Canadian Association of Neuropathologists

Abstracts

of papers presented at

The 26th Annual Meeting

September 1986

Summary

The 26th Annual Meeting of the Canadian Association of Neuropathologists was held September 25, 26, and 27, 1986 at Hecla Island, Manitoba. Approximately 50 members and guests attended the meeting. The meeting was a mixture of abstracts (listed below) and diagnostic case presentations. The slides had previously been sent to members as unknowns. At the meeting, opinions were expressed on each case. The presenter then gave a scientific presentation based on the material. All members felt that this was a rewarding educational experience. A number of presentations, both diagnostic cases and abstracts were given by the residents and fellows in pathology, neuropathology and neurological sciences.

Two awards for presentations by trainees were given:

The Mary Tom Award: Dr. L.C. Ang, London, Ontario: Diffuse Lymphoma Involving the CNS.

The Morris Finlayson Award: Dr. D. Isukawa, Ottawa, Ontario: Immunocytochemical Analysis of Intermediate Filament Protein in Human Ependymal Tumours.

During the meeting there were two special lectures:

Dr. A. Engel, Mayo Clinic, Rochester, Minnesota

The Royal College of Physicians and Surgeons of Canada Lecture

Title: "Immunopathological Studies in Muscle Diseases"

Dr. J. Kepes, University of Kansas, Kansas City

The Jerzy Olszewski Guest Lecture

Title: "Astrocytomas: Old and Newly Recognized Variants. Their Spectrum of Morphology and Antigen Expression"

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1.

Brain Morphology in Duchenne Muscular Dystrophy: A Golgi Study

V. JAGADHA and L.E. BECKER (Toronto, Ontario)

Intellectual impairment in association with Duchenne muscular dystrophy (DMD) is well recognized, although no consistent anatomical lesions in the central nervous system (CNS) have been corroborated. We reviewed the autopsy findings of 13 patients with DMD ranging from 13-18 years at the time of death. Details of intellectual assessment were available in five patients with the following IQ values: 50 (case 5), 75 (cases 10 and 11), 79 (case 12) and 46 (case 13). Gross and microscopic examination of the brain and spinal cord did not reveal a totally consistent pattern of abnormalities. The neuropathology included neuronal loss and gliosis in spinal grey matter and tegmental brainstem (case 1), extensive Purkinje cell loss, and mononuclear perivascular cuffing with gliosis in cortical and subcortical areas (case 5), and cerebral heterotopia (case 9). Quantitative analysis of rapid Golgi impregnations of the visual cortex revealed a significant reduction in the total dendritic length and branching of apical and basal dendrites of pyramidal neurons in one patient (case 12), and attenuated dendritic arborization in another patient (case 11).

A review of the literature suggests that the intellectual deficit in DMD is nonprogressive and unrelated to age or severity of muscle disease, although the performance IQ may deteriorate with progressive muscle weakness. The Golgi analysis in our patients suggests that abnormalities in dendritic development and arborization may underlie the intellectual impairment in DMD. Although the pathogenetic basis of the cellular defect in DMD is not fully known, the coexistence of CNS and muscle pathology raises the possibility of a common molecular mechanism operative in the brain and muscle.

2.

Laurence-Moon-Bardet-Biedl Syndrome Associated with Cerebellar Vermis Aplasia

JACQUES B. LAMARCHE and CHRISTIAN FISH (Sherbrooke, Quebec)

The Laurence-Moon-Bardet-Biedl syndrome is a rare hereditary affection characterized by retinitis pigmentosa, polydactyly, obesity, hypogenitalism and mental retardation. Neuropathological studies are very few and have failed to demonstrate any consistent lesional pattern. The brains have been reported to be either normal or to show a variety of gross and microscopic abnormalities of uncertain significance. The neuropathological findings of a typical case of Laurence-Moon-Bardet-Biedl syndrome are presented. The patient, the first child of a family of 3, was a girl born of healthy French-Canadian parents who were first cousins. A sister 8 years younger than the patient is partially blind and shows macrocephaly, psychomotor and mental retardation, obesity and tapeto-retinal degeneration. At birth, the child weighed 3291 g and the head was noted to be large measuring 36 cm. She was hypotonic and showed a supernumary digit of all 4 limbs which was excised at age 2 years. Mental and motor retardation became evident by age 4 months. At age 6 years, pertinent physical findings included macrocephaly (head circumference 58 cm), retinitis pigmentosa, hypotonia, nystagmus, intermittent strabismus, bilateral ptosis, obesity, genu valgum, and severe mental and psychomotor retardation. She became blind at age 17 years and died from bronchopneumonia at age 19 years following progressive renal failure. At autopsy, the head circumference was 61 cm. The brain weighed 1680 g and no definite anomalies of configuration of the cerebral gyri and ventricular system, hypothalamic structures and pituitary gland were observed. The cerebellum was very large and showed almost total aplasia of the vermis with hypertrophy of both hemispheres. The 4th ventricle was enlarged. Numerous gross and microscopic architectural anomalies were noted in the midbrain, pons and medulla. Examination of the eyeballs confirmed the pigmentary retinitis and both optic nerves showed peripheral atrophy. The malformations observed in the cerebellum and brain stem of this patient are rare and have never been described in the Laurence-Moon-Bardet-Biedl syndrome. The lesions which could partly explain some of the clinical neurological signs mainly represent a defect of migration of the rhombic lip nerve cells. The Laurence-Moon-Bardet-Biedl syndrome should be added to the list of developmental disorders which can be associated with aplasia of the cerebellar vermis.

