Canadian Association of Neuropathologists

Abstracts of papers presented at the 35th Annual Meeting

October 6th - 8th, 1995
Jasper, Alberta

The 35th Annual Meeting of the Canadian Association of Neuropathologists was held from October 6th - 8th, at Jasper Park Lodge in Jasper, Alberta. Local arrangements were made by Dr. Bruce Mielke.

The scientific session consisted of 17 platform presentations, 2 posters and 12 cases for diagnosis. The Royal College of Physicians and Surgeons of Canada speaker was Dr. Clayton Wiley, Professor and Director of Neuropathology, University of Pittsburg, PA. His talk was entitled "Search for Mechanisms of Neurodegeneration in HIV Encephalitis". The Jerzy Olszewski lecturer was Dr. Michael Brooke, Professor and Director of Neurology, University of Alberta, Edmonton. His talk centered on "Some Thoughts on the Etiology of Muscular Dystrophy".

The Association presents two awards annually to trainees/residents giving the best presentations. Dr. Arie Perry received the Mary Tom Award for his paper entitled "Cerebellar Ganglioglioma with a Pleomorphic Xanthoastrocytoma Component". Dr. Patrick Shannon received honourable mention for this award for his presentation of a case of Orthochromatic Leukodystrophy, Pigmentary Type. Dr. Chunhai Hoa received the Morrison H Finlayson Award for the second time for his paper on "Development of Microglia in the CNS".

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Abstracts of Papers Presented at the 33rd Annual Meeting of the Canadian Association of Neuropathologists

PLATFORM PRESENTATIONS

1.

Human Malignant Meningioma Transplanted Into Nude Mice: Effect of Genetically Engineered, Replication-Compentent, Neurovirulence-Attenuated HSV-1.

H.J. MANZ, T. YAZAKI, S. RABKIN and R. MARTUZA
(Washington, U.S.A.)

In the hope of eventually using replication-competent, neurovirulence-attentuated *Herpes simplex* type 1 virus in the treatment of brain tumors in humans, we analyzed the effect of such a mutant in human malignant meningioma transplanted into nude mice. Two models were used, one subcutaneous, the other intracranial subdural; nine or ten animals were used in each group. A 1 mm tumor mass was implanted. In the subcutaneous model, after 7 or 12 days, the tumors had reached size of 6 or 10 mm, respectively. At this time either saline or the attenuated, lac Z HSV-1 mutant G207 (5×10^6 PFU/50 µl) were injected into the tumor; for the 10 mm tumors, the identical dose and 5×10^6 PFU/50 µl were given. Animals were sacrificed up to 28 days later. The ratio of tumor volume between untreated and treated groups was compared by the t-test. For all three treatment groups, tumor growth was markedly inhibited ($p < 0.0001$). In the intracranial model, either saline or G207 at a dose of 2×10^6 PFU/2 µl was injected into the tumor implant on day 7, with 9 animals in each group. By day 31, all animals in the control group had died; in the treated group, three were still alive at day 66; a significant difference in survival was found (Wilcoxon test, $p < 0.01$).

2.

Vascular Permeability Factor/Vascular Endothelial Growth Factor (VPF/VEGF) is Present in Meningiomas and Correlates With the Development of Peritumoral Edema: An Immunohistochemical, Northern and In-situ Hybridization Analysis.

J. P. PROVIAS, K. CLAFFEY[2] and A. GUHA (Toronto, Ontario, [2]Boston, U.S.A.)

Vascular Permeability Factor, (VPF Vascular Endothelial Growth Factor, VEGF) is a recently defined mitogenic growth factor which acts specifically on vascular endothelial cells through high affinity receptors of the tyrosine kinase family. The protein contains a signal peptide and is highly secreted. VPF/VEGF has been shown to be present in a number of solid tumours and plays a prominent role in tumour-associated angiogenesis and the development of tumour-related edema. In the central nervous system it has been best studied in astrocytic tumours. We describe a study of VPF/VEGF in a series of surgically resected meningiomas utilizing combined northern analysis, in situ hybridization and immunohistochemistry for VEGF and its cognate receptors KDR and FLT-1. We find VEGF present in a majority of meningiomas both at the RNA and protein level. Protein immunhistochemistry localizes VPF to meningothelial tumour cells but not vascular endothelial cells. In situ hybridization shows VPF receptors present only in vascular endothelial cells. VPF is upregulated as shown by northern analysis in meningiomas associated with prominent peritumoral edema. Furthermore, VPF/VEGF may play a role in the angiogenesis and vascularization of meningiomas.

