CASE #1

SUBMITTED BY: John J. Kepes, M.D., Department of Pathology and Oncology, The University of Kansas Medical Center College of Health Sciences and Hospital, Kansas City, Missouri 66103

The patient was a 14 year old boy with a "seizure disorder" since age 11. Prior to that, he was said to have been in good general health with a non-contributory family history and normal developmental milestones. For the first two years after the onset of seizures, he received only conservative treatment with Dilantin, but at age 13, he was referred to Kansas University Medical Center for a neurological work-up. Physical and neurological examinations were normal but the EEG showed a "right frontal focus", plain skull films revealed an area of calcification in the right frontal lobe and CAT scans confirmed this finding. A right frontal craniotomy was done and a cherry-sized mass was found superficially in the brain. It appeared to have a fibrous capsule and contained amorphous, rather dry-looking, yellow-gray material. The boy recovered well from surgery and is presently symptom-free.

MATERIAL SUBMITTED: One (1) section stained with H & E and one (1) 2 x 2 Kodachrome of the EMI scan.

POINTS FOR DISCUSSION:

1. What is the diagnosis?

2. What additional investigations may help to elucidate the pathogenesis of this lesion?

CASE #2

SUBMITTED BY: Boleslaw H. Liwnicz, M.D., Ph.D., Department of Pathology (Neuropathology), Stanford University Medical Center, Stanford, California 94305

REFERENCE: #C 2420

A 28 year old Filipino housewife from Fresno Calif had a 1½ month history of severe headaches, with a CT scan indicative of left parieto-occipital lesion. A left carotid and left retrograde brachial arteriograms shows a large, vascular mass, connected primarily with the left posterior cerebral artery and to some extent, with the middle cerebral artery. A left parietal occipital craniotomy was performed, showing a red nodular hard mass, approximately 2 - 3 cms. beneath a somewhat yellow, gliotic cortex. The tumor mass was moderately vascular and well encapsulated. Other than the capsule, the tumor was quite friable. The tumor, although served by multiple arterial feeders, was rather well separated from the brain and was completely removed.

MATERIAL SUBMITTED:

Slide stained with H & E.

POINTS FOR DISCUSSION:

What is the diagnosis?

CASE #3

SUBMITTED BY: Leroy R. Sharer, M.D. and Ellen Kahn, M.D., North Shore University Hospital, Manhasset, N.Y., 11030, (and Stanley Scheartz, M.D. and Robert Good, M.D., Memorial-Sloan Kettering Cancer Center and Dr. Peter G. Bullough, Hospital for Special Surgery, New York, N.Y., 10021).

REFERENCE: A77-77

The patient was a 2½ year old boy who first presented at age 7 months with a short history of fever, rash and vomiting. He was found to have hepatosplenomegaly and thrombocytopnnia (platelets 20,000). No etiology, including viral (the patient's father had concomitant infectious mononucleosis) was found, and fever, organomegaly and thrombocytopneia all responded to corticosteroids. Over the next several months, he had several similar episodes, all responsive to steroids. At age 18 months (at New York Hospital), he was found to have phenotypic type I hyperlipoproteinemia, with chylomicronemia and elevated triglycerides (670 mg/dl). At age 23 months (while on the metabolic unit of the National Institutes of Health), he was first noted to have progressive lower extremity weakness, with induration of muscles and greatly elevated creatine phosphokinase (5060 units, MM isoenzyme). Electromyogram (New York Hospital) revealed decreased insertional activity, occasional fibrillations and positive waves, but no motor unit potentials either at rest or with stimulation. Muscle biopsy (quadriceps) exhibited replacement of muscle by mononuclear cells. Several immunologic abnormalities were observed: peripheral blood lymphocytes (PBL) readily went into extended culture, a property generally seen with viral infection; however, no virus could be recovered. In addition, PBL in co-culture almost completely suppressed allogeneic donor T cell function (blast transformation) and B cell function (immunoglobulin production). T gamma lymphocytes ("supressor cells") were elevated in peripheral blood (22.5%) and in lymph node (24%). Serum immunoglobulins were normal, but a positive FANA was reported. The child was treated with cyclophosphamide, prednisone, methotrexate and vincristine, with 1000 rads given also to the spleen. He developed respiratory insufficiency and died several months later, with necrotizing staphylococcal pneumonia.

AUTOPSY FINDINGS: Non-agressive type lymphocytic infiltrates in portal areas of the liver, in the spleen, in the lymphatic tissue, and in the lamina propria of the small bowel. Myocardium not involved. Diffuse, severe lymphocytic infiltration in skeletal muscles (including those of esophagus and about prostate), with near total replacement in lower extremities and myositic-like picture in upper extremities. (Brain not examined, but spinal cord and peripheral nerves not involved.) Submitted sections, stained with hematoxylin and eosin, are from pectoralis or intercostal (A), and psoas or gastrocnemius (B).