3.

Peripheral Nerve Findings in Neurological Crisis Complicating Hereditary Hepatorenal Tyrosinemia (Type I)

JEAN MICHAUD, GRANT MITCHELL, JEAN LAROCHELLE, SERGE MELANÇON and LOUIS DALLAIRE (Montreal, Quebec)

With early detection and improved treatment, most patients with hereditary hepatorenal tyrosinemia now survive the neonatal period and are followed to childhood and early adolescence. Sixty-one patients identified by neonatal screening in the province of Quebec were reviewed retrospectively and 25 were found to have developed recurrent motor, sensory and autonomic neurological crises. This complication, which was more frequent than and not necessarily associated with renal or hepatic failure, arrived most frequently after infancy. Clinically, two presentations dominate: acute severe pain and paralytic crisis.

We report the peripheral nerve findings in an 18-month-old-girl who developed a complete tetraparesis, six days following admission for fever and vomiting. Cranial nerve function were intact and she remained alert. She had no pain sensation. The following day, peripheral nerve conduction velocities were normal but were completely undetectable two weeks later. Without anesthesia, muscle and sural nerve biopsies were done. Thick sections of the nerve revealed a severe loss of myelinated fibers of all caliber with numerous globular debris. By E.M., severe axonal degeneration and loss was documented with accumulation of cellular debris and lamellar or granular ovoids. Unmyelinated fibres were involved as well. The muscle biopsy showed changes of an acute neurogenic atrophy and intramuscular nerve twigs were either unmyelinated or poorly myelinated. Three weeks after the onset, she began to recover slowly but when discharged 15 weeks after admission she had not completely recovered. During this episode, liver function was stable and blood tyrosine levels were normal. However, urine levels of delta amino-levulinic acid were increased. One year later, she developed a similar clinical picture complicated by renal failure.

Similar clinical and laboratory data from a nine-year-old boy (no biopsy material) and clinical and morphologic data from a two-month-old boy who developed a paralytic crisis at three weeks of age (and who died eight years ago) have also been reviewed.

It is suggested that neurological crisis in hereditary hepatorenal tyrosinemia is secondary to a deranged phorphyrine metabolism. These crises pose a major problem in tyrosinemic children as in other diseases with deranged delta aminolevulinic acid metabolism and episodic neuropathy such as acute intermittent porphyria and lead poisoning.

4.

Amyloid Angiopathy in Alzheimer's Disease

C. BERGERON, P.J. RANELLI and P.N. MICELI (Toronto, Ontario)

Thirty cases of Alzheimer's disease and 30 age-matched controls were studied to determine the incidence of cerebral amyloid angiopathy

and its relationship to age, neuritic plaque formation, and amyloid plaque content. Standardized sections were obtained from three neocortical sites as well as cerebellum, and evaluated semiquantitatively on a scale of 0 to 4 using Congo Red and Bielchowsky stains. Cumulative neocortical scores were then derived for cerebral amyloid angiopathy (CAA), neuritic plaque formation (NP) and amyloid-rich plaques (ARP). CAA was present in 86% of AD cases and 40% of age-matched controls. Its frequent occurrence in AD is not merely a reflection of the advancing age of this group, it is related to the formation of neuritic plaques, without which it is never seen, and represents an integral, though not essential, component of AD. Neuritic plaques, however, did occur in the absence of CAA in 17% of all cases. These results support the hypothesis that brain amyloid is produced locally, rather than hematogenous or systemic in origin. Cumulative neocortical scores for CAA and ARP show that the amount of vascular and plaque amyloid tends to be of comparable severity in many cases, but that significant discrepancies are observed, with preferential deposition of amyloid in either plaque or vessel. Individual variability exists in the amount, localization and perhaps mobilization of cerebral amyloid.

5.

"Ischemic Association Axonopathy: A Pathogenetic Mechanism to Explain White Matter Lucencies in Some Patients with Dementia of the Alzheimer Type"

M.J. BALL, A.J. FOX, V. HACHINSKI, H. MERSKEY, W. BLUME and M. FISMAN (London, Ontario)

A 73-year old florist suffered progressive cognitive decline for about fourteen years before death. Her father had died in his forties from a myocardial infarct, and two siblings suffered from heart disease. The Ischemic Score (of Hachinski) was 0, and the clinical diagnosis was Alzheimer's disease. However, electroencephalography showed typical (rather than the usual atypical) triphasic waves, raising the possibility of a metabolic encephalopathy (? hepatic, ? post-anoxic). CT Scan of the head six years before death showed extensive white matter low densities abutting on the frontal and occipital horns bilaterally, as well as severe enlargement of the lateral ventricles and moderate prominence of the sub-arachnoid spaces.

