CASE 1997 #1

SUBMITTED BY: Dr. Juan M. Bilbao
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CASE REFERENCE NUMBER: B3184 96-S-2111

CLINICAL HISTORY:

This 70 year old woman developed at the age of 58 polyarticular arthritis, butterfly rash, sicca syndrome and was found to be ANA positive, coombs positive and ENA positive. The diagnosis of SLE was made and other investigations revealed IgG lambda paraprotein in serum and urine. A bone marrow biopsy showed 10% plasma cells (1983). Skeletal survey was negative.

Plaquenil, 250 mg/day, was started for treatment of cutaneous manifestations of SLE. At the age of 63, hand tingling developed. At the age of 65, the patient's overall condition improved and all medication was discontinued. Following a flare of skin rash that year, chloroquine was started but symptoms progressed. With a regimen of Prednisone and Isoniazid, the patient's disease was suppressed.

At the age of 68, the patient complained of symmetrical numbness and tingling in hands and feet. Examination was normal and electrophysiological studies (Feb 1994) showed slightly reduced motor amplitudes in the legs. Symptoms progressed, weakness of foot dorsiflexion developed and reduced vibration and pin prick sensation in the feet were demonstrated. Deep tendon reflexes were decreased throughout. In October 1994, electrophysiological studies showed diffuse moderate to severe mixed axonal demyelinating polyneuropathy. The patient was lost to followup and re-examined in November 1995 because of worsening of neuropathy. In March 1996, at the time of sural nerve biopsy, the patient was on Plaquenil 250 mg/day, Prednisone 10 mg/day, Isoniazid 300 mg/day, and Pyridoxine 50 mg/day. A circulating paraprotein was still present, in concentration unchanged from earlier determinations. There was no evidence of active SLE.

Serial paraffin sections (x30) of sural nerve disclosed a focal collection of mature lymphocytes in epineurium, no immunostaining for light chains, no amyloid deposits and no vasculopathy.

MATERIAL SUBMITTED: Plastic resin section of sural nerve stained with Toluidin blue and one kodachrome of two electron micrographs: a myelinated nerve fiber and a smooth muscle cell.

POINTS FOR DISCUSSION:

1) Diagnosis
2) Pathogenesis

CASE 1997-2

Submitted by: Drs. Yves Robitaille, Stéphane Ledoux and Neil Cashman,
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Case Reference no.: NP 96-348

Disease onset for this 19 y.o. right handed female, occurred during pregnancy as a brief episode of abnormal eye movements which, several months later, was followed by a resting tremor, first in the left hand, then in the right arm, both legs, head and tongue. Adequate dosage of L-Dopa brought no significant relief. Tremor was associated with marked fatigue, 40 pds weight loss and generalized joint pains. She also complained of episodic losses of vision in the left eye, which suggested a demyelinating disorder. The past medical history was characterized mostly by abnormal behavior, which led to the diagnoses of borderline personality disorder, anxiety, along with notions of alcohol and street drug abuse, although the latter could never be well documented. The family history could not be accurately expanded, but no specific notion of neurologic disease was recorded.

On examination, she was alert, oriented and there was no cognitive dysfunction. Insight and judgment were rated fair. Ocular movements showed slight limitation of upward gaze, and bilateral nystagmus on lateral gaze. Kayser-Fleisher rings were not seen. Peribuccal myoclonic movements and a tongue tremor were observed. A resting tremor was seen in all limbs, accompanied by a generalized increase of muscle tone and marked cogwheeling, but without significant loss of motor strength. She was described as "extremely" bradykinetic. DTR's were diffusely brisk, and the left plantar reflex was extensor. Besides a stooped posture, the gait was normal. Upper limb movements displayed decreased amplitude on walking. All lab data, which included an exhaustive work up to exclude a wide range of storage disorders, as well as CSF analyses, were within normal limits. MRI of the head was also normal, EMG studies revealed no pathology, but an EEG showed a generalized mild non specific slowing, suggestive of a sub-cortical dysfunction.

She was reassessed 18 months later. A thourough neuroendocrinologic work up was negative. She was diagnosed as an akinetic rigid disorder associated with behavioral abnormalities, consistent with a neurodegenerative disease of undetermined etiology. When last examined a few months prior to death, speech had become dysarthric, and spontaneous hand movements were consistent with myoclonic seizures, although, at times they appeared choreic, with occasionnal dystonic posturing. A few weeks before her final demise, she had become totally akinetic, diffusely hypotonic, hypotensive and mute. Unusual blood pressure fluctuations had been recorded throughout the course of the disease, however. She died suddenly during sleep at age 25. The immediate cause of death was ascribed to bilateral bronchopneumonia. A ubiquitinated section of frontal lobe was submitted.