POINTS FOR DISCUSSION:

1. Can this disease be considered to be a lymphoproliferative disorder? yes
2. Why is there apparent specifity of the disease for skeletal muscle?
3. Why have the lymphocytic cells persisted in the skeletal muscles of the lower extremities.
4. Can viruses produce a similar picture?

CASE #4

SUBMITTED BY: *James S. Nelson, M.D.*
Division of Neuropathology
Washington University Medical Center

REFERENCE: *77-9*

A 35 year old woman was admitted to the hospital with a 3 week history of headaches, nausea and vomiting, and progressive difficulty in walking. At age 21, she had had a large, well circumscribed tumor removed from the right frontal lobe. A precise histological diagnosis was not established at that time, however, the lesion was believed to be a primary CNS neoplasm probably of glial origin. Subsequently, the patient was well until age 28 when symptoms recurred and a histologically similar tumor was again removed from the right frontal lobe. The lesion recurred at the same intracranial site 3 years later. Neuropathologic review of the material obtained at the third craniotomy as well as from the earlier operations disclosed that the histological appearance of the tumor had remained more or less uniform.

Since her last admission at age 31, the patient had had occasional focal seizures and had gradually become more withdrawn and less spontaneous in her interpersonal relationships. No definite evidence of recurrent tumor was seen in a CT scan carried out 2 years after her third craniotomy. She was followed at regular intervals until her final admission at age 35. At that time, a CT scan demonstrated multiple intracranial areas of tumor recurrence above and below the tentorium. In addition, chest x-rays demonstrated multiple tumor nodules scattered throughout both lungs. Cytologic studies of a needle aspirate of a lung lesion showed that the tumor cells were similar to those seen in the previous surgical specimens from the right frontal lobe. A portion of the aspirate was examined by electron microscopy and the results compared with those obtained by ultrastructural examination of small pieces of tumor removed from paraffin blocks of the earlier surgical specimens. The degree of structural preservation was sufficient in the latter specimens to demonstrate the close similarity between the ultrastructural characteristics of the lung lesion and the previous surgical specimens. The patient was given a single course of chemotherapy; however, she deteriorated and died 14 years after the original onset of symptoms. At autopsy, recurrent intracranial tumor and pulmonary metastases were found.

MATERIAL SUBMITTED: *One (1) H & E and one (1) unstained section of recurrent cerebral tumor (autopsy specimen); one (1) 8 x 10 electron micrograph of metastatic lung tumor cells.*

POINTS FOR DISCUSSION:

1. *Histologic diagnosis of the tumor.*

2. *Histogenesis of the tumor.*

CASE #5

SUBMITTED BY: Justin Parr, M.D., Laboratory of Neuropathology, University of Pennsylvania, School of Medicine Philadelphia, Pennsylvania 19174

REFERENCE: UP #OSC 77-58

A 58 year old Caucasian man was admitted to hospital with a 2 day history of nausea, vomiting, abdominal pain and mild bifrontal headache. One day prior to admission, he had blurred vision. Approximately 3 to 4 weeks before, he had had diarrhea and vomiting for about two days. About the same time, he received a swine flu inoculation "at a shopping center". Bilateral optic neuritis and corticospinal tract signs developed and progressed to total blindness, paraplegia with T6 sensory level, incontinence and bilateral Babinski signs. In addition, "right arm monoplegia", right facial paralysis, right hemianalgesia, "dysphasia", bidirectional horizontal gaze nystagmus and areflexia (left arm exception) occurred within ten (10) days. Brain scan (with TcO_4) showed uptake in the left frontal lobe. A CAT scan two weeks later demonstrated decreased density in frontal and calcarine areas, bilaterally and asymmetrically. Other laboratory studies including EEG were normal. He expired during the 15th week of illness.

Visceral Pathology: Bilateral early bronchopneumonia.

Nervous System Involvement: The gross lesions were chalky gray, finely granular, soft and sharply demarcated in white matter of cerebrum (including corpus callosum), cerebellum, brain stem, optic nerves and chiasm, and spinal cord. The sizes ranged from 3.0 cm. (cerebrum) to 0.2 cm. (lumbar) with complete transverse thoracic cord involvement. A confluence of lesions was equivocally discernable in the spinal cord. The lesions were discrete in the brain, multiple, bilateral and asymmetrical. They were not specifically perivenous or subpial in distribution, although most of the brain lesions did abut on the ventricles.

MATERIALS SUBMITTED: One (1) H & E and one (1) unstained section (5u) of left superior frontal, right inferior frontal or left inferior cerebellum are distributed. These are representative of the CNS lesions.

