Case 1993-1

Submitted by: Uma P. Kalyan-Raman, M.D., Robert Cruse, M.D., Tim Miller, M.D. University of Illinois College of Medicine, Peoria, Illinois and Saint Francis Medical Center, Peoria, Illinois 61637

Clinical Summary: This newborn male was born to a 26 year old white woman in good health. She was on no medications. She was supposed to have had polyhydramnios. There was no history of fetal distress. It was not clear whether there was any intrauterine mobility during pregnancy. A baby boy was delivered at thirty-eight weeks gestation by induced labor with vacuum extraction. His weight was about 3,000 gm. His initial APGAR scores were 2 and 7. There was hypotonia at birth and he required supplemental oxygen. Shortly after birth he was transferred to our institution.

Initial examination showed marked hypotonia. He also had a curious tremor of his chin which could be elicited and seemed to be clonus. This persisted for about 24 hours. It also occurred during EEG monitoring and was considered not to be seizure activity. The EEG was normal. Other features of this initial examination included a high arched palate, bland facies and narrow chest, mild flexion of the fingers and limitation of knee extension. This was considered to be consistent with mild arthrogryposis. There was questionable cardiomegaly. The diaphragm appeared to be high bilaterally. There was no evidence of organomegaly. The initial CPK was 1,740 but when repeated four days later was 169. SGOT was 140. His lactic acid was 1.1 mm./l., and pyruvic acid was 0.9 mg./dl. His electrolytes were normal and an EKG was normal. There was no evidence of cardiomyopathy on ultrasound. An EMG was not done. Ultrasound studies of the brain and kidneys were normal. A muscle biopsy was done within four weeks of birth. No definite conclusion could be reached on the muscle biopsy. However, the patient continued to deteriorate and a second muscle biopsy and nerve biopsy were done six weeks later. Soon after the second biopsy, the patient's condition deteriorated and he expired. An autopsy was performed.

Material submitted: 1) Muscle from the second biopsy (cryostat frozen section stained with H&E).
2) Kodachrome photomicrograph of Trichrome stain

Points for discussion:
1. What is your diagnosis?
2. What else needs to be done for a definitive diagnosis?

CASE 1993 - 2

Submitted by: M. Gujrati, M.D., M. Meriggioli, M.D., J. Lee, M.D. Ph. D., C. Thomas, M.D., Loyola University Medical Center 2160 S. 1st Ave. Maywood, IL. 60153

Reference Number: A86-220

CLINICAL HISTORY:

D.L. was a 41 year old white male with a long history of mental retardation and a severe progressive motor disability, who expired in a nursing home.

A childhood history reveals that the patient was slow to develop and required special education classes upto 16 years of age. Progressive deficits in motor strength and gait difficulties were noted in early to mid childhood. Subsequently slurred speech and dysphagia developed. In childhood he had measles and carried a diagnosis of "Galactosemia" He had bilateral cataract extractions at the age of 18 years. He also had history of extraction of multiple carious teeth and bilateral ankle swelling.

The patient's mother died of cancer at age 51 years and father died of heart attack at age 62 years. Both parents had "diabetes". Out of the 5 siblings, a sister (2 years younger than the patient), and a brother (2 years older than the patient) have a similar affliction. Three other siblings are unaffected.

Physical examination revealed severe mental retardation, an ataxic-spastic gait, dysarthria, and evidence of polyneuropathy.

LABORATORY STUDIES:

CBC - normal, serum cholesterol - normal, Galactose tolerance test and Galactose transferase levels were normal; 17 Ketosteroid secretions = 7.9 mg/24 hour (normal 3-10 mg); 24 hour urine for amino acids revealed "uniformly low levels". Chromosomal analysis was normal. Chest x-ray and EKG were normal at age of 27 years. CT scan (brain) showed diffuse, cortical atrophy at age 35 years.

NECROPSY FINDINGS:

At autopsy the brain showed cerebellar atrophy and cut sections reveal multiple ill defined gray-yellow lesions in the basal ganglia and cerebellum.

MATERIAL SUBMITTED:

One H&E stained slide, cerebellum

POINTS OF DISCUSSION: 1) Diagnosis
2) Pathogenesis

CASE 1993-3

Submitted by: Dr. Samuel K. Ludwin and Dr. David Hurlbut
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Case reference number: St. Joseph's Health Centre - A174/92.

