CASE 1990-1

Submitted by: Lucy B. Rorke, M.D. and Commander Donald Lewis, USN
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania 19104

Case Reference # 85-88

Clinical History: A 2 2/12 year old black male was admitted to CHOP because of developmental regression followed by the sudden onset of focal seizures, left hemiparesis and fever.

He was born at term following an uncomplicated pregnancy and delivery, but a tracheo-esophageal fistula, patent ductus arteriosus and coarctation of the aorta were diagnosed. The fistula and cardio-vascular defects were repaired and a gastrostomy was done. The tracheo-esophageal fistula repair broke down several times over the next 18 months, eventually necessitating a colonic interposition and Nissen fundoplication.

Examination showed a rectal temperature of 38.7°C and extreme irritability. Pupils were equal and reacted to light. There was a conjugate right gaze preference but EOMS were complete with oculocephalic maneuver. He did not respond to visual threat nor did he attend to verbal cues. The neck was supple, he moved all extremities semipurposefully and tone was diffusely increased. DTRs were 2/4 throughout and plantar responses were extensor. A draining fistula was present on the left anterior abdominal wall.

Diagnostic studies: WBC 10,000/mm^3 with 67% segs, 23% lymphs, 7% monos and 3% eosinophils; Hgb - 9.9 gm/d; platelets-593,000/mm^3; CSF - 864 WBC/mm^3 (81% segs and 19% lymphs), 3040 RBCs/mm^3, glucose 54 mg/dl and protein over 600 mg/dl. Spinal fluid cultures for bacteria, fungi, mycobacteria and viruses were negative. A CAT scan revealed moderate ventricular dilatation, right frontal lobe enhancement and multiple areas of cerebral infarction of variable ages.

Comprehensive immunologic evaluation yielded no abnormalities, but skin test for Candida antigen was positive.

Infant was treated with Oxacillin, chloramphenicol and Acyclovir, but continued to deteriorate, and expired 3-4 months after onset of symptoms.

Necropsy Findings: Large meningeal mass on ventral surface of brain stem (see kodachrome), smaller nodules at carotid bifurcation and over cervical and lumbar cord.

Material Submitted: Kodachrome of ventral surface of brain, one H&E and one unstained section of meningeal masses.

Points for discussion:

1. Diagnosis
2. Pathogenesis

Fungus type?

DSS 1990-2

Submitted by: P.C. Johnson, M.D., Division of Neuropathology, Barrow Neurological Institute, 350 W. Thomas, Phoenix, AZ 85013

Reference No. N1260-89

Clinical History:

This 62 year old man was well up until August, 1989, when he was seen for a complaint of shortness of breath for which he received a diuretic. Shortly thereafter, he was referred to a Neurology Clinic with a complaint of radiating right arm and left leg pain. Spine films revealed degenerative disc disease and he was begun on corticosteroids with the presumed diagnosis of radiculopathies of right C8 and left L4. The following month the steroids were tapered. However, the pain worsened so the steroid were then increased for a period and then decreased and discontinued. A few weeks later he came to the Emergency Room with an apparent myelopathy. There was a positive Lhermitte's sign, a sensory level at T4-T6, incontinence, neck pain, marked leg weakness with bilateral radiating pain, and weakness of the intrinsic muscles of the hands. Evaluation for spinal cord compression included a negative MRI and a negative myelogram. Lumbar puncture showed a CSF protein of 64 with a normal glucose, 2 white cells and normal cytology. Electro-diagnostic testing revealed changes consistent with axonal neuropathy in a mononeuritis multiplex distribution.

Additional laboratory results included elevated LDH, IgM Kappa monoclonal gammopathy, light chains in the urine on protein electrophoresis and decreased platelets. The ANA titer was 1:160 with nucleolar pattern and decreased C3 and C4. Raji cell assay was positive but the sedimentation rate was normal. Anti double stranded DNA, and hepatitis serologies were normal. The patient underwent sural nerve biopsy.

Material Submitted: H&E section of sural nerve biopsy and unstained section

Points for Discussion: Diagnosis.

CASE 1990-3

Submitted by: Dorothy M. Willis, M.D., Su-Ming Hsu, M.D., and Sozos Ch. Papasozomenos, M.D.
Department of Pathology and Laboratory Medicine,
University of Texas Medical School,
Houston, Texas 77030

Reference No.:S-89-7403

Clinical Abstract:

The patient was a 59-year-old white man, a NASA engineer, with a 3 month history of progressive neurologic deterioration. His initial symptoms were fatigue, balance problems, muscle cramping, myoclonus and spasticity of the lower extremities. He then developed increasing disorientation and lethargy along with declining cognitive function. His condition worsened despite some early mild improvement with steroid therapy.