POINTS FOR DISCUSSION:

1. Diagnosis.
2. What is the relationship, if any, between onset of disease and a) the swine flu inoculation or b) the mild gastrointestinal upset occurring about the same time (3-4 weeks prior to onset of neurological signs)?

CASE #6

SUBMITTED BY: William G. Ellis, M.D., Department of Pathology, University of California-Davis, Davis, California 95616

REFERENCE: SMC U#626715

The patient is a 16 year old White male who was referred for evaluation of headaches and intermittent vomiting of 5 months duration, anemia, fatigue, lack of sexual maturity, and growth arrest which began at age 12 years. Examination: height 150.9 cm. and weight 37.5 kg. (each less than the second percentile), head circumference 55 cm. (50th percentile), right congruous homonymous hemianopsia, bilateral papilledema, slightly decreased visual acuity, spleen and liver enlarged to 5 cm. below the costal margins, immature genitalia with sparse pubic hair, but no neurologic deficits.

Laboratory data: hypochromic microcytic anemia (hematocrit 27%, hemoglobin 8.16) polyclonal hyperglobulinemia, sedimentation rate 140, prolonged partial thromboplastin time, increased numbers of plasma cells and absence of stainable iron in bone marrow, and normal growth hormone. Computerized tomography showed a large intracranial mass extending above and below the left leaf of the tentorium and adjacent to falx cerebri, falx cerebelli, straight sinus and left transverse sinus. Angiography showed a moderately vascular neoplasm, an enlarged tentorial artery and vein of Labbé.

Left parieto-occipital craniotomy revealed a large, spherical, highly vascular extra-cerebral neoplasm which extended at least 7 cm. anteroposteriorly from occipital bone to near the quadrigeminal plate and was solidly attached or merged with the diffusely thickened tentorium as well as other dural reflections. Approximately 85% of the neoplasm was resected. After surgery, the patient had a transient right homonymous hemianopsia, several generalized seizures, brief inappropriate ADH secretion, and a poor plasma cortisol response to insulin, but no permanent neurologic deficit.

In the six months following surgery, his growth rate has increased, sexual maturation has begun, his neurologic status has remained normal, but his hypochromic microcytic anemia and hyperglobulinemia have improved only to a mild to moderate degree.

MATERIAL SUBMITTED: One (1) H & E stained slide and one (1) unstained slide are submitted.

POINTS FOR DISCUSSION:

1. Diagnosis of this neoplasm.

2. Is it benign or malignant?

3. Is there a relationship between the endocrine dysfunction, hepatosplenomegaly, hyperglobulinemia and coagulopathy and the intracranial neoplasm?

CASE #7

SUBMITTED BY: Raymond Clasen, M.D.
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Chicago, Illinois 60612

This 18 year old, right handed, mentally retarded, White male with serious behavioral disturbances, was admitted to hospital on 5/23/77. He was the product of a full-term, uncomplicated pregnancy. At age 4, he developed measles with a fever of 105°F. One year later, he had his first major motor convulsion. This was accompanied by an abnormal EEG. The patient responded to medical management and there were no further major convulsions until the age of 10 when he developed status epilepticus. The EEG at this time showed "temporal lobe damage and spikes". At age 11, he began to develop aggressive behavior which resulted in his expulsion from several schools. His behavior continued to worsen and his seizures remained essentially uncontrolled. At age 16, his IQ was 45. He had a normal brain scan and CT scan. Neurologic examination was within normal limits. The liver and spleen were not enlarged. A right temporal lobectomy was performed on 5/26/77. There were no complications and he was discharged on 6/25/77. The frequency of his seizures has diminished, and he is now under reasonable good medical control. Liver function tests and a bone marrow aspiration were both normal. No amino acid abnormalities were demonstrated in the urine and the fibroblast culture was also normal.

The resected specimen weighed 31 grams. Following fixation, the amygdaloid nucleus appeared white and firm. The slides (stained with PAS - Kluver) submitted are from this nucleus. The changes were confined to the amygdaloid nucleus. Electron microscopic studies were performed on material fixed by immersion in ordinary formalin.

POINTS FOR DISCUSSION:

1. *Is this a storage disease?* No! Axonal spheroids!
2. *Is this a residual effect of measles encephalitis?* Probably!
3. *Is this a congenital malformation or none of the above?* None of these?

CASE #8

SUBMITTED BY: Nancy Peress, M.D.
Veterans Administration Hospital
Northport, New York 11768

REFERENCE: 76A-119

The patient was a 55 year old White male watchmaker by trade who was admitted with the chief complaints of progressive weakness of his lower extremities and urinary incontinence. He had been in good health until eight years prior to admission when he developed urinary frequency and post-void dribbling which progressed to incontinence. He also became impotent at that time. Three years prior to admission, he noted the onset of difficulty in walking with progressive weakness of his lower extremities. He had a shuffling, stooped gait. He followed a progressively deteriorating course with increased weakness of upper and lower extremities to the point of lower extremity paralysis. He developed a slowly evolving sensory deficit in the lower extremities which became severe. He succumbed to sepsis. There were primary sites of infection in the urinary bladder and decubiti.