Clinical History: Following spontaneous rupture of membranes on October 15th, 1992 at 2250 hours, this male infant of 36 weeks gestation was delivered by caesarean section on October 16th, 1992 at 1610 hours. Caesarean section was performed because of a nonreactive nonstress test. The pregnancy for this 30 year old mother (TPAL 1001) was uneventful apart from decreased fetal movements. APGAR scores were 2,3,6 at 1,5 and 10 minutes, respectively. The infant required resuscitation by the neonatal intensivists. He had multiple congenital anomalies including micrognathia, limb contractures and cleft palate. The infant was incubated and ventilated. Subsequent complete neurological examination revealed no spontaneous limb movements, and absent deep tendon reflexes. Echocardiography showed a large atrial septal defect. Following further investigations compassionate care was instituted. The baby died at 1610 hours on Octobr 26th. Consent for a complete autopsy was obtained from the mother.

Necropsy findings: Atrial Septal Defect

Material submitted: 1 glass slide of basal ganglia

Points for discussion:
1. Diagnosis
2. Nosology
3. Is this all one disease?

CASE 1993-4

SUBMITTED BY: Gary S. Pearl, M.D., Ph.D. (Department of Pathology, Orlando Regional Medical Center, Orlando, FL) and William R. Anderson, M.D. (Office of Medical Examiner, District IX, Orlando, FL)

REFERENCE NUMBER: MEN-822-91

CLINICAL HISTORY:

The patient, a 13 year old male, presented to the hospital on 10/5/92 with a one day history of headache exacerbated by movement, fever, gastric pain and nausea. In the emergency room, he was lethargic, confused and his eyes appeared crossed. CSF had 339 WBC with 42% segs, 58% lymphs, protein 495 and glucose 93. Bacterial antigens were not detected.

The patient was transferred, where physical examination revealed him to be lethargic and inattentive, weak and unable to vocalize. Nuchal rigidity was present and he had positive Kernig's and Brudzinski's signs and an equivocal Babinski reflex on the right. Healed insect bites were noted on his legs. Repeat CSF studies revealed 430 WBC with 46% segs, 54% lymphs, protein 490 and glucose 90. Gram stains were negative. Blood and CSF were sent for further studies. Treatment was started with Claforan and Acyclovir.

During the following day, he had a tonic-clonic seizure followed by respiratory arrest. He became unresponsive, with an isoelectric EEG.

NECROPSY FINDINGS:

The general autopsy was non-contributory. The brain weighed 1470 grams, with leptomeningeal clouding, edema and early uncal and cerebellar tonsillar herniation present. On coronal sections, punctate hemorrhages were observed.

MATERIAL SUBMITTED: One H & E slide of basal ganglia.

POINTS FOR DISCUSSION: Diagnosis

CASE 1993-5

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Case Reference Number: A92-7

CLINICAL SUMMARY

Clinical History: This 34-year-old white female was admitted to this hospital on January of 1992. Three weeks prior to admission she developed left eye pain and was diagnosed as having optic neuritis, was given Naprosyn with no response but pain responded to Sudafed and Tylenol. One week later, she developed headache and fever and was admitted to another hospital.

Her past medical history was non-contributory. A lumbar puncture was performed and revealed 40 RBCs; 11,730 WBCs with 86 percent polys; total protein, 131; glucose, 37. She was given Ceftriaxone. CAT & MRI scans of the head showed a lesion in the right medial frontal cortex with thickening of the anterior corpus callosum. Cultures of her cerebrospinal fluid were negative. She was discharged three days later.

Within the next few days the patient became very confused, had brisk reflexes, left ankle clonus and bilateral Babinski's; and was subsequently admitted to another hospital. She was treated with Decadron and Acyclovir. A repeat CAT scan showed increase in the bifrontal lesions and an emergent left frontal white matter biopsy, by drill needle was performed. The biopsy showed sheets of histiocytes, but no polymorphs or viral inclusions. The patient progressively deteriorated and was subsequently intubated. She was given Mannitol, but remained unresponsive. The family requested that the patient be transferred to this hospital for further medical coverage.

The patient arrived at this hospital intubated and unresponsive to stimuli. Blood pressure, 101/55; temperature, 101.9; respiration rate, 18; pulse, 92. Physical examination was remarkable for non-reactive pupils and no response to deep pain. Pertinent laboratory data included a white blood cell count of 12.1 (77 polys, 16 segs, 7 monos). Her EEG was flat line and the patient was deemed brain dead. The family agreed to withdraw supportive measures. The patient as pronounced dead at 7:50 p.m. on the day of admission.

Necropsy Findings: A brain only autopsy was performed. The brain was markedly but symmetrically edematous with evidence of transtentorial and foramen magnum herniation. On coronal sections there were several large greyish plaques in the white matter at several levels which spared the cortex. Secondary brain stem hemorrhage were present.