Points for discussion: 1) Phenotypic diagnosis
2) Pathogenesis

CASE 1997 - 3

Submitted by: Maryam Mohammadkhani, Kathy L. Newell, and E. Tessa Hedley-Whyte. Neuropathology, Massachusetts General Hospital, Boston, Massachusetts 02114.

Case reference number: A96-X68

Clinical History:
An 86 year old hypertensive woman presented to the Massachusetts Eye and Ear Infirmary (MEEI) with weakness and visual complaints characterized by flashing lights and floaters of a few days duration. She was escorted to the MEEI by her son who noticed that her coordination that day was not as good as baseline and that she complained of "not feeling right". While awaiting evaluation in the clinic, she developed substernal chest pain and was rushed to the Massachusetts General Hospital (MGH) emergency room. The EKG revealed ST segment elevations in the inferior leads, and she was admitted with an inferior myocardial infarct. She received aspirin, sublingual nitroglycerin, oxygen, 5 mg intravenous metaprolol and intravenous heparin.
She was started on a lysis protocol with tissue plasminogen activator. Twenty minutes after the initiation of infusion, she developed abrupt onset of weakness in her right arm, cortical blindness and increasing back pain. An emergent head CT scan was negative for hemorrhage. The chest CT was notable for extensive mitral annulus calcification.
She was transferred to the cardiac care unit, where she continued to neurologically deteriorate and required intubation. She rapidly progressed to coma, hypotension and bradycardia, and died approximately eight hours after admission to the MGH.
Autopsy showed massive mitral annulus calcification, and severe aortic and coronary atherosclerosis.

Material submitted: 1 hematoxylin and eosin stained section

Points for discussion: Diagnosis

CASE 1997-4

Submitted by: Dr Jeanne E Bell, Neuropathology Laboratory, Department of Pathology, Western General Hospital, Crewe Road, Edinburgh EH4 2XU.

Case reference number: 1996/03

Clinical History: 29 year old woman with a 17 month history of a progressive dementing illness associated with ataxia and choreiform movements. She deteriorated despite supportive therapy and died in January 1996. Permission for autospy was restricted to the brain and internal organs.

Necropsy findings: Emaciated young woman with muscle wasting and fixed flexion deformities of the limbs. The brain (weight 1122 grammes) showed global atrophy. No focal abnormality was noted on section of the fixed brain.

Material submitted: H&E section of cerebrum.

Points for discussion:

1. Diagnosis.

2. Pathogenesis

CASE 1997-5

Submitted by:

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Ref. # S96-19752 (A-72-96)

Clinical Summary:

A 38 year old homosexual male with AIDS, who, in May 1996, presented with language problems and confusion for 1 month. At presentation he was afebrile and without systemic complaints. On examination the patient was alert, but yawning frequently. He was unable to follow complex directives. He was unable to name, repeat or write. He appeared to neglect the right visual field. Pupils were 4 mm and reactive. Ocular motility was full, but the right gaze was somewhat sluggish. Rest of cranial nerve examination was unremarkable. There was no significant weakness. The tone appeared to be increased in the lower extremities. Ankle jerks were absent and toes were down-going. Sensory examination was limited. His CD4 cell count was 180.

MRI of the head revealed multiple lesions involving bilateral subcortical white matter, some of which were enhancing. The most prominent lesion, however, was a wedge-shaped area of abnormal signal in the left parietal lobe, without enhancement or significant mass effect. Lumbar puncture revealed clear CSF, WBC 1, Protein 33, glucose 54. AFB smear and cryptococcal antigen were negative. CSF cultures were sterile.

Repeat MRI 4 weeks later revealed progression of the large white matter lesion with new enhancement and significant mass effect. At that time, the patient had gait and balance disturbances with progression of his language problems. The patient was admitted for brain biopsy, however, he was found unresponsive with dilated pupils next morning. Resuscitation attempts failed and he was pronounced dead.

Autopsy Findings:

The patient was cachectic and had a few truncal molluscum contagiosum. Further postmortem examination was limited to the brain. The brain was swollen and weighed 1400 grams. There was a left uncal herniation with necrosis. Coronal sections revealed general expansion of the left cerebral hemisphere with compression of the left lateral ventricle and midline shift. There were multiple, bilateral subcortical gray-brown lesions, with focal confluence. A cavitatary lesion in the left frontal lobe was also seen. Cross sections of the brain stem reveal multiple midbrain and pontine hemorrhages.

Materials: One H&E stained section of the left cerebral hemisphere.
One unstained slide.

