lowed by oral prednisolone [OP], oral cyclophosphamide [2 mg/kg per day for 2 to 3 months], and dipyridamole). The other 23 patients with <50% crescent formation were given methylprednisolone followed by OP and dipyridamole. The patients with grade 3 or 4 disease were given OP and dipyridamole. Those with grade 1 or 2 disease were not given any immunosuppressive agent. During the follow-up period (mean: 30 ± 3.5 months; range: 12–96 months), 23 patients with grade 1, 38 patients with grade 2, 2 patients with grade 3, 8 patients with grade 4, and 21 patients with grade 5 disease showed complete remission (59%). Of the 5 patients with extensive fibrosis shown by renal biopsy, 2 (1%) had persistent nephropathy and 3 (2%) developed end-stage renal failure. The remaining 59 patients showed near-complete recovery with minimal urinary abnormalities (38%).

CONCLUSIONS: Although initial presentation of renal involvement determines the prognosis for those with HSN, intensive treatment with triple therapy seems to be effective for severe renal disease, especially if started before the development of fibrotic changes in crescents and tubulointerstitial tissue.

Neurology

THYROID FUNCTION IN EPILEPTIC CHILDREN TREATED WITH SODIUM-VALPROATE MONOTHERAPY: A PROSPECTIVE LONG-TERM STUDY

Submitted by Achilleas Attilakos

Achilleas Attilakos[a], Kontsantinos Voudris[b], Efstathia Katsarou[b], Sotiria Mastroyianni[b], Aspasia Fotinou[c], Alexia Prassouli[a], Anastasia Garoufi[a]

[a]Second Department of Pediatrics, University of Athens, Athens, Greece; [b]Department of Neurology and [c]Hormonological Laboratory, Panagiotis and Aglaia Kyriakou Children's Hospital, Athens, Greece

INTRODUCTION: Sodium valproate (VPA) is widely used for the treatment of partial and generalized epilepsy in childhood and adolescence. The results of studies that have evaluated the effect of VPA monotherapy on thyroid function in children are controversial.

OBJECTIVE: The aim of this study was to investigate, prospectively, whether treatment with VPA has an effect on serum thyroid hormone concentrations in epileptic children.

METHODS: Serum levels of triiodothyronine, thyroxine, free thyroxine, and thyrotropin were determined in 30 epileptic children (aged 2 to 14 years [mean ± SD: 9.10 ± 3.74 years]) before and after 6, 12, and 24 months of VPA monotherapy.

RESULTS: Serum levels of thyroxine and free thyroxine were significantly decreased after 6 (P = .000 and .000, respectively), 12 (P = .000 and .015, respectively), and 24 (P = .000 and .003, respectively) months of treatment with VPA, whereas serum levels of triiodothyronine were significantly decreased only after 24 months of treatment (P = .043). Serum levels of thyrotropin were significantly increased after 6 (P = .000), 12 (P = .000), and 24 (P = .000) months of treatment with VPA. Thirteen children (43.3%) had thyrotropin values higher than the normal-range maximum after 6, 12, and 24 months of VPA monotherapy. Serum VPA concentrations remained within the therapeutic range during the period of study.

CONCLUSIONS: Our results showed that VPA monotherapy in childhood may cause early and persistent alterations in thyroid function, which suggests a need for early and careful monitoring of serum thyroid hormone concentrations in epileptic children who receive VPA.

CLINICAL MARKERS THAT ENHANCE ETIOLOGIC YIELD IN GLOBAL DEVELOPMENTAL DELAY

Submitted by B. H. Y. Chung

B. H. Y. Chung, V. Wong

Queen Mary Hospital, University of Hong Kong, Hong Kong, SAR, China

INTRODUCTION: Etiology remains unknown in 30% to 50% cases of children with global developmental delay (GDD). A selective approach has been recommended to increase etiologic yield.

OBJECTIVE: Our aim was to identify clinical markers that enhance diagnostic yield of GDD at initial assessment.

METHODS: The charts of all patients with GDD (N = 577) followed up at the Duchess of Kent Child Assessment Centre were reviewed. GDD was defined as significant delay (<2 SD) in ≥2 developmental domains. Nine clinical items at initial assessment (gender, severity of delay, parental consanguinity, family history, behavioral disturbance, head size, facial dysmorphism, malformations, and neurologic deficits) were correlated with the likelihood of finding an etiology for GDD.

RESULTS: A significant threshold effect was found between mild and moderate GDD (positive likelihood ratio (LR^+]: 1.9; negative likelihood ratio [LR^-]: 0.72). Other items that significantly affected diagnostic yield were (1) female gender (LR^+: 1.62; LR^-: 0.79), (2) behavioral trait (LR^+: 0.24; LR^-: 1.67), (3) microcephaly (LR^+: 2.78; LR^-: 0.79), (4) presence of facial dysmorphism (LR^+: 2.65; LR^-: 0.65), (5) malformation (LR^+: 1.49; LR^-: 0.50), and (6) neurologic deficits (LR^+: 2.86; LR^-: 0.32). A dose-response relationship was found between LR^+ and the number of facial dysmorphisms and malformations.