Material Submitted:
1. H&E section of cerebrum.
2. 1 Kodachrome of inclusions in macrophages from biopsy.

Points for Discussion:
1. What is the diagnosis?
2. What are the elongate structures in the macrophages from the biopsy?

Case 1993-6

Submitted by: Paula E. North, M.D., Ph.D. and Robert E. Mrak, M.D., Ph.D.
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Case reference number: UAMS A92-70

Clinical summary: This 49 year-old black female, with a history of systemic lupus erythematosus, developed generalized edema and stomatitis, and was admitted to University Hospital in Little Rock, Arkansas. A diagnosis of nephrotic syndrome was made, and therapy with high-dose Solumedrol was instituted. The stomatitis was severe, with oral ulcers and erythema involving the oral cavity and lips, fever with spikes to 104^{0}F, and malaise; but this largely resolved and she was discharged on oral steroid therapy. An open renal biopsy, performed one month after the original admission, showed a membranous glomerulonephropathy with focal proliferative lesions. She returned one week later with continued drainage of serous fluid from her biopsy site, peripheral edema, fever and decreasing mental status. Muscle fasciculations progressed to rigidity with flexed arm posturing, and intravenous steroids were reinstituted for suspected lupus cerebritis. Blood, urine and cerebrospinal fluid cultures were negative, and computed tomographic scans of her head showed only old lacunar infarcts bilaterally. A four-vessel arteriogram found no evidence of cerebritis. A brain biopsy was performed, which showed lesions similar to those later found at autopsy (see below). Cultures of biopsied brain tissue, including viral cultures, showed no growth.

Acyclovir therapy was added to broad-spectrum antibiotic therapy, but attempts to taper her steroid dosage were complicated by acute thrombocytopenia. Two years previously the patient had had a well-documented episode of thrombotic thrombocytopenic purpura which had been treated with steroids, but the present episode was accompanied by hypocellularity and decreased megakaryocytes in her bone marrow and absence of microangiopathic changes on peripheral smear. This resolved when high-dose steroids were restored. The patient continued to decline, developing a terminal Candidal sepsis, and expired 41 days following admission.

Postmortem findings: Postmortem examination showed no significant gross changes. Histological examination showed numerous small necrotizing lesions throughout the grey matter of the cerebral cortex, basal ganglia, midbrain, medulla, spinal cord and neurohypophysis. Somewhat similar lesions were found in the spleen, pancreas, liver and adrenal. The bone marrow showed mild hypocellularity. Cultures of brain tissue obtained at autopsy, including viral cultures, showed no growth.

Material submitted: Section of cerebral cortex, hematoxylin & eosin.

Points for discussion:

1. Diagnosis
2. Etiology

CASE 1993-7

Submitted by: R.M. Uht*, J. Garvey+*, and R.L. Davis.* *University of California, San Francisco, CA 94143-0506, +Permanente Medical Group, San Francisco, CA 94118.

Clinical History: The patient was a 33 year old female who was diagnosed with AIDS after developing thrush and esophageal candidiasis. Her T-helper cells numbered 10 and she was found to be HIV positive. Three months later she presented with difficulty walking. She also complained of fatigue and shortness of breath. On exam she was found to have slightly slowed repetitive movements in her upper extremities. Her lower extremities displayed a mild spastic catch, and her gait was markedly ataxic. Laboratory evaluation revealed an acellular CSF with a protein of 20 and glucose of 41 (serum=87). Her CMV titer was positive and liver function tests elevated. An MRI of the head, cervical and thoracic spine were normal. A culture of bronchial biopsy material was positive for histoplasmosis. She was treated with amphotericin and responded well.

Her lower extremity ataxia progressed and truncal ataxia developed. By five months after presentation she was confined to a wheelchair. Attempts to move her upper extremities produced movements which were almost ballistic. Titubation was present as was mild dysarthria. Her eye movements and cognitive abilities continued to be normal. Anti-neuronal antibodies were not found. An MRI performed a month later revealed cerebellar atrophy and T2 prolongation in the middle cerebellar peduncles. By the next month, her speech was virtually uninterpretable. She developed saccadic intrusions and all movements became ataxic. Her cognitive ability appeared to remain intact for the remainder of her course; she was able to communicate with eye-blinks until her death. She died of aspiration pneumonia, 10 months after the development of her neurologic symptoms.

Necropsy findings: Autopsy was limited to the brain only. The fixed brain weighed 1240 grams. The cerebrum appeared normal; cerebellar atrophy was present. Histologically, the centrum semiovale displayed white matter vacuolation. Occasional microglial nodules and multinucleate giant cells were present, sometimes associated with each other. There was an extensive loss of neurons in the pontine nuclei associated with a reactive astrocytosis. Other features seen in the pons may be found in the submitted slide of cerebellum.

