Canadian Association of Neuropathologists

Abstracts
of papers presented at
The 28th Annual Meeting
September 29th, 30th, October 1st, 1988
Toronto

Summary

The 28th Annual Meeting of the Canadian Association of Neuropathologists was held September 29th - October 1st, 1988 at the Novotel Toronto Center, Toronto, Ontario. The meeting was attended by 79 members and guests. The scientific program consisted of 11 diagnostic cases and 19 scientific papers.

Two guest lectures were presented:

The Royal College of Physicians and Surgeons of Canada Speaker

Dr. Donald L. Price, Neuropathology Laboratory, The Johns Hopkins University School of Medicine, Baltimore, Maryland.

Title: "Aging and Alzheimer's Disease"

The Jerzy Olszewski Guest Lecture

Dr. Ronald G. Worton, Geneticist in Chief, The Hospital for Sick Children, Toronto, Ontario

Title: "Duchenne Muscular Dystrophy: Identification of the Responsible Gene and its Protein Product"

Two awards for presentations by trainees were given:

The Mary Tom Award: Dr. Douglas Kondziolka, Toronto, Ontario: "An Immunohistochemical Study of Neuroepithelial (Colloid) Cysts: Primary Lesions of Neuroectodermal Development"

The Morrison H. Finlayson Award: Dr. T.E. Edgar Huang, Royal Oak, Michigan: "Optic Glioma: A View of 53 Children"

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Canadian Association of Neuropathologists Abstracts

1.

Variations on the Theme of Agenesis of the Corpus Callosum

ELLSWORTH C. ALVORD, JR. and CHENG MEI-SHAW (Seattle, U.S.A.)

The present study was stimulated by a medico-legal case involving the differential diagnosis of the causes of profound microcephaly: perinatal hypoxia, neonatal hypoglycemia or congenital malformation. That agenesis of the corpus callosum (CC) may be entirely incidental and accompanied by no neurological deficit led some to think that the malformation was of no clinical importance.

Although many investigators have noted that many abnormalities that may accompany agenesis of the CC, none appears to have sought clusters that may represent more or less homogeneous syndromes. Subdivisions of our 65 cases of abnormal CC (complete or partial agenesis or hypoplasia) by weight of the brain (macrencephaly, normal, micrencephaly or unknown) and then by accompanying agenesis or hypoplasia of cranial nerves, hypothalamus, cerebral white matter and/or cerebellum as well as gyral abnormalities (agyria, pachygyria or microgyria) and hydrocephalus reveal two major clusters: 1) Complete agenesis of the CC (31 cases, only 5 known to be micrencephalic) with hydrocephalus (13 cases, including 6 cases with Dandy-Walker malformation) and 2) Hypoplasia of the CC (18 cases, 6 known to be micrencephalic), with hypoplasia of the cerebral white matter (9 cases) and agenesis of the olfactory (7 cases) or optic nerves (3 cases). Summarized another way, these cases included 19 hydrocephalics, 13 of whom had complete agenesis of the CC. Of 13 cases with agenesis or hypoplasia of the olfactory nerves, 7 had a hypoplastic CC and 4 had complete agenesis of the CC. While it is clear that there are no constant correlations, it is equally clear that some variations are permissible within these two major clusters.

2.

An Immunohistochemical Study of Neuroepithelial (Colloid) Cysts: Primary Lesions of Neuroectodermal Development

DOUGLAS KONDZIOLKA and JUAN M. BILBAO (Toronto, Ontario)

Continuing debate surrounds the pathogenesis of intracranial colloid cysts. For fifty years the term paraphysial cyst remained in common usage with the seemingly constant finding of these lesions from the roof of the anterior third ventricle. However, demonstration of cysts in areas elsewhere within the ventricular system, led to theories proposing derivation from neuroepithelium like choroid plexus or ependyma. Previous studies have used routine histochemistry and comparative anatomy in reaching their conclusions. In this study, immunohistochemistry was utilized to analyze the specific cell markers of the cyst wall in comparison to normal structures of the third ventricle.