3.

Pleomorphic Xanthoastrocytoma Developing in Gangliocytoma and Cortical Dysplasia of Temporal Lobe.

N. DUGGAL, B. LACH, V.F. DA SILVA and Z.A. DHALLA (Ottawa, Ontario)

We present a 52-year-old female with a 32 year history of epilepsy and no focal neurological signs or lesions on previous CT. An MRI study 6 yrs later demonstrated a 1.5 cm nodule in the right amygdaloid n. area. Light microscopy of the lesion revealed a pleomorphic, predominantly spindle cell tumor, focally extending to cortex and leptomeninges. There were no mitotic figures, necrosis or vascular proliferation. Reticulin fibers and cell lipidization were sparse. The tumor was strongly immunoreactive for vimentin, S-100 protein and, to a lesser extent, for GFAP. There was no neuronal differentiation in PXA. In addition, the amygdaloid area showed subcortical gangliocytoma, approximately 1 cm in size. The neoplastic neurons appeared mature and showed no mitoses or MIB-1 immunoreactivity. The adjacent cortex revealed focal dysplasia characterized by disorganization of neuronal architecture and the presence of neurons abnormal in size, shape and polarization. The perikarium of some of these neurons was strongly NF70 positive. Moreover, mature heterotopic neurons were scattered throughout the white matter of the temporal lobe. The ganglionic tumor and the dysplastic cortical areas showed increased reactivity for synaptophysin.

Occurrence of neuronal component associated with PXA has been previously reported. To our knowledge this is the first example of PXA developing in pre-existing cortical dysplasia and gangliocytoma of the temporal lobe. This association of neuronal hamartoma with astrocytic neoplasm supports the hypothesis that PXA arises from multipotential precursor cells, common to neurons as well as astrocytes.

4.

Brain Necrosis in Hypoxia and Ischemia.

R.N. AUER and O. MIYAMOTO (Calgary, Alberta)

Hypoxia is generally accepted to cause brain damage. We used Wistar rats to determine whether hypoxia can, by itself, cause irreversible (necrotizing) brain damage, and to define the

relationship between hypoxia, ischemia and brain necrosis. In a hypoxia only group, the FiO_2 was lowered to obtain a pO_2 of 25 mm Hg. This induced immediate and profound hypotension to a mean arterial blood pressure (MABP) of 30 mm Hg, and the pO_2 was adjusted to keep MABP at 30 mm Hg for 15 minutes. No necrotic neurons were observed histologically after 1 week survival (n = 13). Thus, in additional groups, ischemia was added to hypoxia, by unilateral ligation of the common carotid artery combined with hypotension. Ischemia without hypoxia was also studied, and graded levels of both hypoxia and hypotension were investigated in multiple groups, to determine the relative contributions of hypoxia and ischemia to the pathogenesis of damage. Four of 12 ischemia only rats had brain damage in spite of a $pO_2 > 100$ mm Hg. The quantity of necrosis was dependent on both MABP and pO_2. Lowering the pO_2 at a fixed MABP of 30 mm Hg augmented ischemic neuronal damage. Reducing the MABP at a fixed pO_2 also augmented brain damage. The results demonstrate that hypoxia facilitates brain damage when blood flow is impaired, but hypoxia alone, in the absence of arterial occlusion, is incapable of causing brain damage in intact animals.

5.

Incidence and Significance of Amyloidosis of the Temporal Artery: a Study of 170 Consecutive Biopsies.

K.L. BURNS and V.J.A. MONTPETIT (Ottawa, Ontario)

Amyloidosis of the temporal artery can present with symptoms of giant cell arteritis (GCA) and there may be evidence of both in the same vessel. The nature of the amyloidosis varies. We reviewed 169 temporal artery biopsies: 28 had GCA; 30 had "senile amyloidosis of the internal elastic lamina (IEL) of the temporal artery" (SATA); only three had both. In one case SATA occurred with primary amyloidosis. Deposits of amyloid were present in the media and focally in the IEL. Lambda light chains were demonstrated in the media but not in the IEL. Rare giant cells and small clusters of lymphocytes were present at the medial-adventitial border. Staining for beta-amyloid was negative in this case and in others with SATA. Amyloid has been described in the IEL in temporal arteritis and now also in the absence of GCA. The type of amyloid here and its significance is not known.

