CASE 1998-1

SUBMITTED BY: Rebecca D. Folkerth, MD
Boston Veterans Affairs Medical Center
150 S. Huntington Avenue
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CASE REFERENCE: BVAMC SP97-4295

CLINICAL HISTORY: This 50-year-old veteran, with a past medical history of hypertension, presented with recent onset of headaches, dysarthria, and right-sided weakness. A head CT scan, performed elsewhere, showed "tumor with edema", and the patient was transferred to the Boston VA. Head MR revealed a 7 cm left hemispheric mass within the left ventricle, possibly involving parenchyma on the left, and extending into the pineal recess and superior vermian cistern. The lateral ventricles were expanded. The tumor had an inhomogeneous signal, with interspersed hypointense areas on T2-weighted images, and uniform gadolinium-enhancement. Prominent vascular flow voids and mass effect were seen, also. Preoperative work-up disclosed a cyst in one kidney. The patient underwent gross total resection of the mass.

MATERIAL SUBMITTED: One H&E-stained glass slide, and one unstained glass slide (baked at 37C).

POINTS FOR DISCUSSION: Nosology, grading, and treatment recommendations for such tumors.

CASE 1998-2

Submitted by: Drs. Barbara H. Amaker, M. Gary Hadfield, and Nitya R. Ghatak
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Richmond, Virginia 23298-0017

Case Reference Number: S97-13832

Clinical History: This 6 year old girl was the product of a normal spontaneous vaginal delivery born to an HIV positive woman after an uncomplicated pregnancy. She remained healthy until she was 2 years old. At that time, she suffered several episodes of interstitial pneumonitis, necessitating an open lung biopsy. No viral, bacterial or fungal etiology was found. She was found to be HIV positive and has subsequently been diagnosed with AIDS based on a low CD4 count of 69/cu mm. She has also had diagnoses of failure to thrive, esophageal candidiasis, and c. difficile colitis. There is no history of significant neurologic changes but a head CT was done to rule out any indolent lesions. A mass discovered in the left portion of the cavernous sinus was further studied with MRI. MRI characterized the lesion as a well circumscribed, enhancing 1.5 cm extra-axial mass. She had a craniotomy with excision of the mass.

Material Submitted: 1 Hematoxylin and eosin stained section
1 Unstained section

Points for discussion: 1. Diagnosis
2. Pathogenesis

CASE 1998 #3

Submitted by: Waldemar Radziszewski, Pier-Luigi DiPatre, Alexander Brooks & Harry Vinters.
Department of Pathology and Laboratory Medicine, UCLA Medical Center, 10833 Le Conte Ave., Los Angeles, CA 90095-1732

Case reference number: 97S-4857

Clinical history: A 50-year-old female presented with a progressively enlarging right frontal mass under her scalp. The mass was non-tender and the scalp was otherwise normal. She was afebrile with no focal neurological symptoms. Her past medical history was significant for systemic lupus erythematosus (SLE) and myocardial infarction in January 1997. An MRI suggested a meningioma with trans-ostial extension involving the cranium, epidural and subgaleal spaces. She was admitted to UCLA Medical Center for surgical resection of the mass and cranioplasty.

Pathologic findings: A dural based mass with focal hemorrhage. H&E stained sections showed a lesion composed of sheets and lobules of meningothelial-like cells with prominent areas composed of spindle-cells forming whorls and short fascicles. Areas of multifocal acute inflammation and necrosis were evident.