Monoclonal and polyclonal antisera were used against twelve cases of colloid cysts to determine the specific antigenic profile of the cyst epithelium. In four cases, adjacent choroid plexus was available for analysis as controls. The epithelial markers mab lu-5 and epithelial membrane antigen demonstrated positivity to cyst epithelium (in 12/12 cases), in contrast to choroid plexus or glial tissue which remained negative. This difference was statistically significant. Less specific was the intermediate filament marker for cytokeratin which showed positivity in both types of neuroepithelium. No reaction to GFAP, neurofilament, or vimentin was seen in cyst epithelium. Vimentin was positive in all choroid plexus samples. S-100 protein, neuron-specific enolase, and anti-Leu-7 were not helpful in distinguishing between epithelia. However, anti-Leu-7, which can be used as a marker of neuroectodermal tissue via its recognition of a myelin-associated glycoprotein, was positive in 2/4 choroid plexus specimens. Routine histochemistry showed PAS positivity in 11/12 and Alcian blue reaction in 8/12 cases. Both stains were negative in choroid plexus. Routine studies demonstrate a functional difference between epithelia but do not help in determining cyst origin.

This immunohistochemical study has shown that colloid cyst epithelium is antigenically distinct from that of choroid plexus or ependyma and therefore does not represent of product of their development, nor does it represent a form of immature glia. We suggest that colloid cysts in any ventricular location represent lesions of the primitive tela choroidea neuroepithelium — which develop as a primary anomaly, separately and independently from its normal contiguous structures.

3.

Neuronal and Astrocytic Cytopathology in Selected Cases of Early Onset Pediatric Epilepsy

V. MAH, D.L. SECOR and H.V. VINTERS (Los Angeles, U.S.A.)

Among cerebral hemispherectomies performed in children for intractable epilepsy, several have shown hamartomatous collections of abnormal hypertrophic neurons or gemistocytic astrocytes, often within subcortical white matter or at the cortex-white matter junction. Many of these neurons were distended by PAS negative filamentous material which displaced the nucleus and Nissl substance. Staining with monoclonal neurofilament antibodies showed these neurons to contain collections of phosphorylated neurofilaments in the perikarya which was not seen in the adjacent normal neurons. In one case definite neurofibrillary tangles were present on Bielschowsky stained sections. Electron micrographs showed collections of cytoplasmic straight filaments. Paired helical filaments were not seen. The abnormal astrocytes in these cases contained abundant cytoplasm, large and sometimes multiple nuclei and tended to localize in deep layers of cortex and U-fibers. Their astrocytic origin was confirmed by immunoperoxidase stain for glial fibrillary acidic protein. The findings appeared to be due to a congenital abnormality, possibly severely disordered cell migration. Further immunocytochemical studies will elucidate the nature of the abnormal cellular constituents, neurofibrillary tangles and astrocytes and allow for comparison with other disorders in which similar types of changes may be seen (i.e. trauma, degenerative disorders).

4.

Basophilic Bodies of Skeletal Muscle in Hypothyroid Myopathy. Enzyme Histochemical and Ultrastructural Studies

K.L. HO (Detroit, U.S.A.)

In addition to non-specific alterations of the skeletal muscle, such as type II fiber atrophy, increased central nuclei, glycogen and mitochondrial aggregates and focal myofibrillar degeneration, basophilic bodies (BB) are also occasionally observed in patients with hypothyroid myopathy. Previous morphologic and histochemical studies of BB of hypothyroid myopathy (Arch Pathol Lab Med 108:239, 1984) have revealed the following features: 1) BB occur predominantly at the myotendinous junction, 2) BB are not membrane bound and composed of straight fibrils of 6-7 nm and dense granules of 15 nm, and 3) BB has staining character of polysaccharides or amylopectine-like material. They are morphologically and histochemically similar to Lafora bodies of neurons, corpora amylacea of astrocytes and hepatic and cardiac inclusions of type IV glycogenosis. With enzyme histochemistry and ultrastructural studies of ultrathin sections stained with periodic-acid-thiocarbohydrazide-silver proteinate (PA-TCH-SP stain) for polysaccharides, the present study of two cases of hypothyroid myopathy revealed additional characterizations of BB: 1) BB were found exclusively in type I fibers, 2) BB were devoid of myofibrillar ATPase, oxidative enzyme and myophosphorylase, and 3) both the fibrillary and granular components of BB stained strongly with PA-TCH-SP method for polysaccharides. The polysaccharide nature of BB is in keeping with previous suggestion that the formation of BB is related to an

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impairment of glycogenolysis which has been reported in patients with hypothyroid myopathy. Their selective involvement of type I fibers and preferential occurrence at the myotendinous junction remain obscure.

5.

