CASE 1994-1

Submitted by:
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Mailing address:
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Case reference number:
93-A-42

Clinical History:

26 year old white male presented with severe left thigh pain. Radiographic studies showed numerous skeletal lytic lesions. A bone marrow aspirate and biopsy, Cytochemical and immunophenotyping studies were consistent with Acute Myelogenous Leukemia, Mo subtype. The patient was started on induction chemotherapy with Idarubicin and Ara-C. He tolerated chemotherapy well.

On day 7, patient had significant thrombocytopenia (14K), neutropenia (ANC .98), anemia (Hgb 8.0, Hct 24.2) and fever which was treated with Ceftazidime. On day 14 bone marrow aspirate and biopsy showed minimal cytoreduction and induction chemotherapy was reinstituted with high dose Ara-C, Vincristine and Decadron.

The patient went home on weekend leave. On day 6 he developed mild shortness of breath and chest pain with nausea and vomiting. Same afternoon he started having decreased visual acuity and dizziness, and in the evening he became unresponsive with sluggishly reacting pupils and nystagmus. Head C.T. scan showed diffuse, multiple ring enhancing lesion. He developed focal, and subsequently, generalized seizures requiring intubation. He developed ventricular tachycardia with no palpable pulses or blood pressure, and died within 12 hours of the onset of his neurological symptoms

EXAMINATION OF THE BRAIN:

The brain weighed 1500 gms. fresh and 1575 gms. following fixation. There was diffuse subarachnoid hemorrhage bilaterally over the frontal and parietal lobes. A few areas of discrete grey-brown discoloration were present on the inferior surface of the temporal lobes. The cerebellar tonsils were prominent and the left cerebellar lobe was larger than the right. There were several punched out lesions on the external surfaces of both cerebellar lobes. Subarachnoid hemorrhage extended along the entire length of the spinal cord. Sectioning showed all lobes of the cerebrum and cerebellum, bilaterally to be studded with hemorrhagic necrotic lesions ranging in size from 0.4 x 0.4 cm. to 1.1 x 1.3 cm. Many of these lesions were associated with the subarachnoid. Multiple sections of the brain stem showed similar type lesions.

Material submitted:
H & E section of cerebrum

Points for discussion:
1. Diagnosis
2. Pathogenesis

CASE 1994-2

Submitted by: Marius P. Valsamis M.D. Dept. of Pathology and Harold W. Horowitz M.D. Dept. of Medicine Infectious Disease Unit
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Case reference number: A93-27

Clinical History:

A 29 year old HIV positive male was admitted to Westchester County Medical Center on January 2, 1991 with a 6 month history of right sided weakness, 3 months of mental status changes. He had sustained a seizure 1 week prior to admission. He had dysphagia for 1 week. Seven weeks prior to admission he was seen at a local hospital where a lumbar puncture was performed. The cerebral spinal fluid (CSF) demonstrated a protein level of 140 mg/dl, normal glucose, 4 white blood cells (WBC) (100% lymphocytes), and a negative venereal disease research laboratory test (VDRL). His serum contained treponemal antibodies by Fluorescent Treponemal Antibody test (FTA-ABS). In 1984 he was treated for primary syphilis and in 1988 neurosyphilis was diagnosed by a reactive CSF-VDRL. Treated with 12 x 10^6 units of intravenous penicillin for 10 days. CD4 cell count was 9 cells/mm^3 and computed tomography (CT) of the brain was negative. ELISA and Western blot studies for HIV were positive.

Currently he was afebrile, pulse 100, respiratory rate 24. Thrush was noted. Neck was supple and retinal exam normal. Skin, chest, heart, and abdominal examination were unremarkable. Neurologic examination: disoriented, tremulous patient with poor memory. Cranial nerve examination intact but the lower extremities appeared weak. Reflexes intact and symmetric. Plantar reflexes downgoing. Fluconazole was the only medication on admission. Laboratory examination showed a WBC of 3,500 cells/mm^3, hematocrit of 31.7%, and platelets 73,000/mm^3. Biochemical blood analysis (SMAC) normal except for gammaglutamyl transferase of 249 U/L. Toxoplasma titers negative but a serum RPR was 1:8 and an FTA was reactive. A CT scan of the head revealed multiple enhancing lesions with a hyperdense nodule in the left centrum semiovale. Surrounding edema caused mass effect on the body of the left lateral ventricle. Additional lesions were noted in the right parietal area. CSF showed 12 WBC (11 lymphocytes) with a normal glucose, protein level of 178 mg/dl, and VDRL reactive at 1:2. CSF was negative for cryptococcal antigens.