At autopsy, an acute myocardial infarct was associated with severe coronary atherosclerosis, 95% stenosis of the right coronary artery, complete thrombotic occlusion of one of its segments, and 75% stenosis of the left anterior descending and circumflex coronary arteries. The brain weighed 1030 grams, and showed all the gross and microscopic features typical of Alzheimer's disease.

In addition, however, hundreds of leptomeningeal branches of the anterior, middle and posterior cerebral and superior cerebellar arteries showed old thrombotic stenoses with "double lumina"; and an extensive laminar necrosis of the superficial layers of the neocortex was seen in all lobes, especially in association areas. This neuronal depletion was accompanied by huge numbers of neuroaxonal "spheroids", and iron pigment both free and in hemosiderophages. A single large, old hemorrhagic infarct was present in the left temporal lobe.

The severe pallor of the myelin in much of the deep white matter was not accompanied by any significant abnormalities of the white matter vessels themselves. However, massive secondary demyelination and gliosis throughout the white matter were secondary to axonal depletion.

It is proposed that in this case, the hypodense lucencies of the white matter now being referred to as "leukoaraiosis" reflect a destruction of axons originating from the neurons of the external pyramidal layer of the cortex, whose perikarya have been damaged due to leptomeningeal ischemia.

This Ischemic Association Axonopathy may contribute significantly to the cognitive deterioration of patients who have suffered from repeated episodes of systemic hypotension. (Supported by NIH Grant #2 R01 AG03047 and MRC Grant #PG 21).

6.

Morphological and Biochemical Correlates of Pre-Frontal Biopsies in a Betanechol Perfusion Program for SD/SDAT

Y. ROBITAILLE, R. QUIRION, R. LEBLANC and S. GAUTHIER (Montreal, Quebec)

A cohort of 9 patients diagnosed as Alzheimer's Disease on the basis of minimental state scores were selected for a trial program of intraventricular betanechol perfusion. A pre-frontal 2.0 cm. large biopsy was submitted during insertion of an intraventricular catheter. The cortex was dissected from white matter, snap frozen and stored at -80 for biochemistry and diced into 0.2 cm. cubes for gluteraldehyde fixation. The rest was fixed in 10% buffered formalin. Histopathological criteria for inclusion within the AD/SDAT group were neurofibrillary tangle (NFT) and senile plaque (SP) indexes of at least 20/mm^3 and 10/mm^2 respectively on sections stained by the modified Bielschowsky technique. Accordingly 6/9 patients could be classified in the AD/SDAT group. Screening of thin epon sections revealed large amounts of neuronal paired helical filaments with frequent intrasynaptic extensions involving both pre and post synaptic components. Non diagnostic cases were characterized by high densities of unpaired straight filaments, mostly within neurites but not involving synapses. ChAT activity was markedly reduced in 8/9 patients (mean ± SEM AD/SDAT = 0.68 ± 0.07 mmol/mg. Pr./h, control non demented epileptic patients = 2.4 ± 0.2). Total muscarinic binding Bmax values measured by [^{3}H] QN3 binding were within range of control values (mean ± SEM AD/SDAT = 962 ± 147 fmol/mg. Pr, control 1188 ± 124) in 6 patients. In a cluster of 4 patients, Bmax values were markedly reduced (mean ± SEM = 577 ± 52 fmol/mg. Pr.). Correlations of NFT and SP indexes with muscarinic binding by regression line analysis were highly significant for NFT indexes ($r = 0.915$) but not for SP indexes ($r = 0.4878$). NFT indexes were also correlated significantly with minimental state scores ($r = 0.850$) vs 0.3362 for SP indexes. In conclusion, these results show that AD/SDAT is associated with early neurofibrillary degeneration in pre-frontal cortex which suggests its simultaneous involvement of presynaptic cholinergic afferents and post-synaptic intracortical neurones in the dementing process.

7.

Electron Spectroscopic Imaging (ESI) of Phosphorus on Neurofilaments (nf) and on Paired Helical Filaments (PHF) of Alzheimer's Disease (AD).

A. CLARK, I. PARHAD, M. SCHOEL and D. BAZETT-JONES (Calgary, Alberta)

Phosphorylation of the neuronal cytoskeleton is important to normal structure and function. Biochemical studies have defined the amount of phosphorus present in the nf protein subunits (Julien & Mushynski 1982). Immunohistochemical studies have mapped the distribution of certain phosphorylated epitopes of the nf within the neuron (Sternberger & Sternberger 1983), and have extended this phosphorylated research into the field of neuropathology. Specifically, certain phosphorylated nf epitopes appear to be components of the PHF of AD, suggesting that aberrant phosphorylation may be significant in the pathogenesis of the PHF (Sternberger 1985). None of these studies or techniques provide information on the spatial distribution of phosphorus on the normal nf or on the PHF of AD. We have used recent advances in ultrastructural imaging of chemical elements (Bazett-Jones & Ottensmeyer 1982; Ottensmeyer FP 1984) to obtain direct imaging of phosphorus on the normal nf and on the PHF of AD.