Medulloblastoma with Neuronal, Glial, Striated Muscle and Pigment Epithelium Differentiation

J.M. BONNIN, E.R. WILSON and JH GARCIA (Birmingham, U.S.A.)

Cerebellar medulloblastomas developing in children may differentiate along neuroblastic or glial cell lines and sometimes may express a divergent differentiation to both. Rarely, they may contain an abundance of striated muscle fibers. Such neoplasms have been variably designated as medullomyoblastomas, rhabdomyosarcomas, teratomas or "teratoid tumours". Exceptionally, medulloblastomas may also contain melanin-laden cells. We have examined an example of a melanotic medullomyoblastoma occurring in the cerebellar vermis of a young child who is alive and free of recurrence seven years after the initial excision and radiation therapy. Immunohistochemistry, silver impregnation studies and electron microscopy disclosed cells with neuroblastic and glial maturation. In addition to an abundance of striated muscle fibers in various stages of maturation, numerous clusters, tubules and paillary formations made up of pigmented epithelial cells were encountered. Ultrastructurally, the epithelial component displayed a well developed but incomplete basement membrane, a rich endowment of smooth and rough endoplasmic reticulum, abundant mitochondria and a numerous premelanosomes and melanosomes. The presence of melanin-laden epithelial cells resembling the pigment epithelium of the eye may indicate a differentiation potential of medulloblastomas along cell lines present in the primary optic cup in the embryo. Expression of the retinal S antigen, a marker for retinal photoreceptor differentiation, has been recently reported to occur in medulloblastomas (Korf H-W et al, Cancer, 1987; Bonnin JM and Perentes E, Acta Neuropathologica, 1988).

6.

Meningeal Tumours of Childhood

G.S. DAVIDSON (Toronto, Ontario)

Meningeal tumours occurring in a pediatric hospital over a period of 18 years were studied. The incidence of meningeal sarcomas was much lower than has been previously reported. A histological subtype of meningioma was found which has not previously been described. In these "sclerosing" tumours, only a very small portion of the lesion contained viable cells. The bulk of the lesion consisted of whorling collagen bundles produced by the tumour. Diagnosis at the time of resection was confounded by failure to recognize the architectural pattern of the collagen, which is readily identifiable as meningeal in the absence of tumour cells. Recognition of this histological subtype may prevent the use of unnecessary postoperative radiotherapy or chemotherapy. All meningiomas showing brain invasion fell into this category, and yet their prognosis was similar to conventional tumours, casting doubt on the use of brain invasion as a criterion for malignancy in meningiomas. The absence of other features of malignancy in the tumours in this series is also in contrast to the consensus in the sparse literature on this subject, which maintains that childhood meningiomas are more malignant than adult ones.

7.

Optic Glioma: A Review of 53 Children

T. EDGAR HUANG, LEE-CYN ANG, GEORGE S. DAVIDSON and LAURENCE E. BECKER (Toronto, Ontario)

Fifty-three patients with histologically confirmed astrocytoma in the optic nerve region occurring at The Hospital for Sick Children between 1939 and 1988 were studied. Clinical charts, Tumour Registry data, and slides of the tumour were reviewed. The ages ranged from 6 months to 17 years 5 months and the male to female ratio was 26 to 27. The most common presenting symptoms included blindness (42%) and proptosis (36%). Other symptoms were optic atrophy, papilloedema, hydrocephalus, precocious puberty, diabetes insipides, and seizures. Onset of symptoms prior to surgery ranged from one month to 11 years 5 months. Sections examined were from total resection (13), partial resection (12), biopsy only (27), and autopsy (1). Multiple separate tumours were present in three cases (1 neurofibromatosis (NF)) and massive tumours (>.1.5 cm) in 13 cases (1 NF). The major sites of involvement included right optic nerve (42%), left optic nerve (47%), chiasm (57%), hypothalamus (23%), thalamus (9%), and others (optic tract, brainstem, basal ganglia, orbit). Radiotherapy (4,000 - 5,256 rads) was administered in 23 patients. Growth patterns could be evaluated in 28 specimens because the size was sufficient: circumferential, 50%; infiltrative/expansile, 85%. Patients with NF showed no special preference for a specific growth pattern. All tumours were composed of spindle-bipolar cells arranged in compact nests segregated by fibrovascular septae of variable thickness. Histological features examined included cellularity (low, 75%; moderate, 23%; high, 2%), pleomorphism (mild, 45%; moderate, 57%; marked, 4%), giant cells (17%), Rosenthal fibers (87%), cystic degeneration (28%), endothelial proliferation (21%), mitoses (21%), necrosis (21%), lymphocytic infiltrate (17%), and calcification (3%). None of these features correlated statistically with recurrence or mortality. Large tumours involving hypothalamus and thalamus were associated with the worst prognosis. The five-year survival of patients with neurofibromatosis (89%) did not differ significantly from those without neurofibromatosis (82%).