Primary amyloidosis may involve the temporal artery. Secondary amyloidosis could conceivably occur as a sequel to altered vascular permeability due to inflammation, but this has not been proven. A foreign-body giant cell reaction to deposited amyloid may cause confusion. Of interest, Salvarani et al. cited one case of amyloid (prealbumin) in a temporal artery in a patient with GCA.

6.

The Histopathology of n-butyl Cyanoacrylate Embolotherapy for CNS Arteriovenous Malformations.

R.R. HAMMOND, J.C.E. KAUFMANN and A.J. FOX (London, Ontario)

Endovascular techniques for the treatment of CNS vascular malformations and aneurysms have increased in their extent and efficacy since their inception in the 1960s. Since 1978, more than 200 arteriovenous malformation (AVM) embolizations have been performed at the University Hospital. Embolization was used as primary or adjunctive therapy to facilitate surgical removal. More than 50 of these lesions were subsequently resected in the early or late post-embolization period. A variety of materials were employed including isobutyl cyanoacrylate (IBCA), polyvinyl alcohol (PVA), avitene (AVT) and more recently n-butyl cyanoacrylate (NBCA). Tantalum (TAN) was admixed as an inert radioopaque tracer.

A recent switch to NBCA alone as the material of choice affords us the opportunity to compare its histotoxicity to that of previous agents. All of the embolizing agents elicit qualitatively similar histopathologic responses, the nature and extent of which is most dependent upon the duration of exposure (i.e., time between embolization and resection). Acutely, any of these agents can incite a prominent acute inflammatory reaction which is frequently associated with frank necrosis of vessel walls. Late tissue reactions are of a chronic, foreign body type. Recanalization of occluded lumina occurs weeks to months after treatment in a minority of cases and may follow embolization by any of the agents used.

7.

The Overexpression of Nestin and Vimentin in the Ependymal Cells in Hydrocephalus.

T. TAKANO, J.T. RUTKA and L.E. BECKER (Toronto, Ontario)

Ependymal immunoreactivity of nestin, vimentin and glial fibrillary acidic protein (GFAP) was examined in normal brains (11 weeks postconceptional age to 6 months of age) and 12 hydrocephalic brains (3 cases each of congenital aqueduct stenosis, Dandy-Walker malformation, Chiari type II malformation and posthemorrhagic hydrocephalus). In normal brains, ependymal immunoreactivity with antisera to nestin and vimentin was detected at 11 weeks of gestation and persisted to term when immunoreactivity declined. In hydrocephalus, nestin and vimentin immunoreactivity with or without GFAP immunoreactivity, was detected along the ventricular surface in areas of ependymal cell loss, glial nodule formation, roof or floor plate of fourth ventricle or cerebral aqueduct, ventral part of third ventricle, and germinal layer of third or lateral ventricles. These results may indicate that the overexpression of nestin and vimentin in hydrocephalus follows two patterns: a reactive pattern associated with ependymal cell loss and glial nodule formation or an abnormal developmental pattern with immunopositivity associated with anatomic regions of the ventricular system.

8.

Fatal Atlanto-Axial Subluxation in Hurler Syndrome.

E. JOHNSON (Edmonton, Alberta)

Atlanto-axial subluxation is a rare complication of mucopolysaccharidosis type I, Hurler syndrome (MPS I H), that radiologically has been attributed to hypoplasia of the odontoid. Nonetheless, there have been no confirmatory pathologic studies. This report records the case of a 5-year-old boy with MPS I H (2½ years post bone marrow transplant), who sustained a

fatal atlanto-axial subluxation after a fall at home. A post-mortem radiologic skeletal survey, compared to a similar study done 3 years previously, showed improvement in bone lesions and hypoplasia of the odontoid. At autopsy, atlanto-axial subluxation with hemorrhagic myelomalacia of the C1-C2 spinal segments was confirmed. However, this subluxation appeared to be caused by a combination of predisposing factors: laxity of the cruciate ligament, hypertrophy of the cartilaginous portion of the odontoid, and consequential narrrowing of the foramen magnum. This case suggests that children treated with bone marrow transplant for MPS I H remain at risk in the early transplant years for atlanto-axial subluxation notwithstanding an improvement in bone lesions and that the mechanism is due to changes in the atlanto-axial joint, including cartilaginous hypertrophy of the odontoid, not readily detected by conventional radiographic techniques.