CONCLUSIONS: Most checklists used for GDD are syndrome specific (eg, fragile X syndrome checklists). These 7 clinical markers are useful in the initial assessment,

even if no specific diagnosis is suspected. Unique statistical characteristics of LRs allow for a wide application in different clinical settings.

EFFECT OF DURATION OF STATUS CONVULSION ON NEURONAL APOPTOSIS AND EARLY APOPTOTIC EVENTS IN HIPPOCAMPUS OF RATS

Submitted by Li Jiang
Li Jiang, Yi Guo, Ai-yun Yuan, Yue Hu
Children's Hospital, Chongqing Medical University, Chongqing, China

OBJECTIVE: Our goal was to explore the influence of duration of status epilepticus on neuronal apoptosis, mitochondrial membrane potential, and cytochrome c release in hippocampus in Wistar rats after status epilepticus (SE).
METHODS: SE that lasted for 30 minutes or 3 hours was induced by intraperitoneal injection with lithium chloride and pilocarpine. Rats were killed at different time points. The apoptosis, mitochondrial membrane potential, and intracellular cytochrome c level were investigated by flow cytometry.
RESULTS: The proportion of apoptotic cells, the decrease of mitochondrial membrane potential, and the release of intracellular cytochrome c significantly changed 30 minutes after 30-minute SE. The peak level was at the 12th hour after SE and 6th hour after SE in apoptosis and the 2 early apoptotic events, respectively. Compared with the same time point after 30-minute SE, the levels of apoptosis and the 2 early apoptotic events after 3-hour SE were much higher. The neuronal apoptosis and the 2 early apoptotic events in hippocampus after SE had a positive correlation with the duration of SE in partial correlation analysis.
CONCLUSIONS: Severe seizures could induce the changes of neuronal apoptosis and the early apoptotic events in hippocampus after SE; the longer the duration of SE, the more serious the change of apoptosis and early apoptotic events were.

PROTEOLIPID PROTEIN 1 GENE MUTATION IN CHINESE PATIENTS WITH PELIZAEUS-MERZBACHER DISEASE

Submitted by Yuwu Jiang
Yuwu Jiang[a], Jingmin Wang[a], Ye Wu[a], Tony M.F. Tong[b], Stephen T.S. Lam[b], Yanling Yang[a], Jiong Qin[a], Xiru Wu[a]
[a]Peking University First Hospital, Beijing, China; [b]Clinical Genetic Service, Department of Health, HKSAR Government, Hong Kong, China

INTRODUCTION: Pelizaeus-Merzbacher disease (PMD) is a rare X-linked recessive disorder that presents with nystagmus, impaired motor development, ataxia, and progressive spasticity.
OBJECTIVE: The objective of this study was to analyze the proteolipid protein 1 (*PLP1*) gene in 6 Chinese patients with PMD.
METHODS: Six unrelated Chinese patients had PMD (P1–P6), and 14 individuals were from family P2. Of these 6 patients, 3 had transitional, 2 had classical, and 1 had connate PMD according to the clinical and MRI features. Genomic DNA was extracted from peripheral blood samples. Gene dosage was determined by multiplex ligation-dependent probe amplification. All 7 exons and exon-intron boundaries of *PLP1* gene were amplified and analyzed by direct DNA sequencing.
RESULTS: *PLP1* duplications were identified in patients 1 through 4 with PMD. Their mothers were *PLP1* duplication carriers. Both duplication carriers and normal genotypes of *PLP1* were identified in the family members of patient P2. A c.517C → T (p. P173S) hemizygous missense mutation in exon 4 was found in patient 5, and his mother was a heterozygote of this mutation.
CONCLUSIONS: We identified 4 gene duplications and 1 missense mutation (p. P173S) of *PLP1* gene in 5 Chinese patients with PMD. This is the first report about *PLP1* mutations in patients with PMD in China.

IRON-DEFICIENCY ANEMIA IS ASSOCIATED WITH CEREBRAL SINOVENOUS THROMBOSIS: A CASE SERIES

Submitted by Fotini D. Kavadas
Fotini D. Kavadas[a], Mahendranath D. Moharir[b], Leonardo R. Brandao[c], Gabrielle de Veber[b]
[a]Department of Medicine, [b]Children's Stroke Program, Division of Neurology, and [c]Division of Hematology/Oncology, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

INTRODUCTION: Iron-deficiency anemia is a relatively common but preventable condition in children that may have significant adverse implications on children's growth and development. Iron-deficiency anemia has also been sporadically reported in association with cerebral sinovenous thrombosis (CSVT).
OBJECTIVE: The objective of this study was to describe the largest case series to date of iron-deficiency anemia in association with CSVT as an advocacy measure for its prevention in children.
METHODS: Patients were identified through the Canadian Pediatric Ischemic Stroke Registry database (Toronto site). Included were patients who were older than 1 month to 18 years, met criteria for iron-deficiency anemia, and had radiographically confirmed CSVT.

CLINICAL MARKERS THAT ENHANCE ETIOLOGIC YIELD IN GLOBAL DEVELOPMENTAL DELAY

B. H. Y. Chung and V. Wong

Pediatrics 2008;121;S145
DOI: 10.1542/peds.2007-2022XXXXX

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