8.

Niemann-Pick disease, type C. Report of Two Cases

DIMITRI P. AGAMANOLIS, HAYNES B. ROBINSON, JR., THIRUVENGADAN KULASEKARAN and G. DEAN TIMMONS (Akron, USA.)

Two patients had hepatosplenomegaly and persistent jaundice in the neonatal period. Liver biopsies showed neonatal giant cell hepatitis in one and fibrosis in the other. Jaundice subsided but hepatic fibrosis persisted. At ages 2 and 5 years respectively, regression of mental and motor abilities, tremor, visual disturbances and seizures appeared. Bone marrow aspirates showed foamy histiocytes. Skin fibroblast assays showed normal levels of sphingomyelinase activity and were negative for other lysosomal enzyme disorders. Neurological deterioration progressed inexorably until the patients' deaths at 4 and 10 years respectively. Autopsies revealed neuronal lipidosis, neuroaxonal dystrophy, cirrhosis and foamy cells throughout the mononuclear phagocyte system.

These cases exemplify Type C Niemann-Pick disease, which is now thought to be a disorder of cholesterol metabolism. Because lysosomal enzyme assays are normal and neurological involvement and foamy cells may be absent initially, diagnosis of this disorder in infancy is difficult and prenatal diagnosis is not possible. Niemann-Pick disease Type C should be considered in cases of unexplained "neonatal giant cell hepatitis".

9.

An Unclassified Case of Lysosomal Storage Disorder

KATHLEEN MEAGHER-VILLEMURE, STIRLING CARPENTER and GORDON WATTERS (Montreal, Quebec)

A female child born at term, without perinatal complications, was showing at one month of age some mild hypotonia. At seven months, microcephaly, motor retardation and hypotonia was revealed on examination. A muscle biopsy done at that time showed some type I fiber atrophy with unusual inclusions in the muscle fibers consisting of membrane-bound bodies with concentric parallel lamellae. At 16 months, the child started developing some intractable seizures. Abnormal liver enzymes and cardiomyopathy was detected at 18 months. A second muscle biopsy done at that age revealed the presence

of storage material in the squeletal muscle, pleiomorphic but definitely lysosomal, taking form of loose membranous concentric lamellar cytoplasmic bodies. A CT scan showed diffuse brain atrophy and cerebellar involvement. The baby continued to deteriorate, suffering repeated episodes of heart failure, otitis media and aspiration pneumonia. She expired at four years of age. The autopsy revealed a severe brain and cerebellar atrophy, diffuse muscle fatty replacement and hemorrhagic bronchopneumonia. Histologically, the cerebral cortex showed diffuse spongiform changes with accumulation of abnormal Sudan Black positive granules in neurons, astrocytes and macrophages and relatively good preservation of the myelination in the white matter. Electron microscopy studies revealed the same abnormal lysosomal material accumulation in the cerebral cortex, squeletal muscles, hepatocytes and cardiac muscle similar to the ones seen in the two muscle biopsies done during life. The differential diagnosis of this abnormal lysosomal content do not correspond to any known characteristic features and the clinical investigation which has been negative for any specific biochemical abnormality also makes of this case a problematic challenge.

10.

Acute Fulminating Encephalopathy of Human Immunodeficiency Viral Infection

ANDERS A.F. SIMA, SCOTT SUTHERLAND and JOHN MAGUIRE (Winnipeg, Manitoba)

A second case of acute fulminating fatal leucoencephalopathy complicating human immunodeficiency virus (HIV) infection is reported in a 31-year-old male patient with known AIDS and previous opportunistic non-CNS infections. There was a fulminating terminal illness with cranial neuralgic pain, bilateral asymmetric optical nerve damage, and dementia. Autopsy demonstrated widespread necrotizing and demyelinating lesions preferably in the centrum semiovale. Although axons were involved they were less affected than myelin. Patchy involvement of the cerebral cortex showed spongiform degenerative changes. No inflammatory infiltrates, microglial nodules, or giant cells were demonstrated. Macrophages were sparse. No complicating neoplastic or opportunistic infectious organisms were identified. Electron microscopy revealed nuclear viral particles characteristic of HIV.