The sciatic nerves of adult rats perfused with glutaraldehyde were used for studies of nf. A brain biopsy from a patient with dementia, obtained for diagnosis during placement of a shunt, was the source of

PHF. The tissue was processed for electron microscopy as usual; no phosphate buffers were used. The Epon-embedded tissue was sectioned at a thickness of less than 40 nm, and examined with a Zeiss 902 electron microscope equipped with an electron imaging spectrometer. Image pairs (reference and phosphorus enhanced) were photographed and processed on an IBAS image analysis system to determine the net phosphorus distribution.

Both the normal nf and the PHF of AD show phosphorylation sites generally in a uniform distribution along the respective structures. The core as well as the sidearms of the normal nf are phosphorylated, and our preliminary data show no distinct differences between these components. On the PHF of AD, there were sites of significant attenuation; these were most common at crossover points.

The technique used in this study corroborates biochemical and immunohistochemical evidence that nf and PHF are phosphorylated. It is capable of imaging phosphorus at a spatial resolution of 5 A and a sensitivity of detection of 2×10^{-21} g, corresponding to about 50 atoms of phosphorus. The high spatial and quantitative resolution provided by ESI make it a useful technique in the study of protein phosphorylation in normal and pathologic settings.

8.

Jakob-Creutzfeldt Disease Associated with Wernicke's Encephalopathy

S. GAYTAN-GARCIA, J.J. GILBERT and J.C.E. KAUFMANN (London, Ontario)

Wernicke's Disease (WD) is a complication of alcoholism and malnutrition. On the other hand, Jakob-Creutzfeldt Disease (J-C) results from infection with an unconventional agent with a long incubation period and is characterized by a rapidly progressive dementia and histologically by a spongiform encephalopathy associated with neuronal destruction and pronounced astrogliosis.

We report 2 cases with typical findings clinically and neuropathologically of J-C disease and WD was an unexpected autopsy finding in both cases.

The first patient was a 67 year old lady who developed progressive unsteadiness of gait, receptive and expressive aphasia, marked deterioration in her intellectual capacity and impaired memory. She deteriorated progressively and eventually became mute, spastic and developed myoclonic jerks in response to startle. She expired 5 months after the onset of her illness.

The second patient was a 68 year old woman who was admitted to the hospital 3 months prior to death with speech disturbance, decreased memory, gait disturbance and odd posturing. An EEG showed periodic sharp waves; she deteriorated rapidly and was eventually unable to communicate.

Several possibilities should be considered in the pathogenesis of WD in association with J-C disease. It is possible that Wernicke-type pathology may be commoner than suspected in the brains of J-C disease and other disorders with dementia and develops surreptitiously without clinically obvious episodes or perhaps cannot be recognized because of overlapping symptoms. It may be that the bedridden demented patient is simply malnourished and vitamin deprived. On the other hand WD is not often seen in the Alzheimer disease bedridden patient.

9.

Combined Thyrotroph and Lactotroph Hyperplasia Simulating Prolactin-Secreting Pituitary Adenoma in Longstanding Primary Hypothyroidism

E.P. PIORO, B.W. SCHEITHAUER, E.R. LAWS, R.V. RANDALL, K. KOVACS and E. HORVATH (Toronto, Ontario and Rochester, Minnesota)

Longstanding primary hypothyroidism accompanies more than 50% of clinically significant pituitary thyrotroph adenomas.[5] Lack of thyroid hormone secretion has also been shown to produce pituitary enlargement with clinical manifestations of a sellar mass and/or hyperprolactinemia.[1,2,6] Three patients with longstanding primary hypothyroidism are reported herein who presented with clinical evidence of prolactin-producing adenomas. Although some hypothyroid patients with pituitary enlargement have shown resolution of laboratory and radiologic abnormalities upon treatment with thyroid hormones,[1] the patients we report showed no clinical improvement and therefore underwent transsphenoidal surgery. Histologic examination of the pituitary revealed no adenomas but features of both thyrotroph and lactotroph hyperplasia. It is suggested that thyrotroph hyperplasia results from at least two factors related to thyroid hormone deficiency: a) release of excessive amounts of thyrotropin releasing hormones (TRH) from the hypothalamus[3] and b) dopamine deficiency, which inhibits thyroid stimulating hormone (TSH) release.[4] The cause of lactotroph hyperplasia in hypothyroidism is unknown but may result from similar causes: a) excess TRH stimulates lactotrophs with resultant hyperprolactinemia[3] and b) reduction in hypothalamic dopamine which inhibits secretion of prolactin. In summary, we suggest that hyperprolactinemia in hypothyroid subjects is not due to "stalk section effect" secondary to pituitary enlargement because of thyrotroph hyperplasia. We conclude that patients with longstanding primary hypothyroidism and evidence of pituitary dysfunction should initially be managed medically so that potentially reversible pituitary hyperplasia is not mistaken for adenoma.

[1]Bilaniuk LT, et al. J Neurosurg 1985; 63: 39-42.

[2]Khalil A, et al. J Endocrinol Invest 1984; 7: 339-404.