He was transferred to Hermann Hospital in Houston, Texas on October 25 for further evaluation. Physical examination at this time revealed that he was oriented to person only and able to follow one-step, but not two-step, commands. Dysnomia, unclear speech, and poor memory were evident. The patient had several myoclonic jerks during the examination. His cranial nerves and motor strength were intact. His tendon reflexes were brisk and symmetrical with bilateral upgoing toes and no clonus.

Initial laboratory results were as follows: Hgb 16.4 g/dl, Hct 49%, WBC 15.7 cumm (88% polys, 9% lymphocytes, and 3% monocytes), platelets 251,000, LDH 302 U/L and electrolytes within normal range. Cultures of blood and CSF revealed no growth. Spinal fluid analysis revealed 10 WBC, 110 RBCs, protein 107 mg/dl and glucose 77 mg/dl. No oligoclonal bands were present in the CSF. During his hospitalization the patient had a fluctuating mental status without notable improvement. A magnetic resonance imaging scan demonstrated multiple extensive abnormalities which were mostly present in the white matter and principally involved the frontoparietal area. A brain biopsy was performed on November 1.

Material submitted: One H + E and 1 unstained slides from the brain biopsy.

Points for Discussion:
1. Diagnosis
2. Pathogenesis

CASE 1990-4

Submitted by: David N. Louis, MD, E. Tessa Hedley-Whyte, MD, and E.P. Richardson, Jr., MD
Department of Pathology (Neuropathology)
Massachusetts General Hospital
Boston, MA

Case reference number: MGH autopsy # 46019

Clinical history:

A 58-year-old woman had a 12-year history of myelofibrosis and myeloid metaplasia. Because of increasing RBC transfusion requirements, a splenectomy was performed on 9/28/89. At operation, a colovesical fistula was discovered. On 10/24/89, the colovesical fistula was excised and a colostomy was performed. Her post-operative course was complicated by shaking chills and fevers. Hematologic studies revealed a hematocrit of 27 with 16 nucleated RBC's/100 WBC, platelet count of 550,000, white blood cell count of 15,000 with 3% blasts, 4% metamyelocytes, 31% bands, 2% segs, 16% lymphocytes, 2% monocytes, and 42% abnormal neutrophils showing the Pelger-Huet anomaly. An abdominal CT scan showed a fluid collection posterior to the uterus; aspiration of the fluid yielded purulent material and cultures positive for enterococcus and alpha-hemolytic streptococcus. She was treated with antibiotics and drainage of the abscess fluid. She did well and was transferred to a rehabilitation hospital on 12/7/89. She had no neurological symptoms or signs, and neurological examination was normal. She died suddenly on 12/10/89.

Autopsy findings:

An acute infarct involved the ileum and right colon, and extensive acute and organizing pneumonia was present in the right upper and middle lobes. The marrow spaces were replaced by firm, tan tissue, and no marrow could be expressed. The liver was massively enlarged (3980 g.) and was a mottled, red-tan color. The distal right ureter contained multiple, smooth, less than 0.4 cm., white-tan nodules.

Neuropathological examination revealed bilateral thin, rust-colored subdural membranes, and one 2 X 2 X 0.2 cm. collection of old blood. Six smooth, white, round, firm, subdural nodules, each measuring less than 0.5 cm., were loosely adherent to the dural convexities bilaterally. Examination of the brain and spinal cord was otherwise unremarkable.

Material submitted: One kodachrome to illustrate the cut surfaces of the two largest subdural nodules; one H and E stained slide of nodules. The gross photo and H and E slide are of the same two nodules.

Point for discussion: Diagnosis

CASE 1990-5

Submitted by: Drs. Gerald Minkowitz, Powers Peterson, Carol K. Petito, and
Susan Morgello
Department of Pathology
Cornell University Medical College
New York, New York 10021

Reference No.: A89-210

Clinical History:

A 62-year-old white male was evaluated at The New York Hospital (NYH) for an asymptomatic anemia 12 months antemortem. His past medical history was significant for a myocardial infarction three years antemortem, and gout. The patient had a ninety pack-year history of smoking.

Initial evaluation included a bone marrow biopsy with aspirate and cytogenetic studies. The marrow was interpreted as refractory anemia with excess blasts (RAEB). Cytogenetic analysis revealed the following abnormalities: 5q-, iso 8q, and ring 8. For the first five months following diagnosis the patient required red cell transfusions every four weeks. As his transfusion demand increased, treatment with 6-thioguanine and cis-retinoic acid was initiated with little response. Physical exam at that time (6 months antemortem) revealed a palpable spleen. An episode of spontaneous epistaxis five months antemortem required surgical packing.