11.

Familial Giant Axonal Neuropathy

A. LACSON, C. NEAVE, J. GIBSON, P. CAMFIELD, J. DOOLEY and J. PELEKANOS (Halifax, Nova Scotia)

The familial incidence of human giant axonal neuropathy (GAN) has only recently been demonstrated with two families recorded in the literature. An autosomal recessive inheritance has long been suspected, however. This has further been observed in the naturally occurring disease in dogs. We report five patients with GAN, four of whom belonged to two related families and one to an unrelated family in whom parental consanguinity is suspected. Of the five, three followed the typical neurological sequence of late-infantile onset, progressive muscular weakness and electroencephalographic dysrhythmias. As in most reported cases, these three patients demonstrated variable sensory abnormalities; they all developed scoliosis and were wheelchair-bound between ages 10-12 years. All had mental retardation. The other two patients presented in early infancy with progressive hypotonia and failure to thrive; one of these died at age four months and showed minimal cerebral, cerebellar and brainstem pathology. However, widespread axonal distension were noted in the long tracts of the spinal cord, and the dorsal nerve roots near the entry zone. The last patient is still alive at 5 years of age, with mental retardation and hypotonia. A biopsy done at 1 year of age showed typical giant axons in the intramuscular nerves. None of these patients had kinky hair.

Detailed neuropathological examination was carried out on one patient who died at 22 years of age. This confirmed previous pathological descriptions, with the additional feature of multifocal demyelinated foci in the centrum semi-ovale and subcortical white matter. Rather prominent autonomic nervous system involvement could help explain earlier clinical features such as peripheral vasoconstriction and trophic ulcers. The number of central nervous system spheroids increased in a rostral-caudal progression, emphasizing distal axonal involvement. A review of the skin ulcer biopsy from 1969 showed giant axons in a subcutaneous nerve. The metabolic abnormality remains unclear; the variability of onset and progression of disease in one family suggests that an allelic gene may be responsible for quantitative differences in axonal transport and/or proximal pathways of neurofilament degradation.

12.

Diabetic Neuropathy: Vascular Pathology and Lack of Response Following Aldose Reductase Inhibitor Treatment

ANDERS A.F. SIMA, VERA BRIL and DOUGLAS A. GREENE (Winnipeg, Manitoba; Toronto, Ontario; Ann Arbor, U.S.A.)

Endoneurial vascular abnormalities have been invoked in the pathogenesis of diabetic neuropathy. The morphometry of endoneurial capillaries in sural nerve biopsies from 11 patients with IDDM (mean age 39) and 16 patients with NIDDM (mean age 56) were studied and compared with that of 15 carefully age-matched control nerves. The frequencies of capillary lumenal closure and the number of endothelial cells per unit length of capillary circumference were not increased in diabetics, but increased with age independent of diabetes. Capillary basement membrane thickness and diffusion distance were increased in both diabetic groups compared with their respective controls. Repeat biopsies in 15 patients following 1 year of treatment with ARI Sorbinil (10 treated; 5 placebo) were compared with their respective baseline biopsy. No effect of ARI could be demonstrated on capillary closure, endothelial cell number, basement membrance thickness or diffusion distance. The results show that capillary closure and/or endothelial cell proliferation are not features of diabetic neuropathy, whereas increased basement membrane thickness and diffusion distance may be significant in explaining focal nerve fiber loss in older diabetic subjects.

13.

The Frequency and Significance of Alpha Subunit in Pituitary Adenomas

K.K. BERG, B.W. SCHEITHAUER and G.G. KLEE (Rochester, U.S.A.)