9.

Rhabdomyolysis and Dystrophic Calcification of Skeletal Muscle.

H.J. MANZ (Washington, U.S.A.)

A retrospective analysis of autopsy cases showing myofiber necrosis or dystophic calcification during the past 12 years was undertaken. The index case was a 50-year-old man with severe ischemic coronary artery disease ultimately requiring orthotopic cardiac transplantation. Three weeks later, flaccid tetraplegia was treated with plasmapheresis and ventilator care; myoglobinuria developed. A muscle biopsy was performed on day 27. He died on day 34 after progressive ARDS, pneumothorax and bronchopneumonia. The biopsy and autopsy depicted massive rhabdomyolysis, minimal inflammation, brisk regeneration and extensive dystrophic calcification frequently evident in mitochondria. There was also focal necrosis and calcification of cardiac myocytes. An additional 10 cases depicted variable degrees of myofiber necrosis and/or calcification. Rhabdomyolysis occurred in a variety of clinical settings, such as organ transplantation, hematologic malignancies, shock, sepsis and influenza. A necrotizing myopathy has been documented by others in critically ill patients. The multitude of drugs used in organ transplantation may act synergistically or idiosyncratically to induce myofiber necrosis and myoglobinuric renal failure. The pathogenesis may be nondepolarizing blocking agents, infusion of blood products, vascular and tissue compression, venous thrombosis and post-ischemic swelling, reduced L-carnitine levels, and elevated interleukin-1. Dystrophic calcification may be precipitated by the massive calcium influx across leaky cell membranes with activation of intracellular proteases and calcium overload in mitochondria.

10.

Chronic Systemic Atropine Treatment Raises ß-APP mRNA Levels in The Rat Hippocampus.

T.G. BEACH and D.G. WALKER (Vancouver, B.C.)

ß-amyloid deposition is a pathogenetic step common to Alzheimer's disease (AD) arising from diverse etiologies. Although several specific genetic alterations have been identified that result in increased deposition of ß-amyloid and an earlier onset of AD, a large fraction of cases of sporadic AD do not possess such risk factors. In addition, ß-amyloid deposition is a virtually universal accompaniment of aging. We hypothesize that ß-amyloid is deposited in both normal aging and AD as a result of age-related cholinergic terminal loss causing upregulation of ß-APP in the denervated regions. Upregulation of ß-APP mRNA and protein induced by lesions of the cholinergic basal forebrain or pathways has already been reported in the literature. In this study, we found that ten days treatment with s.c. atropine (20 mg/kg/day) resulted in an approximately 20% increase in ß-APP mRNA levels (autoradiographically determined after in-situ hybridization) in the granular cell layer and CA1. This supports our hypothesis and suggests that cholinergic enhancers may prevent or slow ß-amyloid deposition. Supported by the Alzheimer Society of B.C.

11.

The Relationship Between Trinucleotide Repeat Sequences and Neurodegeneration in Huntington's Disease.

S. FURTADO, O. SUCHOWERSKY, N.B. REWCASTLE, L. GRAHAM and A. GARBER (Calgary, Alberta)

Little is known about the relationship between the number of trinucleotide CAG repeats and neurodegeneration in the basal ganglia in Huntington's disease (HD). Nineteen HD brains were identified through the Foothills Hospital and Canadian Brain Tissue Bank and each was graded for macroscopic degeneration according to Vonsattel's scale (1985); neuronal counts were performed on sections of anterior striatium. All were evaluated in a blinded fashion with respect to the DNA results from blood (n = 7) and/or frozen and/or paraffinized (n = 12) CNS tissue. Age at death varied from 11 to 84 years; trinucleotide repeats varied from 39 to 93; neuronal counts per 0.25 mm^2 ranged from 3.6 to 24.6 (controls 28.5-38.6).

When correction was made for age at death, greater numbers of trinucleotide repeats were associated with greater neuronal loss in both caudate and putamen suggesting that in HD, longer repeat lengths are associated with faster rate of deterioration and greater pathological severity. Data on duration of formalin fixation and repeat number variation in geographic brain areas will be given.