The patient was treated with sulfadiazine and pyrimethamine. On the 5th day intraveneous cefotaxime was initiated. Decadron was begun on the 9th day. After 11 days of cefotaxime, 12 x 10^6 units penicillin daily was started. He received 10 days of penicillin therapy. Amphotericin B and ceftazidime were subsequently given. Four days prior to his death, a CT demonstrated obstructive hydrocephalus at the level of the fourth ventricle. CSF cultures negative for mycobacteria and fungi. An autopsy limited to the brain was performed.

Gross examination of the brain revealed several greenish masses ranging in size from 1.5 to 3 cm in diameter. They were located in the left frontal (2) lobe, basal ganglia, right occipital lobes, pons and cerebellum (2). The pontine mass obstructed the fourth ventricle.

Material submitted: 1 H & E slide, 1 Kodakchrome, 1 blank slide.
Points for discussion: 1. Diagnosis
2. Histopathologic correlation

CASE 1994-3

Submitted by: Ronald L. Hamilton, M.D. and Clayton A. Wiley, M.D. Ph.D. , Presbyterian University Hospital A-506, Division of Neuropathology, 200 Lothrop, Pittsburgh, PA 15213.

EB was a 40 year old white male who presented to another hospital in July 1992 with disorientation, difficulty speaking and fevers. He was found to be HIV seropositive in November 1991 when evaluated for shingles in a T6 dermatome distribution. He denied any risk factors for HIV infection. Additional clinical history included hepatitis B, peripheral neuropathy and legionella pneumonia. Admitting neurological examination was unremarkable. On admission he was treated for pneumonia. Sputum cultures grew Psuedomonas aeruginosa, but were negative for legionella. Liver function tests were found to be abnormally high. His T4 count was 4 (normal range 370-1482). He suffered a seizure and was placed on phenobarbital. His serum and CSF toxoplasma titers were negative. CSF VDRL was negative and no cryptococcal organisms were identified. MRI scan showed a focal lesion in the left basal ganglia consistent with infarction. He was discharged after 9 days, however, his neurological symptoms progressed and he developed fever and lower extremity weakness. He was unable to stand on his own and was admitted to University of California, San Diego Medical Center. Admitting physical examination showed dysphasia, but was otherwise unremarkable and there were no focal neurological signs. CT scan of the head was unremarkable (the MRI scan from his initial admission was not available for comparison). Phenobarbital levels were not elevated. His respiratory function worsened and he expired that evening.

Systemic autopsy revealed severe pulmonary edema, chronic severe adrenalitis and splenomegaly. The fresh brain weighed 1500 gm and showed no external abnormalities. Coronal sections showed a lesion in the left putamen and globus pallidus. Microscopic examination of sections of the brain showed subacute lesions in the left basal ganglia, thalamus and mamillary bodies with mild perivascular lymphocytic infiltrate. Similar microscopic lesions were present in the right basal ganglia. There were scattered microglial nodules in the basal ganglia and medulla.

Enclosed is an H&E stained glass slide of one of the lesions and a kodachrome slide of a Bielschowsky stain of a similar lesion.

Points for discussion:

1. What is the pathogenesis of these lesions?
2. What further studies might be done to prove the diagnosis?

CASE 1994-4

Submitted by: Janet M. Miles, M.D.
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Reference #: W92-379

Clinical Abstract: This 31-year-old Caucasian female was admitted for lethargy, acute confusion and new onset of generalized seizures. Past medical history is significant for hypertension, glaucoma and a 25 year history of Type I diabetes mellitus leading to a renal-pancreatic transplant approximately three months prior to admission. Two months prior to admission, an episode of graft rejection was successfully treated with high dose steroids, radiation and anti-CD3 antibody and maintained on Cyclosporin. Significant laboratory studies upon admission include elevated liver functions (GGT 2097, AST 31, ALT 87, alkaline phosphatase 533), elevated pancreatic enzymes (amylase 322 and lipase 80) and hyponatremia. BUN and creatine were 25 and 1.9, respectively. CT scan of the abdomen and pelvis revealed hepatic steatosis and gallbladder sludge. CT scan of the chest was negative. MRI of the brain revealed multiple, bihemispheric enhancing lesions. Echocardiogram revealed a mass in the right atrium measuring 2 x 2 cm. apparently adherent to the atrial wall. A stereotactic brain biopsy was obtained. The patient was treated with Amphotericin B and received 50gs of whole brain irradiation. Liver and pancreatic enzymes normalized; however, hyponatremia persisted. The patient became increasingly obtunded and unresponsive. Repeat MRI revealed multiple new intracranial lesions and hemorrhage. Despite all efforts, the patient subsequently expired.

