#### Abstract 1

# Congenital CMV Infection Presenting with Massive Intracerebral Hemorrhage

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Cytomegalovirus (CMV) is among the most common of intrauterine infections against which we have no effective preventative or therapeutic options. The developing nervous system is a frequent target of CMV and while most injuries are subclinical, severe insults leading to microcephaly and migration defects are well known. A 20-week gestational age fetus was found to have several abnormalities on prenatal ultrasound, the most prominent of which was a large echogenic focus in one cerebral hemisphere. Congenital CMV infection was identified by amniocentesis and maternal serology. The pregnancy was ended by early induction of labour for a 368g stillborn infant. Postmortem examination revealed massive intracerebral hemorrhage as the correlate for the sonographic finding. The microscopic examination of the brain was also striking for extensive polymicrogyria, a high burden of CMV and abundant angiocentric CMV pathology. Catastrophic intracerebral hemorrhage has not been previously reported in association with congenital CMV infection. The present case expands the range of potential injuries the developing brain is subject to in the setting of CMV infection and raises the possibility of a direct vascular injury.

## LEARNING OBJECTIVES

- Consider intracerebral hemorrhage in the range of potential outcomes in congenital CMV infection
- Describe how polymicrogyria may result from an insult during proliferation and migration
- Discuss possible mechanisms of injury to the developing brain by CMV

#### Abstract 2

# Brain Toxoplasmosis Comorbid with Autoimmune Disease: Complicated Immune Response And Case Demonstration

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Toxoplasmosis is an opportunistic infection caused by Toxoplasma gondii (TG), commonly involving the brain. Symptomatic clinical disease of TG infection is much more commonly associated with immunodeficiency; clinicopathological

manifestations of brain toxoplasmosis are linked to individual immune responses including brain infiltration of T-cells that are thought to fight against toxoplasmosis. In patients with autoimmune diseases, immune status is typically characterized by T-cell infiltration and complicated mainly by immunosuppressant and/ or immunomodulatory treatment. In this study, we demonstrate clinical and radiological features correlated with pathological features of brain toxoplasmosis at different disease stages in a patient with coexisting autoimmune diseases, including systemic lupus erythematosus and autoimmune hepatitis. The infiltration of CD8+ T-cells in toxoplasma immunostaining-positive acute lesions was greater than that in toxoplasma immunostainingnegative chronic lesions. We also review previously reported cases of brain toxoplasmosis with comorbid autoimmune diseases. Our present case and literature review suggest that brain toxoplasmosis in patients with autoimmune diseases may be asymptomatic unless disease complications occur; it may present as an incidental finding at postmortem examination of rapidly developed lesions. T-cell infiltration in patients with autoimmune diseases and coexisting toxoplasmosis may be at least partially reduced; ultimately, the roles of T-cell infiltration in brain toxoplasmosis deserve further investigation.

#### LEARNING OBJECTIVES

- Discuss complicated immune response to toxoplasmosis in patients with autoimmune diseases.
- Describe clinical, radiological, and pathological features of brain toxoplasmosis in patients with autoimmune diseases.

#### ABSTRACT 3

# Small Vessel Vasculitis in Biopsies Of Anti-mog Encephalitis.

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We report the neuropathology of two pediatric brain biopsy cases associated with serum anti-myelin oligodendrocyte glycoprotein (MOG) positivity. Descriptions of anti-MOG associated neuropathology are limited, with initial reports describing various patterns of inflammatory demyelination. Our first patient presented with confusion, speech abnormalities and personality changes following a treated strep throat infection. Our second patient had a past medical history of neurofibromatosis type 1 (NF1) and presented with hypersomnolence and focal neurological deficits. MRI abnormalities included diffuse scattered T2 FLAIR hyperintensities +/- enhancement. CSF was positive for anti-MOG antibodies in both cases, while one case exhibited additional anti-NMDA-R antibodies. Brain biopsies revealed vasocentric mononuclear inflammation featuring a predominance of lymphocytes that included intramural forms, as well as diffuse microglial activation, but no evidence of microglial nodules or microorganisms. One case demonstrated mild perivascular demyelination. The prevailing pattern in both cases was suggestive of "small vessel childhood primary angiitis of the central nervous

system" (SVcPACNS). Our results parallel recent reports of anti-MOG neuropathology describing small vessel vasculitis, contrary to initial and subsequent reports that describe "encephalitis". The foregoing suggests that the neuropathology associated with serum anti-MOG positivity may be broader than first appreciated. Moreover, this pattern of vasculitis might have implications for the natural history of this nascent disorder.