12.

Neuropathological Changes in Chronic Adult Hydrocephalus.

M.R. DEL BIGIO and W.C. HALLIDAY (Winnipeg, Manitoba)

Twenty-nine patients with suspected "normal pressure hydrocephalus" (age 64-88) consented to cortical biopsy. Eleven exhibited neuritic plaques and/or neurofibrillary tangles. The presence or absence of such changes did not correlate with the clinical response to shunting (p = 0.63). Twelve hydrocephalic adults (age 26-92) were autopsied. Neuritic plaques and neurofibrillary tangles were found in 5/12 brains in the absence of

Alzhiemer's Disease. Neurofibrillary tangles in midbrain neurons were also found in 2 brains. Grumose degeneration in the substantia nigra was identified in 5 brains. None of these features are specific for hydrocephalus. However, they indicated that long-standing hydrocephalus can be associated with neuronal degeneration in addition to the well documented white matter degeneration.

13.

Wallerian Degeneration in the Human Adult CNS.

E.C. ALVORD, JR. (Seattle, U.S.A.)

Wallerian degeneration of the corticospinal (pyramidal) tracts of adult humans begins about 2 weeks after a major stroke with swelling of axons and vacuolization and clumping of myelin. Although the abnormal myelin stains heavily with antibodies to CD68, a macrophage and lysosome marker, sudanophilic macrophages do not appear until at least 3 months. Atrophy is measurable only after about 1 year and progresses for several more years to a decade. The time course is longer in humans than reported in experimental animals.

The early physico-chemical changes compare well with those reported in living patients by magnetic resonance imaging (MRI): 1) no abnormality within the first few weeks, 2) decreased intensity on T2-weighted images for the next few weeks or on proton density images for the next 2 months (corresponding to the swelling of axons, clumping and vacuolization of individual myelin sheaths and activation of CD68 epitopes in the abnormal myelin, all probably resulting in decreased mobility of water molecules), and 3) increased intensity on T2-weighted images beginning about 10 weeks after the stroke (suggesting a liberation of water molecules as the early axonal and myelin changes are absorbed and converted to sudanophilic lipids by macrophagic digestion).

14.

Development of Microglia in CNS.

C. HAO and D.G. MUNOZ (London, Ontario)

Microglial cells are increasingly recognized as playing a critical role not only in infectious diseases, such as HIV encephalopathy, or inflammatory diseases, such as multiple sclerosis, but also in degenerative diseases, such as Alzheimer's and amyotrophic lateral sclerosis. However, our knowledge of the normal development and anatomical distribution of microglia is limited. We have addressed this issue by studying the development of microglia in murine brains, utilizing the new histochemical technique of inosine diphosphatase on vibratome sections. Microglia were first seen in the brain at the newborn stage, as amoeboid cells closely associated (on or in) penetrating blood vessels. This is in contrast with descriptions in the literature, based on ultrastructural identification, indicating that microglia appear at the time of vascularization of the brain, during the embryonic period. Our results suggest that microglia derive from blood cells, rather than neuroglial precursors, but that maturation of either hematogenous precursors, or the brain must occur to enable microglia invasion. Over the next two weeks microglia differentiated into ramified forms covering the grey and white matter of the cerebral hemispheres in a closely knit, orderly network. Differences in the density and morphology of the cells between grey and white matter reflected adaptation to specific CNS environments. This microglial network is a prime candidate for the structural substrate for the interactions between neural and immune systems of the organism.

15.

Lymphomatoid Granulomatosis of the Temporal Lobe: Possible Confusion With Herpes Simplex Encephalitis.

R.J.B. MACAULAY and H.G. DENEER (Saskatoon, Saskatchewan)