Submitted: One H&E stained section and one unstained slide.

Points for Discussion:

1. Diagnosis
2. Pathogenesis
3. Radiographic correlation

Case 1994-5

Submitted by: P.V. Gould and D.G. Munoz, University Hospital, University of Western Ontario, London, Ontario N6A 5A5

Clinical History:
The patient was a 40 year old male who developed bilateral sensorineural deafness at age 11. By age 20 he had an ataxic gait and progressive loss of vision. His brother underwent an orthotopic heart transplant for cardiomyopathy in January 1990. The mother reportedly also suffered from cardiomyopathy and ataxia.

By age 36 our patient had marked external ophthalmoplegia with slight residual lateral gaze only — more so on the left. He had bilateral ptosis with facial weakness and prominent dysarthria. His motor strength was rated as 4/5 in all extremities. Sensation was intact except for the left hand which showed decreased pin prick, light touch and vibration. His gait was wide based and his coordination was impaired. An MRI scan revealed moderate cerebellar atrophy but no other lesions. He had no evidence of cardiomegaly. By June 1992 his condition had deteriorated; he required a wheeled walker despite coenzyme Q therapy.

In August 1992 the patient developed pneumonia and went into acute respiratory failure. He remained dependent on mechanical ventilation thereafter due to significant respiratory muscle weakness. In October 1992 he suffered a cardio-respiratory arrest but was successfully resuscitated. Following this episode he regained consciousness but had marked myoclonus and bouts of seizure activity which responded to standard anticonvulsant therapy. He was transferred back to his community hospital in January 1993, still respirator-dependent following tracheostomy. He suffered a terminal cardiac arrest there in April 1993.

Necropsy findings:
General autopsy revealed cerebellar atrophy and hypertrophic cardiomyopathy. The fresh brain weighed 1260 g. The brain was referred to our institution for further evaluation. The external examination confirmed symmetric atrophy of the cerebellum, but was otherwise unremarkable. Upon sectioning the brain we noticed multiple small areas of rarefaction in the tectum of the midbrain.

Material submitted:
- H&E stained section of cerebral cortex (a)
- H&E stained section of midbrain (b)

Points for discussion:
- Diagnosis
- Molecular defect

CASE 1994-6

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

Case reference number: A86-133

Clinical History:

The patient was a young white female with a history of movement disorder following a viral syndrome at the age of 21 years, when she started having excessive drooling and involuntary lip smacking. Later on she developed involuntary tongue movements, tongue biting, difficulty with articulation and involuntary movement of her limbs and occasional dystonic posturing. She also had strange bizarre speech and behavior and tendency to unintentionally injure herself. At age 28, she had severe choreiform movements of arms and lips. Since she was not able to take care of herself, she was admitted to a nursing home. She continued to deteriorate with increased athetoid movements and self destructive behavior with chewing and biting her cheeks and died at the age of 31.

Past History:	Infectious mononucleosis 1975.
Family History:	Grandmother had oral involuntary movements in later years.
Physical Exam:	Thin white female, emotionally labile, showing lip smacking, drooling and repetitive movements of lips, dysarthric speech, unable to stand.
Neurological Exam:	Cranial nerves - normal, no nystagmus Motor - mild decrease of tone, no focal weakness, reflexes-hypoactive diffusely. Sensory exam - normal Mental - IQ 106
Labs:	Chest x-ray normal, EKG - normal Blood Glucose 100, LDH 268, Cholesterol 176 Copper and ceruloplasmin (serum and urine) - normal CSF - normal

Necropsy Findings:

Degeneration of basal ganglia

Material Submitted:

1. Kodachrome of corpus striatum (gross)
2. H&E stained section of corpus striatum

Points for Discussion:

1. Differential Diagnosis
2. Plan for further workup.

CASE 1994-7

Submitted By : Cheryl P. Harris, MD [University of Alabama at Birmingham], Jeannette J. Townsend, MD [University of Utah, Salt Lake City] and E. Tessa Hedley-Whyte, MD [Massachusetts General Hospital, Boston]

Case Reference Number : NP 2262

Clinical History : This 45 year old man had a ten year history of steady progressive cognitive decline. Initially, family members noticed that the patient's memory was failing and he seemed nervous and unable to concentrate. He was evaluated by a neurologist in 1984, who described weight loss, insomnia, and anhedonia but a normal neurological examination. He was referred to a psychiatrist and was diagnosed with a major depressive episode. In 1986, a magnetic resonance imaging scan revealed diffuse white matter disease and moderate cortical atrophy. Laboratory studies at that time included flourescent Treponemal antibody test, Vitamin B12, erythrocyte sedimentation rate, heavy metal screens, serum copper, ceruloplasmin, serum lactate, urine arylsulfatase levels, very long chain fatty acid levels, urine homocystine and a HIV antibody titer, all of which were unremarkable. The diagnosis of possible multiple sclerosis was entertained due to the presence of four oligoclonal bands in the cerebrospinal fluid, although the CSF protein was only 39 mg%.

The patient's cognition continued to worsen and eventually he required placement in a protected care setting. In late 1991, a misunderstanding with local police resulted in his incarceration, who did not recognize his dementia and did not realize he lived in the nearby care center. He was assaulted in the jail that night by a fellow inmate and suffered a frontal intraparenchymal hemorrhage and diffuse subarachnoid hemorrhage. He remained comatose until his death in late 1992.

Autopsy Findings : At autopsy, evidence of the old cerebral trauma was seen with remote subarachnoid hemorrhage and a hemosiderin-lined cavity in the frontal pole. The white matter was discolored, more prominently anteriorly.

Materials Submitted :
1 - H & E section of cerebrum
1 - Unstained slide

Points For Discussion :
1. Diagnosis?
2. Pathogenesis?

CASE 1994-8

Submitted by: Roberta Seidman, M.D., Department of Pathology, University Hospital- SUNY at Stony Brook, Stony Brook, NY 11794-7025

Reference number: ME 93-0357

Clinical History: This patient was well until age 42, when she was first noted to have a change in personality. Over the next two years, she developed a progressive dementia that resulted in an inability to function in her job as a secretary and eventually to be limited to the point of even having difficulty shopping. In her early thirties, there had been a transient episode of numbness and tingling in her left upper extremity, but she had no other history of medical problems. There was no prior history of hypertension.

When she was 44 years old, she was admitted to New York Hospital for neurologic evaluation. At that time, she was normotensive and general physical examination was normal. Neurologic examination revealed moderate cognitive impairment without aphasia. There was diffuse symmetric hyperreflexia, bilateral Hoffman's signs and bilateral Babinski signs with normal strength and gait.

CT scan revealed "white matter degeneration". Two years later, MRI of the brain revealed diffuse increase in signal on T2-weighted images throughout the cerebral hemispheric subcortical white matter. CBC, electrolytes, general chemistry panel, VDRL, B12, folate, thyroid function tests were normal. "Metabolic studies" were normal. CSF protein, glucose and cell count were normal.

She experienced further decline in neurologic function and was placed in a nursing home at the age of 48 years, when she was no longer able to ambulate. She died of pneumonia at age 56.

Autopsy findings: Gross autopsy findings revealed bilateral acute bronchopneumonia, mild systemic atherosclerosis and nephrolithiasis. External examination of the 1061 gram brain revealed bifrontoparietal and ventral brainstem atrophy. Internal examination revealed diminution in amount and gray discoloration of cerebral subcortical white matter, with multifocal cavitation, sparing U-fibers and polar regions. The basal ganglia, thalamic nuclei and pontine base had multiple small cavitary lesions.