Serum levels of alpha subunit (aSU) were studied in 271 cases of sellar disease (211 consecutive pituitary adenomas; 60 nonadenomatous lesions). Adenomas were immunostained for GH PRL ACTH glycoprotein hormone (LH FSH TSH) and aSU: E/M was selectively performed. Elevations of aSU (normal<1.2 ng/ml) were seen in 18 cases of adenoma (8.5%) and in 3 nonadenomatous cases (5%); elevations in the latter were minimal. Immunoreactivity was seen in 105 adenomas (50%) and in 78% of cases with aSU elevation. Reactivity was seen in 105 adenomas (50%) and in 78% of cases with aSU elevation. Reactivity was seen in 91 cases (48%) with normal aSU levels. All but one tumour associated with increased serum aSU were macroadenomas; adenoma immunotypes included: GH, 33% (n=3); GH/PRL, 0%; GH/+ PRL/glycoprotein, 92%; PRL, 10%; ACTH, 23%; glycoprotein, 95%; null cell, 50%. Features of cases with aSU immunoreactivity included: age 16 - 78 (mean, 52) 59% male, 14% microadenomas (87% noninvasive, 13% invasive) 86% macroadenomas (49% noninvasive, 51% invasive). Comparatively aSU immunonegative tumours demonstrated: age 14-70 (mean, 35), 34% male, 44% microadenomas (77% noninvasive, 23% invasive) 56% macroadenomas (49% noninvasive, 51% invasive). We conclude that 1) aSU elevations are highly suggestive but not pathognomonic of adenoma, 2) aSU is more often noted immunocytochemically than biochemically, 3) aSU immunoreactivity predominates in glycoprotein, plurihormonal and null cell tumours, 4) among patients with aSU elevation, levels provide no information regarding tumour size or invasiveness, but may provide a marker of recurrence, 5) there is no specific ultrastructural correlate to aSU production, and 6) aSU adenomas are not a specific clinicopathologic entity.

14.

Ultrastructural Studies of Two Cerebral Biopsies of "Binswanger's Disease"

S. COMMONS, V.J.A. MONTPETIT, R. NELSON and S. DANCEA (Ottawa, Canada)

Subcortical arteriosclerotic encephalopathy (SAE) is an ill defined condition characterized by progressive dementia, transient focal neurological deficits and on CT scan, periventricular white matter lucencies (PVWML). It typically affects hypertensive middle aged to elderly individuals. Even at autopsy it is difficult to establish a definite diagnosis as there are no pathognomonic morphological criteria and other conditions present similar clinico-radiological features. An ultrastructural study of cerebral biopsies from two demented patients with PVWML was performed to determine if indeed there are electron microscopic markers for SAE. The patients were two middle aged men who fulfilled clinical criteria of SAE. The clinical history and light microscopic findings have been reported.[1] A cerebral biopsy from one revealed minor nonspecific histologic abnormalities while cerebral biopsy material from the other was characterized by severe arteriosclerosis with microinfarcts of white matter, pallor of myelin and sparing of cortex and subcortical U fibers. At the ultrastructural level the latter disclosed splitting of myelin sheaths, axonal degeneration and proliferation of oligodendroglial cells which contained an increased number of polymorphous bodies. Minimal pericapillary edema, proliferation and swelling of oligodendrocytes together with patchy structural changes of myelinated processes were noted in the other case. Huang et al[2] felt that myelin sheath splitting was due to edema. This hypothesis does not explain the proliferation of oligodendrocytes in our cases which appear to be a reactive phenomenon secondary to white matter destruction. Perhaps the absence of significant findings in the second biopsy indicates that the PVWML may precede ultrastructural changes. These findings support the contention that arteriolar changes are not a constant feature of SAE. The extensive pallor of white matter with sparing of U fibers is morphological evidence of a syndrome caused by many disease entities. Splitting of myelin sheaths together with proliferation of oligodendroglial cells are best explained on the basis of reaction of brain tissue to injury such as hypoxia and/or ischemia with or without acidosis as postulated by Huang et al.

1. Nelson R, Montpetit V., et al. Can J Neurol Sci 1988; 15, 231.
2. Huang K, Wu L, Luo Y. Can J Neurol Sci 1985; 12: 88-94.

15.

Profound Hypoglycemia Increases Brain Quinolinic Acid Levels

R.N. AUER, M. PAPAGAPIOU and M.P. HEYES (Calgary, Alberta; Bethesda, U.S.A.)

There is ample evidence that the mechanism of neuronal death in brain damage due to profound hypoglycemia involves the production by the brain of an endogenous excitotoxin. Brain levels of aspartic acid have been measurably increased in profound hypoglycemia. Quinolinic acid, a more potent excitotoxin produced from tryptophan by metabolism in the kynurenine pathway, has not been measured in hypoglycemia. We undertook gas chromatographic-mass spectometric measurements of quinolinic acid and related metabolites after 40 min. of EEG isoelectricity due to hypoglycemia, and 30 min. after recovery with glucose administration.