Material submitted: Section of the mass (1 H&E-stained, 1 unstatined)

Points for discussion: 1. Diagnosis
2. Pathogenesis

CASE 1998-4

Submitted by: Sozos Ch. Papasozomenos, M.D.
The University of Texas-Houston Medical School
Houston, Texas 77030

Case reference numbers: S96-11029, SU96-949, EM96-300

Clinical History:

A 26 year old Latin American man with a one year history of progressively worsening polyuria and a three week history of memory loss presented with increasing somnolence and dizziness upon standing. Further information included a decreased libido and impotence within the past eight weeks. He had recently been evaluated by an endocrinologist and was found to have hypernatremia and hypogonadism [testosterone, 15.5 ng/dL (200-1200 ng/dL)]. The patient denied any visual symptoms, nipple discharge, or headaches. His past medical history was unremarkable. His physical exam was remarkable for orthostatic dizziness, unequal pupils, and partial loss of short and long term memory, with confabulatory amnesia. He was oriented to self, but not to place or situation. Extraocular movements were intact in all directions. No visual field deficits were noted. Cranial nerve examination was normal. No motor or sensory deficits were noted. Cerebellar function was normal, and deep tendon reflexes were normal and symmetrical. Abnormal serum values were: sodium 161 meq/L, chloride 121 meq/L, osmolality 315 mOsm/kg, phosphorus 4.9 mg/dL, ALT 47 U/L, AST 57 U/L, and prolactin 52.1 ng/mL (2.2-18.5 ng/mL). Abnormal CSF values were: glucose 165 mg/dL, and protein 87 mg/dL. An MRI showed a brightly enhancing hypothalamic lesion with extension into the third ventricle, and distortion of the region of mammillary bodies. The patient then underwent a bifrontal craniotomy for biopsy-resection of the hypothalamic lesion.

Material submitted: One H & E stained slide and one kodachrome of an electron micrograph from the surgical specimen.

Points for discussion: 1. Diagnosis
2. Prognosis

CASE 1998 - 5

Submitted by: Brent Harris, M.D., Ph.D. and Dikran Horoupian, M.D.
Div. of Neuropathology, Dept. of Pathology, Stanford University Hospital, Stanford, CA 94303
and L.T. Smythe, M.D., Kaiser Hospital Redwood City, CA 94063.

Case ref. #: NP7878

Clinical History:

The patient is a 52 year old gentleman who works as a machinist. He presented in May, 1996 with left eye pain without visual deficit and intermittent mild headaches for approximately one year. He underwent surgery for a right scleral/lacrimal gland lesion. The pathologic diagnosis was reported as: "inflammatory nodule with stromal fibrosis and histiocytic response; special stains negative for organisms". As part of the workup, he had a MRI scan which showed an apparently incidental, 3 cm, dural-based, contrast enhancing, left temporal mass without any obvious bony involvement. This was felt to be suspicious for meningioma.

Other medical problems include hypertension and gout for which he takes an ACE inhibitor, Zesteril, and allopurinol, respectively. The patient smokes and drinks (amounts not known). His family history is positive for diabetes and tuberculosis. His review of systems was significant only for the mild headaches with no difficulties with vision, hearing, or weakness.

On physical exam he had: BP - 140/70, pulse - 80, resp. rate - 20, afebrile. He was generally alert and cooperative in no acute distress. His HEENT, chest and lung, cardiac, abdominal, and neurologic exams were normal.

Laboratory values showed: glucose - 81 mg/dL, K - 4.2 mEq/L, Na - 143 mEq/L, WBC - 14 K/uL, HCT - 43.1%, MCV - 101 fL, Plt - 476 K/uL, granulocytes - 67%, lymphs - 24%, monos - 8%, eos - 1%, baso - 0%.

The temporal lesion was resected one month after the eye surgery.

Material submitted: 1 H&E stained section from the intracranial mass.

Points for discussion: Differential diagnosis, prognosis

CASE 1998-6

Submitted by: Edwin S. Monuki and Umberto De Girolami, Joint Program in Neuropathology, Brigham and Women's Hospital and Children's Hospital, Boston, Massachusetts 02115

Case reference number: A97-26

Clinical History: The patient was a 42 year old male with a history of intravenous drug abuse, alcohol abuse, and AIDS. He was diagnosed with AIDS in 3/93 when he presented with *Pneumocystis carinii* pneumonia, pneumococcal pneumonia, and hepatitis. Toxoplasma and CMV titers at that time were both high positive for IgG and negative for IgM. Serologies were also positive for hepatitis B and C viruses. In 7/95, he developed pulmonary tuberculosis, which was multidrug-resistant by culture. Sputum samples also suggested colonization by *P. aeruginosa*. His CD4 count was less than 20 when last measured in 9/95.