[3]Reichlin S. Neuroendocrinology. *In*: Wilson JD and Foster DW (eds), Williams Textbook of Endocrinology, Seventh Edition, W.B. Saunders Co. 1985; pp. 510-512.

[4]Scanlon MF, et al. J Clin Endocrinol Metab 1981; 53: 360-365.

[5]Scheithauer BW: Surgical Pathology of the Pituitary: The Adenomas, Pt II. *In*: Somers SC and Rosen PP (eds), Pathology Annual, Volume 19, Pt 2, Appleton-Century-Croft 1985; pp 269-329.

[6]Stoffer SS, et al. Fertil Steril 1981; 36: 682-685.

10.

Pituitary Adenoma and the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

D.D. EISENSTAT, M.L. SCHWARTZ, K. KOVACS, A.J. LEWIS and I. FETTES (Toronto, Ontario)

A 64 year old man presented with a 2 month history of weakness, lethargy and confusion. Serum sodium (Na) was 117 mEq/L, plasma osmolality was 250 mOsm/kg, urine Na was 81 mEq/L and urine osmolality was 274 mOsm/kg. Hyponatremia responded to fluid restriction and demethylchlortetracycline (demeclocycline), 300 mg qid, but serum Na fell to 124 with a fluid intake of 1500 cc/day. Nevertheless, the patient's sensorium cleared and he was discharged. A CT scan showed a pituitary tumour with slight suprasellar extension.

Nine months later, the patient returned with similar symptoms, decreased right visual acuity (20/200) and a left temporal field defect. Serum Na was 118, osmolality 238; urine Na was 32, osmolality 360. Demeclocycline and fluid restriction were begun. Serum Na rose to 131 mEq/L after 1 week. CT scan was unchanged. Pituitary function was normal.

Three months later he returned with a history of falling episodes, weakness, confusion and unsteady gait. Visual acuity was diminished bilaterally and bitemporal hemianopsia was evident. Serum Na was 117, osmolality 240; urine Na was 75, osmolality 330. After transsphenoidal tumour excision, demeclocycline and fluid restriction were stopped. Histology showed an FSH and LH-storing adenoma with

choristoma cells. Five weeks post-surgery, serum Na, osmolality and urine osmolality were 140, 284 and 167, respectively. Vision had improved, lacking only colour vision in the superior temporal quadrants. He was on testosterone replacement.

SIADH has been associated with experimental preoptic lesions, hypothalamic glioma, neurohypophyseal choristoma and "chromophobe" adenoma. This is the first case where SIADH has been reversed with tumour excision.

11.

In-Situ DNA Hybridization Versus Immunoperoxidase Methods for Localization of Herpes Simplex Virus

B. CURRY, M. ONOUE, A. KOSSAKOWSKA and N.B. REWCASTLE (Calgary, Alberta)

Using paraffin embedded material, 25 cases (this retrospective analysis included both surgical and autopsy material) were examined for the presence of Herpes Simplex Virus by in-situ hybridization (using a biotinylated DNA probe) and immunoperoxidase methods. Ten of these cases were positive using both techniques; these same cases were also proven by viral culture and/or electron microscopy to contain Herpes Simplex virus. Two other varieties of proven Herpes virus infection (CMV and Herpes Zoster) were used as negative controls. Other controls included an acute infarct and several varieties of degenerative disorders. The remaining ten cases consisted of a variety of inflammatory encephalitidis for which the etiologic agent was unknown. These were all negative with immunoperoxidase and no virus was identified by the in-situ hybridization method. Both methods were shown to have a relatively similar sensitivity, were performed in a short time, and were highly reproducible. No false positives or false negatives were detected. Unlike the immunoperoxidase method, there is no background staining with the "in-situ" technique. In our experience with Herpes Simplex encephalitis, the immunoperoxidase technique has already, in occasional cases, provided an earlier specific diagnosis than standard virology culture and E.M. techniques. To date the in-situ hybridization method would appear to be an equally valuable diagnostic tool. In an attempt to improve its sensitivity and thus perhaps pick up more subtle or latent Herpes Simplex infections, we are currently comparing the in-situ DNA hybridization method with the southern blot technique.

12.

Oncotic Cerebral and Systemic Arterial Aneurysms

H.J. MANZ, S.L. COHAN, D. SCHELLINGER and J.L. FOX (Washington, D.C.)

Eight months after an uncomplicated full-term pregnancy, a 28-year old woman presented with a rapidly evolving neurologic catastrophe. At autopsy, intracranial hemorrhages were related to oncotic aneurysms due to choriocarcinoma also metastatic in left ventricular myocardium. Aneurysms were present in kidneys and intestine.