Material submitted: One color 2x2 slide and one H&E section of cerebrum.
Points for discussion: 1. Diagnosis 2. Pathogenesis 3. Prognosis for family

CASE 1994 - 9

Submitted by: M.G. Norman, Department of Pathology
BC's Children's Hospital
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Vancouver, BC V6H 3V4

Case reference number: A93-121

Clinical History: This infant was the product of a normal, 36 week pregnancy in 38 year old gravida ii woman. Amniocentesis and fetal karyotyping for advanced maternal age showed a normal fetal karyotype. Apgars 6, 8 and 9. Birth weight 2270 gms. Length 70 cm (90%ile) and head circumference 25 cm (1½ cm below 10%ile). Referred at 16 days of age for dysmorphic features and congenital nephrotic syndrome. Dysmorphic features were ? posteriorly rotated ears, small palpebral fissures with microphthalmia, high-arched palate, micrognathia, wide-spaced nipples, flexion deformities ge MPJ of thiembs, (also described as arachnoidactyly). The renal problems were edema, including orbital puffiness, proteinuria, and impaired renal function. The kidneys were palpable and ultrasound showed enlarged kidneys. Head ultrasound showed that the contour of both cerebral hemispheres appeared smooth and simple with lack of sulcal formation, and the Sylvian fissure also appeared simple. Over the last 15 days of life hemoglobin fell from 158-172 to 91 g/L, serum sodium potassium and calcium tended to be slightly under the lower limit of normal, urea varied form 14.6 - 15.0 mmol/L, creatinine rose from 169 to 269 umol/L. Total protein was 32 g/L; serum albumin ranged from 19-25 g/L and beta and gamma globulins were also low. Urine protein was more than 5.00 g/L. Alkaline phosphatase ranged from 93-55 U/L. Investigations for various viral and bacteriological agents were negative. The EEG was severely abnormal.

The infant was treated with many infusions of albumin. A feeding jejunostomy was performed at 23 days of age because of hiatus hernia, gastric reflux and esophageal motility problems in the hopes that this would allow the baby to be sent home to die, the diagnosis having been made clinically. After the operation he required intermittent positive pressure ventilation. Seizure activity was seen. He became oliguric, and his condition deteriorated, with gasping respiration. He was extubated and died at 31 days.

Necropsy findings: Failure to thrive (weight 2890, normal 3634 g) Brain weight 172.3 g (normal 431 +/- 117.7). Pachygyria, kidneys showed glomerulosclerosis, tubular ectasia, renal hyperlobation. Other findings: hiatus hernia, thyroid dysplasia, adrenal hypoplasia, facial dysmorphisms (microgthia, posteriorly rotated ears, high arched palate), flexion deformity of thumbs, wide-spaced nipples, generalized edema with pleural effusions and ascites, acute pneumonia, hepatic cholestasis with ductular proliferation.

Material submitted: 1 Kodachrome of brain.
1 H & E section of frontal lobe.

Points for discussion:
1. Diagnosis
2. Pathogenesis

B:CASE1994.#9

CASE 1994-10

Submitted by: Marius P. Valsmais, M.D.
Department of Pathology
New York Medical College
Westchester County Medical Center
Valhalla, NY 10595

Case reference number: A-93-22

Material submitted: One H&E stained slide

Points for discussion: #1: Diagnosis
#2: Pathogenesis

Clinical History:

This was a 10 year old hispanic boy, a resident of the Gosher Group Home in Rockland County, with a history of attention deficit disorder, hyperactivity and asthma. A week before admission to WCMC he developed an upper respiratory tract infection for which he was receiving Penicillin. On 2/10/93, he was playing basketball when he suddenly complained of headache with dizziness and he collapsed. He was taken to the Emergency Room at a nearby hospital. He was found to be unresponsive, tachycardic to 140 BPM and apneic. He was immediately intubated. His laboratory values were within the normal range. A chest x-ray showed bilateral pulmonary infiltrates consistent with pulmonary edema. A CT-scan showed a cerebral hematoma with some bleeding into the third ventricle and acute hydrocephalus. He was then transferred to WCMC for further management, where he was taken to the Operating Room for an emergency right frontal ventriculostomy placement. The CSF was found to be under high pressure and was bloody. On the operating table, the patient was noted to have no spontaneous respirations, no response to deep painful stimuli and had fixed and dilated pupils, consistent with absence of all brain stem functions. The patient remained comatose. An EEG showed minimal cortical activity at this time. He was maintained on ventilatory support. Neurological criteria for brain death were evaluated on 2/13/93 and he was declared dead on 2/13/93 at 4:00 pm On 2/14/93, multiple organ harvesting was carried out and the liver with gallbladder, kidneys with adrenal, spleen, pancreas, and mesenteric lymph nodes were removed. Subsequently an autopsy was performed, 67 hours after death.