The patient's neurologic history began in 3/96, when he experienced sudden-onset of left-sided weakness and brief loss of consciousness. He was unable to ambulate for the next few days, then came to the Brigham and Women's Hospital (BWH). Physical examination findings included a left facial droop, left hemiparesis, and brisk reflexes. Multiple brain lesions were detected radiographically, which involved bilateral frontal and parietal cortex and subcortical white matter, thalamus, and cerebellum. He was treated for presumptive Toxoplasmosis, with subsequent clinical improvement and radiographic regression of the CNS lesions. He was eventually discharged on an anti-Toxoplasma regimen.

In 12/96, the patient was readmitted to BWH complaining of poor balance following a period of complete noncompliance with his medical therapy. Further history revealed fever, chills, dry cough, weakness and lethargy. The patient was alert, oriented and slightly dysarthric, with a right facial droop and left pronator drift. Brain imaging revealed new lesions, including a large one in the right basal ganglia. After reinstituting anti-Toxoplasma therapy, the patient again improved clinically and was discharged.

On 1/29/97, the patient was readmitted after experiencing a probable seizure despite reported compliance with medications. Additional history revealed only mild fever and headache. He was alert with a temperature of 102. Examination was notable for diffuse cervical and supraclavicular lymphadenopathy. Laboratory examination revealed a therapeutic Dilantin level, and toxicologies were negative. Cerebrospinal fluid analysis showed elevated protein, normal glucose, and rare blood cells; studies for organisms (Gram stain, bacterial culture, AFB, fungal culture, cryptococcus, and RPR) were negative. Brain imaging revealed the old right basal ganglia lesion, which had increased in size, as well as new lesions in the cerebellum and cerebrum. On hospital day 2, the patient had increasing unresponsiveness and speech difficulty. On hospital day 3, brain biopsy was considered, but the patient deteriorated rapidly and died later that day.

Necropsy findings: The fresh brain weighed 1340 grams. External examination of the brain revealed mild cerebral edema, but was otherwise unremarkable. Sectioning revealed over 20 discrete lesions in the cerebrum and cerebellum, the largest of which involved the right basal ganglia and measured 4 cm in greatest dimension. The lesions were hemorrhagic, soft, and slightly to moderately expansile. All of the lesions looked similar grossly, except for the presence of small, yellow, overtly necrotic areas within two of these lesions. No lesions were detected in the brainstem, and the remainder of the macroscopic brain examination was unremarkable. General autopsy findings included a hemorrhagic necrotizing pneumonia with macroscopic abscesses involving both lungs, interstitial nephritis with microabscesses, generalized AIDS lymphadenopathy, and mild hepatitis consistent with the history of hepatitis B and C virus seropositivity. Immunohistochemical studies demonstrated scattered Toxoplasma cysts within the lung and kidney abscesses. Postmortem lung cultures were also positive for *S. aureus* and *P. aeruginosa*.

Material submitted: H&E section of a representative cerebral lesion.

Points for discussion: 1. Diagnosis
2. Classification and epidemiology of the etiologic agent

CASE 1998-07

Submitted by:
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Department of Anatomic Pathology (Neuropathology)
The Cleveland Clinic Foundation, L25
Cleveland, OHIO 44195

Clinical History

A 45-year-old woman with long-time, but stable, asthma presented on 12/14/1996 with shortness of breath, cough and chest tightness. ABG showed severe acidosis and hypoxia. She was intubated and treated for status asthmaticus with IV steroids and theophylline. She then developed fever with a right perihilar infiltrate on chest X-ray and was given multiple antibiotics following a positive sputum culture for H. influenza and Staph. aureus. In subsequent days, her course was complicated by GI bleeding, tension pneumothorax, cardiomyopathy with EF of 25% and fluctuations in mental status, at times unresponsive. Ten days after admission, she was noted to be very weak on all 4 extremities. Neurological examination revealed diffuse weakness (graded 3-4 / 5 globally) with a normal sensory exam, and 2+ DTRs throughout except for absent ankle jerks. By 1/2/97 her weakness improved and she was able to walk with a walker.