The general necropsy findings included bilateral bronchopneumonia, chronic pyelonephritis, calcific hilar lymphadenitis and bilateral apical pulmonary scarring.

The brain weighed 1370 gms. External examination revealed normal gyral configuration. The tissue, however, had a diffusely glassy appearance which was more obvious when coronal sections were examined. Coronal sections disclosed multifocal single and confluent areas of rarification, usually granular in consistency, throughout centrum semiovale with greatest concentration in fronto-parietal lobes. Arcuate fibers appeared intact.

There was a rim of depressed, firm, white glistening tissue, up to 0.3 cm. thick, surrounding the superior angles of the lateral ventricles and the superior aspect of the cerebral aqueduct. This periventricular gliosis was more prominent on the right side. The pontine base and medulla appeared reduced in size. It was difficult to define the cerebellar dentate nucleus The middle cerebellar peduncle appeared reduced in substance. No focal lesions were seen in the cerebellum, pons or medulla. The lateral and third ventricles and cerebral aqueduct were moderately enlarged.

MATERIALS SUBMITTED: Slide stained with H & E.

POINTS FOR DISCUSSION:

1. Diagnosis.

CASE #9

SUBMITTED BY: *Leopold Liss, M.D.*
The Ohio State University, Columbus, Ohio 43210

REFERENCE: *#7329*

The patient was a 55 year old mail carrier who was described as always moody. Family History - Patient's one brother was epileptic, and died of unknown cause at the age of 20; his four sisters are living and well. Patient was married and had three children who are well; one daughter is hospitalized for schizophrenia.

At the age of 52, the patient had a car accident and required some stitches but was not hospitalized. Following this trauma, his behavior changed. He developed strange ideation of a religious nature, would disappear from home and would tell people bizarre stories, taking delight in frightening them. This verbally assaultive behavior led to a visit to a psychiatrist and subsequent retirement. At that time, he was described as suspicious with increased psychomotor activity, mannerisms with gestures of face and eyes. He would laugh and cry inappropriately, had flight of ideation and perseveration of thought. His sense of perception and comprehension were impaired. General knowledge and calculation ability, limited. Memory was defective both for recent and intermediate events. He had no insight into his condition. The impression was organic brain syndrome secondary to trauma with psychosis.

The condition progressed and two years before death, led to hospitalization because he became confused, poorly oriented and actively psychotic. At that time, his memory was severely impaired. His behavior became bizarre. Psychological examination stated that the patient was psychotic, confused and totally disoriented. His EEG was read as normal.

About a year and a half prior to death, patient had a single seizure. He was placed on Dilantin. Following the seizure, there were two (2) EEG's which were described as markedly abnormal with suggestion of lateralization and encephalopathy. A second admission to a hospital for workup for brain tumor followed, a carotid angiogram was performed showing an ulcerated atheromatous plaque in the right internal carotid artery. Patient refused surgery and remained in VA Hospital for 1½ years. During this time, he gradually deteriorated, became totally bedridden, developed bed sores, thrombophlebitis. His cause of death was bronchopneumonia. The total duration of his disease was less than three years. The autopsy confirmed the diagnosis of bronchopneumonia as cause of death. The organs were described as normal, both on gross examination and histologically. The brain weighed 1310 grams.

MATERIAL SUBMITTED: *Section from frontal lobe and spinal cord stained with LFB-PAS; one (1) 2 x 2 Kodachrome.*

POINTS FOR DISCUSSION:

1. *The nature of the disease.*

2. *Does it represent a separate clinicopathological entity?*

CASE #10

SUBMITTED BY: William C. Shoene, M.D.
Peter Bent Brigham Hospital
Boston, Massachusetts 02115

REFERENCE: A 77-47

The patient was a 67 year old White female with multiple subcutaneous nodules which secondarily became infected. Severe osteoarthritis with multiple compression fractures of the vertebrae, anemia and a peripheral neuropathy were also present. In October, 1976, the patient developed a right sixth nerve palsy. A left sixth nerve palsy then was noted at the beginning of February, 1977. Both the right and left sixth nerve palsy persisted until death, approximately two weeks later in mid-February, 1977. The patient died of pneumonia and a pulmonary embolus.

MATERIALS SUBMITTED: *The slide was obtained from the 6th cranial nerve.*

POINTS FOR DISCUSSION:

1. *Differential diagnosis.*

2. *What are the other possible primary and secondary effects of this disease process on the nervous system?*