perfused brain were verified histologically. Upper respiratory infection and mouth-breathing accompanied the pneumonia, with ongoing choking on formula or food in three cases, and vomiting in an additional five cases. In eight of the 10 cases, the pre-terminal event was a quiet respiratory arrest while sleeping, or being carried in the arms. Adrenaline was given up to 7 times during CPR lasting 44±32 minutes, with up to 2 hours CPR and fall in body temp to <32°C. Mean survival was 1.9±1.5 days and heparin was given for organ donation in 3 cases. The lungs showed chronic interstitial pneumonia as described by Katzenstein, with superadded acute bronchiolo-alveolar infiltrates in two cases of aspiration. The court permitted recuts and cellular characterization of the interstitial cells in one case, revealing the infiltrate was ~40% histiocytes, 5% T or B cells, and ~50% vimentin+ mesenchymal cells. All brains showed features of non-perfused brain and retino-dural hemorrhage. The observed features of non-perfused brain were blurring of the gray-white junction, edema, gross friability, histologic pallor, closure of the microcirculation, patchy acidophilic neurons and recent demarcated pan-necrosis, and pituitary infarction in one patient where hypophysis was sampled. Normally, from birth to 30 months, cerebral blood flow increases to 55% of cardiac output, accompanying physical brain growth. Restoration of high cardiac output using adrenaline-CPR means that on resuscitation, re-routing of blood that can no longer go through the non-perfused brain detours through dura, face, scalp, eyes and optic nerve sheaths. The diversion of blood around non-perfused brain results in facial bruising and retino-dural hemorrhage that can be misinterpreted as head trauma, and a common inference of child abuse in the courts. In the present series from Australia, Canada and the USA, outcomes ranged from acquittal to life imprisonment.

References

Katzenstein AL, et al. (1995) Chronic pneumonitis of infancy. A unique form of interstitial lung disease occurring in early childhood. Am *J Surg Pathol* **19**:439–447

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Investigate infant deaths including workup for interstitial pneumonia.
2. Know cerebral blood flow changes in development, and cranial blood flow dynamics in non-perfused brain.

Abstract 7

Epilepsy Related Death: the London Health Sciences Center Experience

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Premature mortality among epilepsy patients is well recognized. Except a few identifiable causes of unnatural death, more than half of the epilepsy related death remains unexplained after extensive workup. These cases are classified as sudden unexpected death in epilepsy (SUDEP). SUDEP incidence varies significantly depending on the population, the methods documenting cause of death and the availability of Neuropathological examination. An accurate diagnosis of the cause of death is needed for epilepsy related death. The goal of this study is to present the relevant clinical data, the general autopsy and Neuropathology findings of epilepsy related death investigated in London Health Sciences Center during the period of 2000 to 2011. We identified 71 cases with known history of chronic epilepsy. In the 29 cases of epilepsy associated death, the causes of death have been classified as cardiac, pulmonary, accidental (e.g. drowning), toxic (e.g. drug overdose) and non-related causes. Forty two cases are considered to be SUDEP, and were categorized according to the recently proposed SUDEP Definition and Classification. Half of the SUDEP cases have no specific Neuropathological findings. The most common identifiable lesions in SUDEP cases are perinatal/neonatal destructive lesions (29%), hippocampal sclerosis (24%), and focal cortical dysplasia (20%). These are followed by neuronal heterotopia (9%), previous head trauma (9%), and cavernoma (5%).

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Review cause of death in epilepsy related deaths
2. Discuss the practice guideline in neuropathology autopsy of epilepsy related deaths

Abstract 8

Medial Temporal Lobe Dysgenesis and More in a Man with Hypochondroplasia and Epilepsy

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Hypochondroplasia, achondroplasia, and thanatophoric dysplasia are related at the molecular level, all caused by fibroblast growth factor receptor 3 (FGFR3) gene mutations. They differ in severity. FGFR3 has critical roles in fibroblast growth factor (FGF) signalling pathways during bone growth and cerebral cortical development. Mutations of the FGFR3 gene lead to constitutive activation of FGFR3. The well-described brain malformation in thanatophoric dysplasia is characterized by gross abnormalities of temporal lobe patterning and severe dysplasia of the hippocampus. Experimental models suggest that increased proliferation, abnormal migration, and decreased apoptosis are involved. However, reports of the brain findings in hypochondroplasia are based solely on radiologic imaging.