## LEARNING OBJECTIVES

- Define anti-MOG encephalitis.
- Recognize the pathologic spectrum of reported cases of anti-MOG encephalitis.
- Contrast the pathologic features of pediatric and adult CNS vasculitis.
- Describe the histologic overlap of vasculitis and encephalitis.

## Abstract 4

## Spectrum Of White Matter Changes In Ischemic Lesions

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Morphological studies on cerebral ischemia concentrate mainly on the grey matter and white matter changes are regarded as secondary or overlapping injuries. Immunohistochemical (IHC) studies to highlight the combination of various cellular changes in ischemic white matter but have not well documented. We selected 11 archival cases of 3 different ischemic processes (i.e. large vessel occlusion, small vessel occlusion, and hypoperfusion) with survival period range 2-35 days from the ischemic event. The white matter was examined using HE-LFB histochemistry, APP, GFAP, and HLA-DR immunostains focusing on myelin, axonal, astrocytic and microglial changes respectively. The various white matter changes are probably reflective of the different mechanism, duration, severity and extent of ischemia. The APP-IHC shows patchy axonal expression, swelling, and finally complete axonal loss. HLADR-IHC highlights early microglial injuries (fragmentation of processes), complete cell loss, and subsequent replacement by cells of macrophage phenotype. Surrounding the ischemic areas are reactive microglia. Astrocytic changes range from fragmentation of processes (clasmatodendrosis) to different stages of cell loss. Astrocytic swelling tends to occur with cerebral edema. Large vessel occlusion results in complete tissue loss while in small vessel disease the damage is more selective. The injury is generally more subtle in hypoperfusion but can be pronounced focally. Our study has documented the spectrum of white matter injury in different scenarios of cerebral ischemia.

## LEARNING OBJECTIVE

 Describe the cellular and immunohistochemical changes in the ischemic white matter

## ABSTRACT 5

## Relevance of tissue eosinophilia in subdural hematomata

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Chronic subdural hematomata (CSDH) are treated by evacuation. Recurrence occurs in 3-20% of cases, but the factors determining its occurrence have not been determined. Having observed that eosinophil cell infiltrates are often present in the outer membrane of CSDH, our aim was to determine whether such infiltrates are associated with risk of recurrence. Histological sections of the resections from 72 patients with primary CSDH (Mean age 73.4) and 16 with recurrent CSDH (Mean age 72.1) stained with H&E were graded by blinded observers for eosinophilic cell infiltrates using a semiquantitative 0 to 3 scale. The risk of recurrence requiring reoperation (RrR) in primary CSDH was 11.1%, and 12.5% in recurrent CSDH (meaning third surgery was required). A dense (grades 2 or 3) eosinophilic infiltrate was present in 22.2% of primary CSDH; the RrR was 0% in these cases, as compared with 14.8% in cases with sparse (grades 0-1) eosinophilic infiltrate. Among recurrent CSDH cases, 12.5% (2/15) showed a dense eosinophilic infiltrate; the RrR was also 0%, contrasting with 14.3% in those with sparse eosinophilic infiltrate. We conclude that eosinophils either play a role or are a marker of a process leading to stabilizing CSDH, making them less prone to rebleeding. Abstract not previously published

#### LEARNING OBJECTIVES

- Describe the risk of recurrence following surgical evacuation of chronic subdural hematomata
- Recognize the variable presence of eosinophils in chronic subdural hematomata
- Cite the presence of eosinophils is predictive of absence of recurrence

#### ABSTRACT 6

# Subpial Thorn-shaped Astrocytes Are Prevalent In Guam ALS/PDC

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Guam amyotrophic lateral sclerosis/parkinsonism-dementia complex is a progressive neurodegenerative disorder characterized by neuronal and glial tau pathologies. With the aim to