The patient's transfusion requirements increased in the ensuing two months to one unit packed cells/week. Three months antemortem the patient presented to NYH with a fever, cough and weakness. Physical exam was notable for a greatly enlarged spleen. A repeat bone marrow biopsy and aspiration were performed. Broad-spectrum antibiotic therapy and other medications were administered. Repeated epistaxis and oozing from catheter sites complicated this admission. He was discharged 1 month antemortem.

Nine days antemortem he presented with chest pain, left upper quadrant abdominal pain, fever, lethargy, and oral thrush. The WBC count was elevated and the platelet count markedly decreased. All blood cultures were negative. Four days antemortem the patient was described as disoriented. Two days antemortem, the patient was oriented to person only and had a nonfocal neurological exam. One day antemortem he was more lethargic. The patient suffered a cardiorespiratory arrest, and as per the his prior request no resuscitiative efforts were made.

An autopsy was performed.

Material Submitted: One H&E and one unstained slide from cerebral cortex

Points for discussion: Diagnosis

Case #6.

Submitted by: John J. Kepes, M.D., Department of Pathology and Oncology, University of Kansas Medical Center, Kansas City, Kansas 66103

Case reference number: KUMC S-89-12357

Clinical history: This 69 year-old gentleman developed left sided facial paralysis 4 weeks prior to admission, this was followed by gradually worsening numbness of the left hand and the inability to carry out fine movements with that hand. He had a long history of being a heavy smoker, and had a 15 lb. weight loss over the last 3-4 months. On examination he was alert and oriented. The visual fields showed extinction on the left side to double simultaneous stimulation. CT scans showed a round mass superficially located in the right parietal lobe with massive edema surrounding the mass at its deep aspects. Craniotomy with excision of the mass was performed.

Material submitted: 1. H&E stained section of the surgical specimen.
2. CT scan of the head with enhancement.

Points for discussion: 1. Diagnosis.
2. Significance of individual histologic features of this case.

Case 7

Submitted by: Roy C. Sutton III, M.D. and Lucien J. Rubinstein, M.D.
Division of Neuropathology
University of Virginia Medical Center
Charlottesville, Virginia 22908

Reference No. A19049

Clinical Abstract:

A 25 year old woman presented to another hospital in July 1980 with progressively worsening headaches, galactorrhea and amenorrhea. Previous medical history was unremarkable.

Laboratory tests were notable for a serum prolactin of 5000 ug/L (normal < 20 ug/L). A CT scan of the head showed a large pituitary mass with suprasellar and third ventricular extension. The scan was otherwise unremarkable.

In August 1980, partial resection of a chromophobe pituitary adenoma was performed by transfrontal craniotomy. Postoperatively, the patient received conventional megavoltage therapy delivered by a 6-mV linear accelerator unit. Large 5 x 7.5 cm parallel-opposing temporal ports were used to a total dose of 6200 centigray (cGy), delivered in fractions of 200 cGy 5 days a week for 6 weeks, because of the suprasellar extension. She improved after surgery and radiation therapy with resolution of the headaches and galactorrhea, although she never regained normal menstrual cycles.

A follow up CT scan of the head one year after surgery showed residual pituitary tumor and irregular enhancement in the left frontal lobe, interpreted to be post-surgical changes. Shortly afterwards, the patient began to develop progressive blindness with eventual total loss of vision in the right eye and partial loss in the left. She also developed clinical and laboratory evidence of hypopituitarism requiring replacement therapy. She received a course of bromocriptine without effect.

In March 1987 the patient presented to the University of Virginia complaining of recurrent severe headaches, lethargy, dizziness, inappropriate affect, expressive aphasia and right ear deafness. CT and MRI studies of the head revealed a large pituitary mass with extension to the suprasellar region, both cavernous sinuses and both internal carotid arteries. In addition, there was marked thickening of the cortex of the left posterior frontal, insular, superior and middle temporal gyri. The patient was admitted to the hospital, but died suddenly.

At general autopsy, visceral examination showed a massive pulmonary embolus but was otherwise unremarkable.