Oncotic cerebral aneurysms represent a rare type of aneurysm, an uncommon manifestation of systemic neoplasia, and an unusual cause of intracranial hemorrhage. While berry aneurysms are present in 5% of the adult population, only a few dozen cases of neoplastic aneurysms exist. Among patients with systemic malignant neoplasms, 20% have intracranial metastases, most commonly the result of (arterial) hematogenous dissemination. Massive cerebral or subarachnoid hemorrhage occurs in a relatively small proportion of cases with cerebral metastases; only a fraction of these has been linked to oncotic aneurysms. The latter develop from progressive destruction and weakening of the arterial wall as the neoplastic emboli proliferate and infiltrate, causing aneurysmal dilation and eventual rupture. In analogy with septic emboli, neoplastic emboli tend to lodge at bifurcations of smaller, distal cerebral arteries.

While breast and lung carcinoma are preponderant as intracranial metastases, it is cardiac myxoma and choriocarcinoma which account for the majority of oncotic aneurysms. Intuitively, one might suggest that cardiac myxoma, as a neoplasm with a purely intravascular location, would not cause much invasive growth in the capacious left atrium, but tumor emboli in the lumen of a small artery would readily invade the vessel's wall. Somewhat analogously, gestational trophoblast is programmed to invade maternal blood sinuses at the placental site; when trophoblast undergoes malignant transformation, this biologic behavior is accentuated so that hematogenous dissemination is a hallmark of choriocarcinoma.

On the other hand, it is difficult to conceptualize why neoplastic aneurysms do not occur more commonly, since, in the process of the development of a matastasis from a tumor embolus, a complex of interdependent events operates; portions of this staircase phenomenon must be common to the formation of oncotic aneurysms and metastases.

13.

Eosinophilic Polymyositis (EP) and Eosinophilic Fastitis (EF): A Comparative Ultrastructural Study

S. DANCEA*, V. MONTPETIT and D. CLAPIN (Ottawa, Ontario)

Our recent electron microscopic findings in two cases of EP led us to believe that eosinophils or their products play a major role in the tissue pathology of the skeletal muscle.[1] Similar histological features have been described by V.J. Ferrans in the endocardium of cardiac biopsies from patients suffering from the hypereosinophilic syndrome (HES).[2] Although EF appears to be a distinct entity, it shares many light microscopic characteristics with EP. Consequently it is appropriate to compare the ultrastructural findings of EF with those of EP. A 57-year-old man developed myalgias and muscle weakness mainly in his legs over a period of six months. This was followed by swelling of his left knee, ankles and wrists accompanied by pain and a maculopapular rash over the legs, thighs and forearms. Skin felt tight particularly over the shins. Laboratory investigations disclosed a mild leukocytosis with 49.7% eosinophils and a SR of 40. The ANA was positive at 1:160. A biopsy of the left quadriceps displayed the classical findings of EF, characterized by a thickened and edematous fascia infiltrated by mononuclear inflammatory cells and abundant eosinophils. While perifascicular atrophy was pronounced, the inflammatory cells were relatively sparse especially in the center of the muscle fascicles. At the ultrastructural level, the capillary basement membrane was thickened and the endothelial cells swollen. The latter displayed numerous pinocytotic vesicles, dense bodies and prominent luminal cell processes. Structural abnormalities of eosinophils indicating activation and degranulation, such as the reversal of their normal staining pattern were observed. Free granules or their contents were noted in the interstitial space. Mast cells were increased in number and disclosed evidence of fusion of their granules and discharge into the pericellular space. These findings, which are similar to our observations of EP, indicate that eosinophils and mast cells play a significant role in the tissue injury. However, immunological studies are required in order to define more precisely the initial events and possible common denominators which mobilize these cells.

*Research Fellowship from the Ottawa General Hospital Research Fund.

[1]Dancea S, Montpetit V and Olberg B (1986). J Neuropath Exp Neurol 45: 371 (Abstract 163).

[2]Fauci AS, et al. Ann Int Med (1982); 97: 78-82.

14.

Multicore Disease Associated With Axonal Neuropathy

K. MEAGHER-VILLEMURE and S. CARPENTER (Montreal, Quebec)

The coexistence of a CNS disease with Multicore disease has not so far been reported in the literature to our knowledge.

The neuropathological investigation of a deceased ten year old boy who suffered a progressive unusual neuromuscular disease since the age of 3½ is reported. Muscle biopsies done during life had revealed involvement of both histochemical types with Z disc streaming, foci of mitochondrial absence and foci of focal denervation. Abnormalities were found in the sural nerve biopsy with some Wallerian degeneration and focal enlargement of the axons. At autopsy, diffuse skeletal muscle disease confirmed the previous diagnosis of Multicore disease and cardiac muscle involvement was also identified. The central nervous system revealed a diffuse unusual form of axonal neuropathy consisting mainly of foci of neurofilament accumulation.

Histological and biochemical findings will be discussed with emphasis on the ultrastructure and immunocytochemical findings. A review of the literature will complete this unusual case.

15.

Myopathy With Ring Fibers: A Report of Three Cases

D.P. AGAMANOLIS, A.C. RAYNOR and R.W. SHIELDS, JR. (Akron and Cleveland, Ohio)

Three young adult males had longstanding myalgias, tightness and cramps involving axial and proximal muscle groups, particularly the low back. There was no muscle tenderness and only one had muscle weakness. These symptoms were present for several years without progression. Creatine kinase was persistently moderately elevated. Nerve conduction was normal. Electromyography showed nonspecific myopathic changes. Radiographic studies were negative. There was no family history of neuromuscular disorder. Muscle biopsy revealed frequent small ring fibers, all type 2, and rare degenerating fibers. Phosphorylase and phosphofructokinase histochemical stains were normal and there was no lipid storage.