Her family history was unremarkable. She's married with two children. She had a history of 15 pack years of smoking (none for 13 years). There was no EtOH use.

Her medication included antibiotics (Gentamycin, Timentin, Vancomycin, and Cipro), Solumedrol (>6000 mg total dose), Theophylline, Ativan and Versed PRN, Insulin, Pepcid, Capoten then Lisinopril, and Digoxin.

Lab data

1) MRI C-spine - mild spondylosis, no spinal cord compression;
2) EEG - moderately severe encephalopathy
3) Normal head CT
4) Lumbar puncture - normal
5) EGD - mild gastritis and duodenitis
6) ECG - c/w an anteroseptal MI (normal CK-mb fraction)
7) CBC and electrolyte abnormalities which resolved prior to discharge
8) CK - 2,452.

She was discharged to rehabilitation on 1/6/97 and was described as having "diffuse generalized weakness, both proximally and distally with substantial muscle wasting.....reflexes are not brisk, but seem to have improved from where they were recorded when she was admitted which would suggest some type of demyelinating polyneuropathy."

A muscle biopsy was performed.

Material submitted: 3 kodachrome slides labeled A (H&E), B (NADH) and C (EM photograph)

Points for discussion:
a) Diagnosis
b) Pathogenesis

CASE 1998 - 08

Submitted by: Dr. Juan M. Bilbao, Dr. Felix Tyndel and Ms. Sandra M. Cohen
St. Michael's Hospital, Department of Pathology
30 Bond Street, Toronto, Ontario, M5B 1W8, Canada

Case Reference Numbers: B180 and B2678

Clinical History:

In 1977, a 57-year-old man developed recurring and remitting symptoms of polyneuropathy beginning in the legs and then the arms. Family history was negative for neurological disease. Nerve conduction studies showed generalized demyelinating sensory motor neuropathy with motor conduction velocities of 23 and 18 m/s in the median and ulnar nerves respectively, and unobtainable sensory responses in the arms and legs. Investigations showed hypothyroidism, and replacement therapy did not influence the polyneuropathy. Biopsy of left sural nerve showed no inflammation, decreased number of fibers and onion bulbs. Records indicate presence of an IgM paraproteinemia which was not investigated further. Symptoms progressed slowly over the years with worsening numbness, increasing weakness of lower extremity and wide-based gait. A short trial of Prednisone treatment did not alter disease severity, however, the patient improved slightly over subsequent years spontaneously.

At the age of 69 (1989), examination revealed minimal weakness, postural tremor, generalized areflexia, loss of vibration sense and ataxia of lower extremities, and unsteady wide-based gait. Sensory responses were not obtainable. Motor conduction velocity was 15 m/s in the median nerve.

At the age of 72 years (1993), the patient presented with fatigue, anemia, lymphadenopathy and inability to walk unassisted. Laboratory investigation revealed IgM/kappa paraprotein with a total IgM concentration of 54.5 gms per liter and relative plasma viscosity of 12.2. Lymph node and bone marrow biopsies revealed a diffuse small lymphocytic malignant lymphoma with a monoclonal plasmacytoid B cell population expressing immunoglobulin light chain kappa and immunoglobulin heavy chain IgM. Treatment with Chlorambucil and Prednisone was instituted with apparent remission of the lymphoma. Plasma exchanged was performed to treat hyperviscosity syndrome. The patient noted marked subjective improvement. A second nerve biopsy was performed 16 years after the onset of his original symptoms (1993). The patient died in 1996 of disseminated lymphoma.

Material Submitted: Semithin sections stained with toluidine blue of left sural nerve (1978 - close to label) and right sural nerve (1993); and a lantern slide of an electron photo-micrograph.

Point of Discussion: Diagnosis.

