relationship between these markers using multivariate and stratified linear regression analysis for initial and repeated CSF sampling. We also calculated the receiver operating characteristics of CSF glucose and CSF to serum glucose ratios to presumptively diagnose microbial meningitis.

Results We found that increasing levels of CSF inflammation were associated with decreased CSF glucose in the microbial but not aseptic category. Moreover, elevated CSF protein correlated more strongly than leukocyte count with low CSF glucose on initial (R^2 = 36%, $p < 0.001$) and repeated CSF sampling (R^2 = 46%, $p < 0.001$). Hypoglycorrhachia (<40 mg/dL) was observed in 50.1% of microbial cases, but only 9.6% of aseptic cases, most of which were neurosarcoidosis. Absolute CSF glucose and CSF to serum glucose ratio had similar low sensitivity and moderate to high specificity in diagnosing microbial meningitis at thresholds commonly used.

Conclusion The main driver of hypoglycorrhachia appears to be a combination of microbial meningitis with moderate to high degrees of CSF inflammation and proteins, suggesting that the presence of microorganisms capable of catabolizing glucose is a determinant of hypoglycorrhachia in meningitis. A major notable exception is neurosarcoidosis. Low CSF glucose and CSF to serum glucose ratio are useful markers for diagnosis of microbial meningitis.

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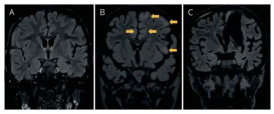
Phenotypic and functional complexity of brain-infiltrating T cells in Rasmussen encephalitis



Objective To characterize the brain-infiltrating immune cell repertoire in Rasmussen encephalitis (RE) with special focus on the subsets, clonality, and their cytokine profile.

Methods The immune cell infiltrate of freshly isolated brain tissue from RE was phenotypically and functionally characterized using immunohistology, flow cytometry, and T-cell receptor deep sequencing. Identification of clonally expanded T-cell clones was achieved by combining flow cytometry sorting of CD4+ and CD8+ T cells and high-throughput T-cell receptor Vβ chain sequencing. The most abundant brain-infiltrating T-cell clones were isolated and functionally characterized.

Results We found that $CD4^+$, $CD8^+$, and γδ T cells infiltrate the brain tissue in RE. Further analysis surprisingly revealed that not only brain-infiltrating $CD8^+$ but also $CD4^+$ T cells are clonally expanded in RE. All 3 subsets exhibited a Tc1/Th1 phenotype characterized by the production of interferon (IFN)–γ and tumor necrosis factor (TNF). Broad cytokine profiling at the clonal level showed strong production of IFN-γ and TNF and secretion of interleukin IL–5, IL-13, and granzyme B in $CD4^+$ and $CD8^+$ T cells.

Conclusions $CD8^+$ T cells were until now considered the central players in the immunopathogenesis of RE. Our study adds to previous findings and highlights that $CD4^+$ T-cell clones and γδ T cells that secrete IFN-γ and TNF are also involved. These findings underline the complexity of T-cell immunity in RE and suggest a specific role for $CD4^+$ T cells in orchestrating the $CD8^+$ T-cell effector immune response.

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