These patients do not have myotonic dystrophy or limb-girdle dystrophy. These cases suggest that ring fibers may be a prominent pathological feature in some myopathic states characterized by myalgia and muscle tightness.

16.

Primary Cerebral Sarcomas

I.R.A. MACKENZIE, L. GASPAR, J.J. GILBERT and J.C.E. KAUFMANN (London, Ontario)

Sarcomas are uncommon CNS tumors and at times pose diagnostic difficulties. In a retrospective study of 11 patients with primary sarcomas confined to the brain and meninges, from 1975-1986, we evaluated the clinical course, histologic appearance and histochemical techniques as a means of tumor characterization.

There were 6 male and 5 female patients with a mean age of 45 years (range 21 to 69). One patient was not diagnosed until autopsy, where as 10 had surgical procedures, often multiple. The neoplasms consisted of 5 meningeal sarcomas, 4 fibrosarcomas (3 intracerebral and 1 arising from the meninges), 1 angiosarcoma and 1 anaplastic sarcoma.

The time to presentation was short, ranging from weeks to months, with the chief complaint being headache in most cases. Two patients also experienced seizures. All patients had CT scans of the head and 6 of 11 had cerebral angiography with the resulting diagnosis of meningioma made in *all* cases. Of the 10 surgically treated, 8 had total gross removal, 1 subtotal removal and 1 only biopsy. One patient was lost to follow-up. Of the remaining 9, 2 survive now at 6 and 24 months. The average survival of the others was 19 months (range 2 to 47 months). Both patients who had less than total initial resection died after 5 months. Local recurrence occurred in 6/9, spread within the CNS in 3/9 and spread outside the CNS in 4/9.

In addition to routine stains, immunohistochemical assessment was performed using the peroxidase-antiperoxidase and avidin-biotin complex methods with antisera to GFAP, cytokeratin, vimentin, desmin, factor VIII, S-100 protein and lectin receptors. The meningeal sarcomas showed no positivity for GFAP, desmin, factor VIII, or lectin receptors. Slight S-100 positivity was present in one of several biopsies of one patient and one tumor was consistently positive for cytokeratin. Vimentin was positive in all cases. The fibrosarcomas were also variable. One tumor showed vimentin positivity at each of several resections and another had focal areas positive for cytokeratin, S-100 and GFAP. The anaplastic sarcoma was negative for all antisera and the angiosarcoma was positive for factor VIII.

These tumors were uncommon in our centre. The prognosis is poor with average survival 19 months. The histologic diagnosis is usually possible with routine stains. The use of immunoperoxidase methods is of limited diagnostic value, although it may help to exclude some other tumor types, such as gliomas. The frequent positivity for vimentin needs to be further evaluated.

17.

Angioblastic Meningioma (Dural Hemangiopericytoma): A Pathologic Study of 41 Cases with Long-Term Followup

B.L. GUTHRIE, B.W. SCHEITHAUER and M.J. EBERSOLD (Rochester, Minnesota)

Forty-one patients with angioblastic meningioma were treated between the years 1938 and 1985. There were 24 (59%) males, and 17 (41%) females, ranging in age from 16 to 76 years (mean, 42.5 years). Tumor location was similar to that of the 40-fold more common meningioma: supratentorial, 26 (63%), most being parasagittal, falcine or convexity; posterior fossa, 5 (12%); tentorial, 4 (10%); spinal, 3 (7%). Duration of symptoms prior to diagnosis averaged 11 months. Plain x-rays were either normal or showed bone erosion; no blastic changes were noted. Angiography showed rapid filling, dense staining, sinusoidal or sunburst patterns and early venous drainage, though rarely were all features exhibited by one tumor. CT features were not diagnostic. Tumors showed the classic light microscopic features of angioblastic meningioma. The reticulin pattern varied greatly from dense to sparse. Three tumors showed rare foci of papillary change, a feature prominent in only one tumor. Necrosis was not evident. Mitoses varied from 1 to 33 per 20 high power fields. Rare psammoma bodies were noted in one lesion, and six tumors showed focal spindling of cells simulating fibrous meningioma. The histology of 15 recurrences showed no tendency to increasing anaplasia. Twenty-nine subjects (71%) developed at least one recurrence. Average time to first recurrence was 47 months; subsequent recurrences arose at increasingly shorter intervals. The probability of first recurrence increased with time: 5 years, 75%, 10 years, 87%; 15 years, 93%. Metastases were noted in 7 patients (17%) at a mean of 103 months after the first operation. The likelihood of metastases increased with time: 5 years, 19%; 10 years, 33%; 15 years, 64%. Metastatic sites included bone,[4] lung,[3] liver[1] and retroperitoneum.[1] In terms of tumor-related death, overall survival diminished with time: 5 years, 63%; 10 years, 37%; 15 years, 21%. No histologic features correlated with prognosis. Radiotherapy did not effect mortality but did lengthen recurrence free intervals. Appropriate therapy appears to be gross total resection with adjuvent radiation therapy.