Materials submitted: One 2 x 2 Kodachrome
One H&E and one unstained slide of cortex

Points for discussion: Diagnosis
Pathogenesis

Case 8

Submitted by: Andrei I. Holodny, M.D., Jeffrey Reich, M.D., Michael Deck, M.D.,
Susan Morgello, M.D. and Carol K. Petito, M.D.
Departments of Pathology and Radiology
The New York Hospital, Cornell Medical Center
New York, New York 10021

Reference No. A 89-153

Clinical Abstract:

This 62 year old white female physician was diagnosed with infiltrating ductal breast carcinoma in the spring of 1987. She underwent a right modified radical mastectomy. On 12/87 the patient received chest wall radiation therapy of approximately 1000 rad for metastatic disease. She developed an idiosyncratic hypersensitivity reaction to the radiation therapy which was manifested by pericarditis, pleuritis and mediastinitis. These symptoms resolved after the radiation therapy was discontinued. She was placed on Tamoxifen. On 12/88, she developed occipital headaches and an MRI scan revealed multiple brain metastases. On 1/89, she was placed on Decadron and began a course of wide beam radiation therapy. She received a total of 2000 rad over 14 treatments. On 4/89, she received an additional 1080 rad over 6 treatments without complications. An MRI scan at that time revealed gadolinium-enhancing mass lesions consistent with metastases without evidence of any vascular anomaly. Her subsequent course was complicated by recurrent pulmonary emboli and steroid myopathy.

The patient's past medical history is significant for hyperextensible joints, hyperelastic skin and a separation of the pubic symphysis during parturition.

On 7/89 she was admitted to the New York Hospital for terminal care. Physical exam at that time was notable for mild cognitive impairments, hyperextensible finger joints, a question of hyperelastic skin and generalized weakness. MRI revealed multiple CNS metastases. 4 days after admission, the patient suffered one generalized seizure and thereafter remained stuporous. Her condition deteriorated until she became deeply comatose. No further diagnostic tests were performed after the seizure. She expired 16 days after the seizure.

Autopsy revealed multiple CNS metastases which were microscopically consistent with the breast primary. A large, fresh subarachnoid hemorrhage was located over the base of the brain and extended over the parietal and occipital lobes (L>R) and posterior cerebellum (R>L). Microscopic sections of this lesion revealed occasional hemosiderin-laden macrophages. The Circle of Willis exhibited multiple aneurysms. Other blood vessels in the leptomeninges and the brain parenchyma, as well as small, medium and large systemic vessels, were histologically unremarkable. Gross and microscopic examination of both lungs and the heart revealed mild pleural thickening but no apparent difference between the right and left sides.

Material Submitted: One H&E stain slide of the M2 segment of the right middle cerebral artery.

Point for Discussion: Etiology of the lesions of the Circle of Willis.

CASE 9

Submitted by: Patricia A. Mozzicato, M.D., Adekunle M. Adesina, M.D. and William W. Pendlebury, M.D.
Department of Pathology (Neuropathology)
University of Vermont College of Medicine
Burlington, Vermont 05405

Reference No.: Medical Center Hospital of Vermont # A89-38

Clinical Abstract:

The patient was a 22 month old girl who was born at term by spontaneous vaginal delivery after an uneventful pregnancy. She was given hepatitis B prophylaxis shortly after birth because her mother is a known carrier. She developed normally until the age of six months when developmental and growth arrest were noted. She had wandering eye movements and ptosis. By 12 months, she was below the fifth percentile in height, weight, and head circumference. A sweat test was negative and thyroid function tests were normal. At 16 months, she had lost previously acquired milestones, was less active, and interacted less with others. Audiometry testing indicated moderate bilateral hearing loss. At 19 months, a karyotype was performed and interpreted as 46,XX. A serum amino acid screen showed an increased alanine level. Evaluation at Children's Hospital in Boston included blood levels of arylsulfatase, galactocerebrosidase, galactosidase, long chain fatty acids, and phytanic acid; all results added no further diagnostic information. A T_1 and T_2 weighted MRI done at the Medical Center Hospital of Vermont (MCHV) at 21 months showed increased signal of the thalamus (bilateral), pons and midbrain with decreased differentiation between grey and white matter. Two weeks after the MRI, she was admitted to MCHV for further studies (1/31/89). Physical examination revealed a lethargic child with symmetrically decreased muscle tone throughout. Elevated serum levels of pyruvate, lactate, and alanine, and elevated CSF levels of pyruvate and lactate, were noted. Serum ammonia was normal. EMG and nerve conduction velocities were unremarkable. She was discharged after a few days, but was readmitted on 2/25/89 following two weeks of decreased tone and decreased responsiveness to verbal and tactile stimuli. On the day before admission, she developed fever, loose black stools, and vomiting. On the morning of admission, her parents found her lying in vomitus, unresponsive, and with cold, blue extremities. She was brought to the Emergency Department where she was noted to be cyanotic with gasping respirations and hypotension. Resuscitation efforts included intubation and pressor support, but she developed decerebrate posturing with loss of pupillary and corneal reflexes. Although pupillary reflexes returned within 24 hours, respirator support was withdrawn in consideration of her generally poor prognosis. She died on 2/27/89.