We present the neuropathology of a 44 year-old man with hypochondroplasia, epilepsy, and significant intellectual disability. The temporal lobes are enlarged, prominent fissures traverse the inferior temporal surface, and the hippocampus is abnormally folded. Microscopically, the dentate gyrus is variably small or

thin and is located near the edge of a gyrus. Ammon's horn is displaced and meandering. Subicular-like clusters are profuse. Complex gyri resemble microgyria. White matter forms a subpial border in some gyri. In summary: medial temporal lobe dysgenesis.

This individual also had many autistic features including stereotypies and head banging. The latter could explain another surprising set of brain abnormalities unrelated to the presumed FGFR3-related syndrome.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Summarize current theories on the pathogenesis of FGFR3-related cortical malformation
2. Describe the brain abnormalities in hypochondroplasia
3. Identify the neuropathology resulting from head banging

Abstract 9

Area postrema: fetal maturation, tumours, vomiting centre, somatic growth and role in neuromyelitis optica

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The area postrema (AP) in the caudal 4th ventricular floor is unique, highly vascular without blood/brain or /CSF barrier. In addition to its function as the vomiting centre, several other important functions are: part of the circumventricular organs for vasomotor and angiotensin II regulation; a role in neuromyelitis optica related to aquaporin-4; contributor to fetal and postnatal somatic growth. Functions are immature at birth.

The purpose of this study was to demonstrate AP neuronal/synaptic/glial maturation in normal fetuses and 3 AP tumours. Transverse sections of the caudal 4th ventricle of 18 normal human fetal brains at autopsy, 6 to 40 weeks were examined; also 3 infants 3-18mos; 2 children. A battery of immunocytochemical neuronal and glial markers: MAP2; calretinin; synaptophysin; vimentin; nestin; GFAP; S-100β protein; were applied to paraffin sections. Two children with AP tumours and one with neurocutaneous melanocytosis, all with pernicious vomiting, were studied. In normal fetuses, AP neurons exhibited cytological maturity and well-formed synaptic circuitry by 14wk gestation. Size/volume increase was disproportionately greater than brainstem growth in 2nd and 3rd trimesters and postnatally. Astrocytes co-expressed vimentin/GFAP but glia were best demonstrated by S-100β protein. Ependyma over the AP in fetuses is simple cuboidal, adjacent to pseudostratified columnar of the 4th ventricular floor. Melanocytes infiltrated AP in the toddler with pernicious vomiting; 2 children had primary AP pilocytic astrocytomas. Though AP is cytologically mature by 14wk, growth increases and functions mature into the postnatal months. We recommend that AP neuropathology include synaptophysin and S-100β at autopsy if AP dysfunction suspected.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Explain the maturation of neurons, synaptic circuits and glial elements of the AP
2. List and recognize tumours that can affect the area postrema
3. Describe functions of the area postrema

Abstract 10

Human brain atlas: miRNA version

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Human brain is a complex organ comprising multiple cell types of differing function. Although histological evaluation remains the mainstay approach for evaluating tissue, comprehensive molecular characterization is now possible due to advanced -omic approaches. microRNAs (miRNAs) are small (~22 nt) RNA molecules that regulate gene expression and mediate cellular differentiation in normal brain development. miRNAs also make excellent tissue markers due to their abundance, cell-type and disease-stage specificity, and stability in solid/liquid clinical samples. To advance our knowledge of miRNA-mediated gene regulation in human brain, we generated comprehensive miRNA expression profiles from 117 fresh normal brain samples through barcoded small RNA sequencing; tissues included neocortex, allocortex, white matter, cerebellum, olfactory bulb, optic nerve, pineal gland and spinal cord. FASTQ sequence files were annotated using state-of-the-art sequence annotation available through the Renwick lab. Following data pre-processing, high expression analysis of miRNA profiles showed that miR-9 was the highest expressed miRNA in neocortex, cerebellum and olfactory bulb, whereas miR-22 was highest expressed in cingulate cortex, optic nerve and spinal cord; interestingly, miR-29 was the highest expressed miRNA in hippocampus. Our analyses showed a trend towards unique miRNA signatures in different anatomical areas of the brain. Our next step is to perform miRNA fluorescence *in situ* hybridization on formalin-fixed paraffin-embedded tissues using a novel method developed in the Renwick lab. Accurate miRNA characterization of normal tissues will provide a firm basis for understanding miRNA changes in neurological diseases.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Describe the function of miRNAs and their suitability as tissue/cell specific signatures
2. Describe the miRNA expression trends in profiling various anatomical regions of the central nervous system