The results demonstrate that quinolinic acid increased markedly in the cerebral cortex, hippocampus, and other brain regions examined. Notably, increases in regional brain QUIN persisted into the recovery period, in spite of glucose administration. The results suggest a profound and prolonged derangement of QUIN metabolism induced by hypoglycemia, with increased degradation of QUIN from tryptophan via the kynurenine pathway. The findings indicate that QUIN is an endogenous neurochemical which should be considered as the possible endogenous excitotoxin responsible for neuronal death in hypoglycemic brain damage.

16.

Multisystem Degenerative Changes and Premature Senile Changes of the Brain Associated with Oculo-cerebro-renal Syndrome

JOHN MAGUIRE, A.E. CHUDLEY and ANDERS A.F. SIMA (Winnipeg, Manitoba)

We present a case of a 23-year-old male of consanguineous parents with congenital ocular defects (glaucoma, cataracts, and nystagmus), progressive renal failure, and a longstanding seizure disorder with mental retardation. Two other siblings had congenital nystagmus and progressive renal dysfunction.

Neuropathological examination revealed marked cerebellar atrophy with loss of the inner granular layer and a marked loss of Purkinje cells with secondary hypertrophy of the inferior olivary nuclei. Other features included marked neuronal loss of the substantia nigra and of the subthalamic nuclei. Unexpected senile changes of the Alzheimer type were widespread in the cortices and marked neuroaxonal dystrophic changes were found in the globus pallidus, substantia nigra and in the gracile nuclei.

In an attempt to identify this case and his siblings with a specific syndrome, an oculo-cerebro-renal syndrome first comes to mind and remains the most likely, despite the many incongruities present in this family. Documentation of the neuropathologic features of such a syndrome is extremely sparse and amounts to only a few case reports. Dementia has not previously been reported in these cases, and affected males and females have not previously been reported in the same family.

Oculo-cerebro-renal syndromes are associated with considerable heterogeneity and more than one mode of inheritance is likely.

17.

Gangliogliomas Associated with Complex Partial Seizures

S. GAYTAN-GARCIA, W.T. BLUME, J.C.E. KAUFMANN and J.P. GIRVIN (London, Canada)

Two hundred and sixty-four lobectomies and corticectomies were done from February 1974 to February 1988, to control intractable partial seizures. Neuropathological examination showed primary brain tumours in 94 (35%). Among these, 8 were gangliogliomas, all of which were located in the temporal lobe (5 right; 3 left).

Partial complex seizures compatible with a temporal lobe origin occurred in 7 patients, and simple partial seizures in the 8th. Four patients had associated grand mal seizures. Median age of seizure onset was 19 months (mean 5.5 years; range 5 months to 13 years). Median age of surgery was 14 years (mean 19 years; range 10 to 41). Five patients are male and 3 are female.

Complex partial seizures arising from the tumourous temporal lobe were EEG-recorded in 5 of the 8 patients while the other 3 had subclinical EEG seizures in this region. All patients had focal ipsilateral temporal delta and spikes on at least one recording. Generalized spike and waves occurred in 3, multiple independent spikes in 2, and bitemporal spikes in 1. Pre-operative CT-scan disclosed temporal lobe lesions in 7 cases; of these calcification appeared in 2. This series of 8 gangliogliomas in the temporal lobe causing seizures appears to be larger than any other published series.

18.

Neuropathological Findings in a Case of Proteus Syndrome

A. LACSON, P. CAMFIELD, M. COHEN and Y. ONG (Halifax, Nova Scotia)

Proteus syndrome is a recently described condition characterized by localized growth disturbances. These include asymmetry in body growth, macrocephaly, macrodactyly, a variety of skin lesions, soft tissue masses, bony abnormalities and others. Nearly half of the reported cases have mental retardation, and about three have had seizures.

Although macrocephaly and EEG abnormalities provide clues to the underlying lesions, the structural basis for these central nervous system manifestations is not known. A 6-year-old boy had been followed since birth because of mild gross deformities which progressed dramatically over 5 years. He had four fingers on the right hand and hemihypertrophy of the face and lower extremities. He developed soft tissue masses on the face, hyperkeratotic skin lesions, macrodactyly particularly of the 3rd and 4th fingers, gyriform soft tissue masses of the plantar aspect of both feet and subcutaneous lipomatosis of the abdomen. He had a seizure disorder since birth and mental retardation since 2 years of age. At autopsy, the soft tissue deformities were confirmed. Vascular malformations were noted in the colon in addition. A microscopic focus of cystic adenomatoid malformation was present in the left lung.