Autopsy Findings:

The major autopsy findings were growth retardation, bronchopneumonia, and left ventricular hypertrophy. The brain weighed 965 grams. In the thalamus bilaterally were focal discolorations measuring 1 to 4 mm, primarily in the ventral aspects. Similar lesions were noted in the pons and midbrain.

Material Submitted: One H & E slide of an autopsy brain section.

Points for discussion: 1. Diagnosis
2. Pathogenesis

CASE # 1990-10

Submitted by: C. Duncan, M.D. (Neurology & Pediatrics); R. Craver (Pathology), and J. S. Nelson (Pathology); mailing address: Department of Pathology, Louisiana State University Medical Center, 1901 Perdido St., New Orleans, LA 70112.

Case reference number: Children's Hospital A89-23

Clinical History: The patient was a 12 year old boy with an incapacitating choreoathetoid movement disorder which began at 32 weeks of age during a brief, systemic illness began characterized by diarrhea, vomiting, and otitis media. Laboratory studies including CSF examination, CBC, urinalysis, serum electrolytes, serum enzymes, uric acid, SMA_{12}, and ceruloplasmin disclosed only a slightly elevated LDH. The EEG was normal. His gestation, birth, and development had been previously unremarkable except that he was delivered without complications following a three hour induced labor. He weighed 10 lbs, 5 oz at birth. A maternal cousin had a seizure disorder but there was no other family history of neurological disease. His parents (who are unrelated) and older sibling were healthy.

During the ensuing twelve years the patient's cognitive and educational attainment reached second grade level. Because of his movement disorder, however, he never developed intelligible speech, had no voluntary use of his upper extremities, and was never able to sit, stand, walk, or keep his head erect without support. In the last four years of his life he had occasional, brief generalized seizures.

A CT of the head at 2 years of age was considered normal. Urine and plasma amino and organic acids were done at 12 years of age and were normal.

While in a spica cast following surgery for subluxation of the hip he developed decubiti and malnutrition. He died at home awaiting repair of the decubiti.

Necropsy findings: The formalin fixed brain was sent by the medical examiner to Children's Hospital of New Orleans for examination. The brain weighed 1390 grams. Grossly, the caudate and lentiform undei were symmetrically atrophic and firm.

Materials submitted: H&E section of corpus striatum

Points for discussion: Diagnosis

CASE 1990-11

Brian W. Little, MD, PhD
Lehigh Valley Hospital Center
Allentown, Pennsylvania

E.Z. is a 22 year old caucasian male. He was the product of a normal, full-term pregnancy with a "complicated delivery". Within the first year of life he developed a myoclonic seizure disorder requiring phenobarbital and steroid therapy. The diagnosis of "spastic cerebral palsy" was made. Motor milestones were delayed; he sat at 19 months and walked at 48 months. A diagnosis of mild mental retardation was made. His seizures were difficult to control, but he stabilized on a regimen of Tegretol, Depakote and Diamox.

In September of 1988 his caregivers complained that he would collapse after walking a short distance. Immediately before falling, he would complain of pain in his hips and thighs. He was evaluated by an orthopedic surgeon who found no evidence of disease in the pelvis or lower limbs to explain the fatigue and pain. A myelogram, CT scan and MRI were performed which showed a C-5 to C-7 stenosis. A cervical decompression was performed in April 1989 with some relief of symptoms for two to three months. In September 1989 his fatigue had progressed to the point where he could not walk 200 feet or climb one flight of stairs. His upper extremities were less affected. He saw a cardiologist who undertook exercise testing and echocardiography. The summary of the exercise testing was: "Marked impaired exercise capacity. It seems to be a neuromuscular rather than cardiovascular basis. No evidence of [cardiac] ischemia. No hemodynamic instability." The echocardiogram was normal.

Examination in October 1989 showed his spastic quadriparesis to be unchanged. The weakness was documented as above. Sensory examination and EMG/NCV were not undertaken due to poor cooperation from the patient. Optic disk pallor and nystagmus were unchanged from prior examinations. Routine laboratory tests were normal, except for a slightly elevated cholesterol [217 mg/dl] and triglyceride [194 mg/dl]. A creatine kinase was 560 U [Ref range 35-232U]. A muscle biopsy was performed.

SLIDES PROVIDED

1. One H&E stained, paraffin embedded slide.
2. One 2x2, 35 mm slide.

FOR DISCUSSION:

1. What is your morphologic diagnosis?

2. What further diagnostic or therapeutic steps would you undertake or recommend?