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Immunocytochemical Analysis of Intermediate Filament Protein in Human Ependymal Tumors

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Immunocytochemical techniques have shown the simultaneous presence of both glial fibrillary acidic protein (GFAP) and Vimentin in human gliomas. GFAP has been established as a reliable marker for normal and neoplastic neuroglia. Vimentin is the earliest intermediate filament protein expressed in embryonic neuroepithelium but is replaced by GFAP in mature astrocytes. Mature ependyma, however, has not shown demonstrable GFAP content despite the presence of abundant intermediate filaments which likely contain Vimentin. The peroxidase anti-peroxidase technique was used for intracellular localization of GFAP and Vimentin in 12 ependymomas, 6 subependymomas and 1 mixed ependymoma/choroid plexus papilloma in order to determine if a unique pattern of intermediate filament expression could be demonstrated. An identically treated group of 23 non-ependymal central neuroectodermal tumors were used as controls. Cytokeratin immuno-reactivity was determined in a subgroup of 11 tumors with papillary or epithelioid differentiation.

Ependymomas showed positive reaction for Vimentin and GFAP in well differentiated ependymal portions of tumor. Subependymomas and astrocytomas were also positive for both markers. Oligodendrogliomas, oligodendroglial portions of mixed gliomas and medulloblastomas were negative for GFAP and Vimentin. Areas of poor differentiation in ependymomas, astrocytomas, oligodendrogliomas and mixed tumors showed weak reaction if any. The mixed ependymoma/choroid plexus papilloma showed the presence of GFAP in the ependymal component and cytokeratin in the papillomatous portion while Vimentin was found in both areas. Four papillary ependymomas in the series were negative for cytokeratin. These results showed no significant difference in intermediate filament expression between human ependymal tumors and other gliomas. However, immunocytochemical intermediate filament protein analysis was found to be valuable in the diagnosis of mixed gliomas and mixed ependymoma/choroid plexus tumors.

TITLES OF DIAGNOSTIC CASE PRESENTATIONS

1. **Stenosis and occlusion of internal carotid artery, associated with sickle cell anemia.**
   DRS. J.H. SHER, C. RAO, P.B. KOZLOWSKI (Brooklyn, New York)
2. **Choroid plexus carcinoma with rapid meningeal spread.**
   DRS. K. DOROVINI-ZIS, M.G. NORMAN (Vancouver, British Columbia)
3. **Ependymoma of the pineal region.**
   DRS. P.J. LEWIS, E.S. JOHNSON, K.E. ARONYK, T.E. HIGA, J.J. AKABUTA (Edmonton, Alberta)
4. **Neuroaxonal dystrophy.**
   DR. W.C. HALLIDAY (Winnipeg, Manitoba)
5. **Mitochondrial encephalomyopathy.**
   DR. B. LACH (Ottawa, Ontario)
6. **Extra pontine myelinolysis.**
   DR. B. CURRY (Calgary, Alberta)
7. **Delayed myelopathy following electrical injury.**
   DRS. G.S. DAVIDSON, J.H.N. DECK (Toronto, Ontario)
8. **Progressive dementia: Diffuse Lewy body disease, Alzheimer and spongiform changes.**
   DR. N.B. REWCASTLE (Calgary, Alberta)
9. **Congophilic angiopathy mediated dementia.**
   DR. Y. ROBITAILLE (Montreal, Quebec)
10. **Hypothalamic hamartoma.**
    DRS. S. KING, L.E. BECKER, G.S. DAVIDSON (Toronto, Ontario)
11. **Diffuse lymphoma involving the CNS.**
    DRS. L.C. ANG, M.J. STRONG, J.J. GILBERT (London, Ontario)
12. **Foreign body giant cell reaction to microfibrillar collagen hemostatic agent.**
    DRS. P. MOZZICATO, D. MUNOZ-GARCIA (Burlington, Vermont)
13. **Thyrotrophic hyperplasia in the setting of hypothyroidism.**
    DR. B.W. SCHEITHAUER (Rochester, Minnesota)
14. **Melanotic Schwannoma of cauda equina.**
    DR. L. LU (Winnipeg, Manitoba)
15. **Metastatic medullary carcinoma of the thyroid with an occult primary.**
    DR. J.J. KEPES (Kansas City, Kansas)
16. **Chordoma, of 12th thoracic vertebrae.**
    DRS. J. WANKLING, V. MONTPETIT, M. RICHARD (Ottawa, Ontario)
17. **Metastatic thymoma.**
    DRS. G.N. HOAG, S. CARLYLE, K. MARTIN (Victoria, British Columbia)
18. **Primary intracranial cylindroma.**
    DRS. W.K. ILSE, B.A. BRODY, J.H.N. DECK (Toronto, Ontario)
19. **Ganglioglioma of cerebellum.**
    DRS. D. ISUKAWA, B. LACH (Ottawa, Ontario)

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