Case 1998 [9]

Submitted by: Professor Francesco Scaravilli, Department of Neuropathology, Institute of Neurology, National Hospital for Neurology & Neurosurgery, Queen Square, London WC1N 3BG

Case Reference no: PM83-89

Clinical History: Female 19years

She fed poorly as a neonate and was hypotonic; she sat independently at 1 year of age and did not walk until 2 years and 3 months. Speech development was normal. Her gait was always ataxic.
12 years: External ophthalmoplegia, retinopathy and cerebellar syndrome.

14 years: Insulin-dependent diabetes.
16 years: Mild bulba weakness, brisk reflexes and exterior plantars.
19 years: Fit after a fall. Admitted unconscious to hospital.
Biochemical and haematological screens normal, including blood lactate concentrations (apart from mild hypoglycaemia) - ECG: bifascicular block, CSF: xanthochromic with 3g/l proteins. EEG: widespread theta and slow activity with superimposed episodes of high amplitude irregular slow waves - CT scan: extensive white matter low attenuation.
The patient did not regain consciousness and died 3 weeks later.

Necropsy findings: General post-mortem examination showed bronchopneumonia and oedema, pyelonephritis and cystitis. The brain weighed 1150g and showed the appearance of a diffuse white matter disorder.

Material submitted: H&E sections

Points for discussion: 1. Diagnosis
2. Pathogenesis

CASE 1998 #10

Submitted by: Martha Quezado, M.D.*, Peter Bryant-Greenwood, M.D.*, Nancy Tresser, M.D.^
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Case reference number: S97-2011

Clinical History

A 39 year old Caucasian woman presented in **December 1997** with a chief complaint of worsening pain of the left leg and perineum, described as "sharp and burning". Review of systems elicited constipation, urinary spasms with increased frequency and incontinence, back pain and dyspareunia. On physical exam she was found to have decreased sensations of the perineum and posterior left lower extremity. She had originally presented in **July, 1996** with chronic back pain and bilateral foot pain, at which time she was given a diagnosis of chromic pain syndrome and referred for PT, acupuncture and analgesics. By **March, 1997** the patient was using daily enemas for constipation. Her diagnosis at this time was changed to mixed dysphoric hypomania complex (personality disorder). After repeated ER visits for symptoms of bowel obstruction, careful neurological examination in **April, 1997** revealed decreased sensations to the back, buttocks, and LLE, with diminished vibratory sense. CT and MRI in **April** were reported as normal. Repeat MRI in **December** demonstrated a bilobed tumor at the S2 nerve root.

Past medical history

1979 bilateral wedge resections for "cystic ovaries" (pathology report not available)
1981 retroperitoneal cyst: encapsulated pink cell tumor with melanin
1985 gastric wall tumor: pink cell tumor, well differentiated hepatocellular carcinoma vs. adrenal rest
1986 left hepatic lobectomy: encapsulated pink cell tumor with melanin
1988 bilateral adrenalectomies: L) adrenal cortical proliferation of uncertain malignant potential.
R) nodular hyperplasia of the adrenal cortex
1988 ear and buttock: myxoid neurofibroma, thigh: dermatofibroma
1989 thyroidectomy: papillary thyroid carcinoma
1991, 1993 wedge resections of RLL of lung: metastatic adrenal cortical carcinoma
1992 gastric submucosa: metastatic adrenal cortical carcinoma
1993 right oopherectomy: serous cystadenoma, leydig cell hyperplasia
1997 breast: myxoid fibroadenoma

Material submitted: One H&E and one unstained slide of sacral mass

Points for discussion: 1. Diagnosis of sacral mass, including pathogenesis
2. Clinical significance of present lesion
3. Clinical significance of past medical history

The authors would like to thank Joseph Watson, M.D., National Institute of Neurological Disorders and Stroke, Surgical Neurology Branch for his awesome intraoperative photographs and detailed operative report and Constantine A. Stratakis M.D., National Institute of Child Health and Human Development, Developmental Endocrinology Branch for his meticulous records of the patient's numerous ailments.