Material submitted:
1. H&E stained section of the cerebellum.
2. Kodachrome of cerebellar ultrastructure.

Points for discussion:
1. Diagnosis
2. Etiology of the cerebellar granular layer cell depletion.

Case 1993-8

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The patient is a 4½ month old boy who was in his usual state of health until approximately one week prior to hospital admission when, according to his mother, he became irritable. She attributed the irritability to recent immunizations. However, over the course of the week, he became lethargic and periods of alertness diminished so that he spent most of the time sleeping. Around that time his mother also noticed that his head seemed to be larger and a caretaker noticed that he used his left hand more than his right.

On admission, he weighed 7.2 kgs, 0.25 kgs less than a week earlier. His head circumference was 47 cm (50th percentile - 42 cm). (At two months of age his head circumference was 40.5 cm with the 50th percentile 39 cm.) His fontanels were full. He was lethargic and would not smile. He moved his left arm and leg much more than his right. He would grasp with his left hand but not with his right and had more flexor tone in his right arm than his left. He would spontaneously kick with his left leg but not his right.

Head MR scan showed a large extraaxial mass centered adjacent to the left cavernous sinus. It was isointense with brain on T1 weighted images and produced low signal intensity on T2. It demonstrated homogenous enhancement after administration of gadolinium. Adjacent to the mass was a large extraaxial fluid collection.

At operation, a tumor extended from just beneath the left temporoparietal cortex to the cavernous sinus to which it was densely adherent. It appeared pink and well encapsulated. It was very hard and the sonicator would not break it up, so it was removed piecemeal.

Multiple fragments of white, firm tissue, the largest, 1.5 cm in greatest dimension were submitted.

Material submitted: 1 paraffin embedded, H&E stained section
1 Kodachrome of a reticulin stained section
1 Kodachrome of a section stained by immunoperoxidase

Point for discussion: Diagnosis

CASE 1993-9

Submitted by Richard A. Prayson, M.D. and Melinda L. Estes, M.D.
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Reference No. S90-24606

Clinical History:

The patient is a 70-year-old woman with diabetes mellitus and atrial fibrillation of eight years duration. Five months preoperatively, she noted a worsening in her vision and an increased frequency of headaches. Several ophthamologists were consulted and most attributed her visual changes to either cataracts or macular degeneration. Approximately one week preoperatively, she experienced an acute worsening of vision. Magnetic resonance imaging performed at an outside hospital demonstrated bilateral occipital lobe enhancing mass lesions with nonhomogeneous signal. Physical examination was notable for bilateral decreased visual acuity, a bilateral superior quadrant defect, an irregular heart rate and venous stasis changes in the lower extremities. A cerebral angiogram showed large avascular bioccipital masses and a left sigmoid dural arteriovenous malformation. The patient underwent an occipital craniotomy with gross total excision of bilateral parasagittal tumors. A firm extraparenchymal tumor attached to the posterior falx immediately below the sagittal sinus measured 2 X 3 X 4 cm. A similarly superficial firm tumor measuring 2 X 4 X 6 cm was excised from the right occipital lobe region. A small amount of tumor adjacent to the superior sagittal sinus was not excised. The patient's immediate postoperative course was unremarkable. The patient presented three weeks later to an outside hospital with an acute pulmonary embolism secondary to deep venous thrombosis and expired. An autopsy was not performed.

Material submitted: One H & E stained section and one kodachrome electron micrograph

Points for discussion:

1. What is the differential diagnosis?
2. What is the nature of this lesion?
3. What is the prognosis for this entity?

CASE 1993-10

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CASE REFERENCE NUMBER: E92-386

CLINICAL HISTORY: This 9-year-old, male Husky dog presented ambulatory with pain at L5-6. The dog was incontinent of urine and feces and the tail was paralyzed. There were no abnormalities of pelvic limb reflexes nor postural reactions. The urinary bladder was easily expressed and the dog dribbled urine. The tail was analgesic and the perineal reflex was depressed. A myelogram, performed from the foramen magnum, revealed interruption to contrast flow at cranial L5. Dorsal laminectomy at L4, L5 and L6 revealed a "swollen dural tube." A specimen was resected and submitted.

MATERIAL SUBMITTED: 1. H&E section of the surgical specimen
2. Kodachrome showing EM features

POINTS FOR DISCUSSION: 1. Diagnosis
2. Nature of the eosinophilic areas of the tissue