Lymphomatoid granulomatosis (LG) isolated to the CNS is rare. The patient, an 82-year-old man, presented with speech difficulties. Imaging revealed left temporal hypodensity. Herpes simplex (HSV) encephalitis was suspected, and acyclovir was administered. HSV DNA was detected in CSF by PCR. After initial stabilization, he again deteriorated and a biopsy was obtained. Histology showed a lymphoplasmacytic infiltrate in the brain and overlying meninges. Penetrating blood vessels showed angioinvasion and destruction, obliteration of the lumen, endothelial hyperplasia, and reticulin deposition. Lymphocytes exhibited moderate pleomorphism. Mitoses were rare, but immunostaining for Ki-67 using MIB-1 revealed up to 20% positive cells. No viral inclusions were identified. Immunohistochemistry showed mostly T-cells with sparse B-cells. Immunostaining and electron microscopy were negative for HSV. The histologic features were characteristic of lymphomatoid granulomatosis. Epstein-Barr virus (EBV) was detected in biopsy material by PCR, consistent with the suggested pathogenetic link between EBV and LG. Because of the suggestion that LG may represent low grade lymphoma, our patient underwent cranial irradiation. No association between HSV and LG has been reported. The rate of false positive results for HSV DNA is not well-established, and the significance of our findings is unclear.

16.

The Effect of Chronic Anti-Inflammatory Drug Use on Brain Microglia.

I.R.A. MACKENZIE (Toronto, Ontario)

Microglia are immune-competent cells which participate in acute inflammatory processes in the CNS and chronic neurodegenerative conditions. In Alzheimer's disease (AD) the association of microglia and immune system proteins with senile plaques suggests that immune mechanisms are involved in AD and that anti-inflammatory drugs may modify the course of the disease. To examine the effect of nonsteroidal anti-inflammatory drugs (NSAID) on brain microglia, the number and degree of activation of cells was compared amongst three groups; non-demented arthritis patients with a history of chronic NSAID use (n = 12, mean age = 73 ± 12 years), arthritis patients who had used only acetaminophen for analgesia or no drugs (n = 10, mean age = 70 ± 12 years) and

a control group with no history of dementia, arthritis or regular NSAID use (n = 15, mean age = 72 ± 10 years). Cases were obtained from the autopsy files at University Hospital, London, Ontario. Quantification was performed on formalin-fixed, paraffin-embedded sections of temporal neocortex. Although the number of microglia labelled with *Ricinus communis agglutinin-1* (RCA-1) lectin was slightly fewer in NSAID users than controls, a more significant difference was seen using CR3/43; an anti-MHC class II antibody which recognizes *activated* microglia. There were few CR3/43-positive cells in the NSAID group (mean = 5 ± 4 cells/mm^2) compared with arthritis controls (21 ± 23 cells/mm^2) and non-arthritis controls (19 ± 14 cells/mm^2). This suggests that chronic NSAID use modifies the base-line level of microglial activation. The implications for treating AD will be discussed.

17.

Primary Non-Hodgkin Lymphoma Arising From the Choroid Plexus.

G. TSE and J. PROVIAS (Toronto, Ontario)

Primary CNS lymphoma is rare in immunocompetent patients, and accounts for less than 5% of primary intracranial malignancies. Most reported cases are of non-Hodgkin types, and most are B cell in origin. The presence of tumour cells in the basal ganglia and corpus callosum with widespread infiltration into the white matter is the usual pattern of spread. We report a case of primary B cell lymphoma which originated from both choroid plexi, which were massively enlarged with the tumour spreading along the ventricular ependymal lining in the direction of the CSF flow to involve the third ventricle, the aqueduct, the fourth ventricle and through the foramina to the subarachnoid space, where the tumour cells focally condense to form a nodule in the cerebello-pontine angle and cause clinical symptoms. In the periventricular white matter, there is only microscopic single cell infiltration. There was no evidence of systemic spread of the disease at autopsy. This case is unique as there is minimal involvement of the cerebral parenchyma with the major tumour load present within the ventricular system as compared to most primary CNS lymphomas, and is also distinct from the recently described primary leptomeningeal lymphomas, in which parenchymal involvement is also absent.

18.

Extensive Telangiectases of Cerebral White Matter in Ataxia Telangiectasia.

B.H. LIWNICZ and R.G. LIWNICZ (Loma Linda, U.S.A.)

A 30-year-old woman with a diagnosis of ataxia telangiectasia since the age of 5 died as a consequence of interstitial viral pneumonia. Post-mortem examination showed cerebellar atrophy with Purkinje cell dropout, extensive gliosis and mild white matter telangiectases. A striking finding in this case was numerous cerebral telangiectases associated with gliosis. This finding is uncommon and to our knowledge was reported only twice before. (Agamanolis and Greenstein, J. Neuropathol. Exp. Neurol., 1979; Amromin et al., J. Neuropathol. Exp. Neurol., 1979). In all three cases with telangiectases of cerebral white matter, patients had a long survival of 30 years and over. In the reported case, telangiectases were confined to CNS with only a single small vascular malformation in an adrenal gland. There were no evident angiomas of the skin, mucosal surfaces or the conjuntiva.