The brain weighed 1609 grams. Asymmetrical gyral abnormalities were at once evident on the convexities. There were multiple foci of large gyri sometimes overlying heterotopic gray matter nodules in the white matter. Lateral ventricular dilatation consisted of asymmetrical size with bilateral rostro-caudal elongation. Cytoarchitectonic configurations of the abnormal gyri followed the four-layered polymicrogyric pattern. Focal dysplasia of the hippocampi were noted. Throughout the cortex, especially in the occipital lobes, randomly scattered, large neurons occupied layers V and VI; similar neurons were seen in the white matter. There was a large right cerebellar abscess from which anerobic organisms were recovered.

The dysplastic brain in this particular case suggests that other patients with seizures and mental retardation may have a similar basis. Proteus syndrome represents another example of a hamartoneoplastic condition.

19.

Hemimegalencephaly, Hemifacial Hypertrophy and Intracranial Lipoma: A Variant of Neurofibromatosis

G.W. ROSS, J.Q. MILLER, S.R. VANDENBERG and H. URICH (Charlottesville, U.S.A.)

Hemimegalencephaly is a rare but well recognized malformation, characterized by unilateral hypertrophy of the cortical neurons, occasionally similar changes in the glia, and a variable degree of disorganization of the cortical cytoarchitecture. In isolated hemifacial hypertrophy, all tissue elements may be proportionately enlarged while retaining their normal relationships to produce a uniform overgrowth of bones and soft tissues. In contrast, it may give rise to a tumour-like hyperplasia of one tissue element, most commonly the peripheral nerves, in which case it forms part of the spectrum of neurofibromatosis. The present case is a 30-year-old, mentally retarded and epileptic patient, with a progressive hemifacial hypertrophy since birth. Multiple biopsies and an autopsy exam revealed the neurofibromatous nature of the facial lesion in addition to meningeal lipomas and esteomas. The striking feature in the tissues recovered from the cheek, lip and tongue was the abundance of abnormal nerve fibres, surrounded by concentric cellular lamallae ("onion bulbs"). Schwannian elements were limited to the sheaths surrounding individual axons and played no part in the formation of the "onion-bulbs". Perineurial cells, as identified with the anti-EMA antibody, were scanty and largely confined to the periphery of the concentric structures which also contained a variable number of vimentin positive cells. Whether these represent fibroblasts or are aberrant expressions of vimentin in neoplastic perineurial cells remains questionable. This case presents an opportunity to carefully examine by immunocytochemistry some of the uncommon manifestations of hemimegalencephaly and to study its relationship to neurofibromatosis.

TITLES OF DIAGNOSTIC CASE PRESENTATIONS

1. **Upper cervical myelopathy in achondroplasia.**
   E.S. JOHNSON, D.B. SINCLAIR (Edmonton, Alberta)
2. **Central neurocytoma.**
   K. BERRY, J.J. KEPES, D.J. CHERCOVER, G.B. PURVES (Vancouver, B.C. and Kansas City, U.S.A.)
3. **Gangliocytoma and mixed growth hormone and prolactin producing adenoma — pituitary fossa.**
   B. CURRY, E. McCRAE (Calgary, Alberta)
4. **Cystic meningioma with ganglioneuroblastoma.**
   A. LACSON, W. HOWES, G. MURRAY (Halifax, Nova Scotia)
5. **Secretory meningoma (query folliculo-stellate adenoma).**
   D.S. Horoupian, H. VOGEL, G. SILVERBERG (Stanford, U.S.A.)
6. **Malignant pigmented epithelioid schwannoma.**
   B.W. SCHEITHAUER (Rochester, U.S.A.)
7. **Hypertrophic brachial plexus neuritis.**
   J.N. BILBAO, M. CUSIMANO, S.M. COHEN (Toronto, Ontario)
8. **Cerebral chromomycosis.**
   J. MULLER (Indianapolis, U.S.A.)
9. **Cerebral fat embolism in acute pancreatitis.**
   S.N. GUARDIA, J.M. BILBAO (Toronto, Ontario)
10. **Pellagra.**
    A.H. KOEPPEN, K.D. BARRON (Albany, U.S.A.)
11. **Oculorenal cerebellar syndrome**
    W. HALLIDAY (Winnipeg, Manitoba)

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