19.

Hemangioblastomas: Immunohistochemical Studies.

S. NAG (Toronto, Ontario)

Hemangioblastomas were studied by immunohistochemistry to determine glucose transporter (GLUT-1) expression. The latter protein is highly specific for cerebral endothelium and not expressed in the majority of noncerebral endothelium with the exception of endothelium in the testis. In addition, expression of the extracellular matrix proteins – laminin, fibronectin and collagen IV, which are normal constituents of vessel walls was studied. The endothelium of normal cerebral vessels were strongly immunoreactive with GLUT-1 antisera. Basement membranes of intracerebral vessels showed mild immunoreactivity with collagen IV, fibronectin and laminin antisera.

In hemangioblastomas, endothelial cells resembled normal cerebral endothelium and showed GLUT-1 immunoreactivity while the stromal cells were nonreactive. There was over expression of all the extracellular matrix proteins studied in tumor vessels, particularly laminin which was present in endothelial cells as well. This study describes two additional markers for endothelial cells in hemangioblastomas – GLUT-1 and laminin. Neither markers were demonstrable in stromal cells, which continue to be an enigma.

20.

Search for Mechanisms of Neurodegeneration in HIV Encephalitis.

C.A. WILEY (Pittsburgh, U.S.A.)

About one-third of AIDS patients develop a dementia complex during the terminal stages of disease. HIV encephalitis is the pathologic substrate of this complex. Unlike other viral encephalitides where virus can be recovered from the central nervous system (CNS) only when it mediates disease, HIV is found in the CNS in the majority of AIDS autopsies. The severity of HIV encephalitis (as assessed by measuring abundance of viral burden) covers a broad spectrum, with CNS viral burden measurements showing a good correlation with the severity of CNS damage. Nevertheless, the primary mediator of neurologic damage in HIV encephalitis remains an enigma. As we have been unable to confirm recent reports of abundant neuroglial infection by HIV, or a specific neurotropic strain of HIV, we have examined a variety of other pathogenic mechanisms that could mediate neuritic damage. At the present time leading theories of the pathogenesis of neurologic damage associated with HIV encephalitis include; toxic viral proteins, toxic activated macrophage factors, and loss of neurotrophic factors.

Titles of Diagnostic Case Presentations

1. **Dermatofibrosarcoma protruberans, metastatic.**
   I. AUER and R.A. AUER (*Calgary AB*).

2. **Cerebellar ganglioglioma with a pleomorphic xanthoastrocytoma component.**
   A. PERRY and B.W. SCHEITHAUER (*Rochester MN*).

3. **Thrombotic occlusion of atherosclerotic basilar artery with calcification, ossification and metaplastic bone marrow.**
   A.H. KOEPPEN (*Albany NY*).

4. **Primitive neuroectodermal tumor.**
   M.G. NORMAN (*Vancouver BC*).

5. **Congenital ependymoblastoma.**
   J. WOULFE, J.C. WALTON and D.G. MONOZ (*London ON*).

6. **Pick's Disease.**
   J.B. LAMARCHE (*Sherbrooke PQ*).

7. **Orthochromatic leukodystrophy, pigment type.**
   P. SHANNON and S. NAG (*Toronto ON*)

8. **Myositis and encephaloyelitis caused by Neospora caninum.**
   P.B. LITTLE and M. GAINES (*Guelph ON*).

9. **Malignant peripheral nerve sheath tumor with glandular differentiation associated with a plexiform neurofibroma.**
   C. GIANNINI and B.W. SCHEITHAUER (*Rochester MN*).

10. **Bilateral lipomas of cerebellopontine angle.**
    E.S. JOHNSON, K. SCOTT, D. OLDRING and R. BROAD (*Edmonton AB*).

11. **Extensive chondromatous differentiation.**
    B. LACH, B.W. SCHEITHAUER and B.G. BENOIT (*Ottawa ON*).

12. **Granular cell neoplasm of 5th cranial nerve.**
    R.D. BROWNLEE and N.B. REWCASTLE (*Calgary AB*).