Points for discussion: 1) What is the diagnosis?
2) Is the patient immunocompromised?

CASE 1997-6

Submitted by: Anthony T. Yachnis, M.D., University of Florida College of Medicine and Brain Institute, P.O. Box 100275, Gainesville, Florida, 32610-0275

Case reference number: A-25-95

Clinical History:

A cachectic 33-year old male with AIDS (CD4+ T cells =2) presented in mid May of 1995 because of sudden onset, transient right-sided hemiparesis and left temporal headache. His temperature was 100 °F, mental status was normal, and a neurologic examination was non-focal. The cerebrospinal fluid showed a protein of 100 mg/100 ml (nl 15-45), glucose of 43 mg/100ml (nl 45-80), and no cells; a negative India ink preparation; and negative AFB, fungal, and bacterial cultures. Magnetic resonance imaging (with and without contrast) showed many well-circumscribed 0.5-1.0 cm, peripherally and diffusely enhancing lesions of the cerebral cortex, deep nuclei, cerebellum and brainstem without significant edema or mass effect. The patient was treated empirically for toxoplasmosis, but therapy was discontinued because of intolerance.

He was readmitted at the end of May after new-onset complex tonic-clonic seizures. Neurologic revealed a sluggish left ocular light reaction and a left eyelid lag. The white blood cell count was 900/mm^3 with 74% neutrophils, 8% monocytes, and 2% lymphocytes; hematocrit was 24%; and platelets were 4200/mm^3. Other blood studies revealed normal electrolytes and liver function tests and negative RPR, ANA, cryptococcal antigen, AFB, bacterial, and fungal cultures. Computed tomography scans with contrast performed at the beginning of June were essentially unchanged from the may MRI studies, except for occasional punctate foci of calcification suggestive of neurocysticercosis. Serum toxoplasma and cysticercosis titers were 1:16 and <1:10, respectively. Seizures were controlled with phenytoin. The patient was discharged in stable condition and died at home about 4 weeks later; 2 months after his initial hospital presentation.

Necropsy was restricted to examination of the brain.

Material submitted: H&E-stained and unstained sections of the cortex and subcortical white matter.

Points for discussion:

1. Diagnosis
2. Pathogenesis

CASE 1997-7

Submitted by: Dr. Leila Chimelli
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Case reference number: HC327/94

Clinical History :

A 30-year-old Brazilian hemophiliac patient had received several transfusions of factor VIII cryoprecipitate. At the age of 28, he had positive serological tests for the HIV and was having AZT.

He presented with dizziness, generalized weakness, headache, fever (39° C), nausea and vomits, and had left hemiparesis.

A CT scan showed an extensive ill-defined right parietal hypodense lesion, with contrast enhancement, and edema of the adjacent tissue.

Treatment for toxoplasmosis was introduced, but he developed convulsions, did not respond to stimuli and died in coma 20 days after admission to hospital.

During this period, serological tests showed that he was infected with the *Trypanosoma cruzi* (the agent of Chagas' disease).

Necropsy findings:

There was an extensive ill defined necrotizing and hemorrhagic lesion in the right parieto-occipital lobes, involving both cortex and white matter. The other organs were macroscopically normal.

Material submitted: H&E section of the cerebrum

Points for discussion: 1. Diagnosis

2. Pathogenesis

CASE 1997-8

Submitted by: James M. Henry, M.D.
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Department of Neuropathology
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Case reference number: 2471833

Clinical History:

A 24 year old caucasian female was seen in the emergency room with a chief complaint of musculo-skeletal pain involving the left hemithorax. A root canal procedure had been performed two weeks prior and she was also in the sixth week of pregnancy. While in the emergency room she developed a focal seizure involving the left arm which rapidly progressed to generalized seizure activity with loss of conciousness, emesis, and respiratory failure requiring intubation. She subsequently spiked fevers to 107° and experienced a spontaneous abortion.

She did not recover conciousness. Multiple examinations of serum and CSF failed to reveal evidence of rickettsial, viral, syphilitic, or HIV involvement of the central nervous system. She was treated empirically with antibiotics and steroids, developed disseminated intravascular coagulation followed by multi-organ failure and expired ten days later of a fulminating illness of undetermined etiology.

Necropsy findings:
The dura mater was unremarkable with no evidence of thrombosis.

The brain weighed 1225 grams and had a dusky, congested appearance. The leptomeninges were free of infiltrate. The external surface of the cerebrum was unremarkable. Examination of the base of the brain revealed herniation of the right uncus and both cerebellar tonsils. The large vessels of the anterior and posterior circulation were unremarkable as were the cranial nerves and brainstem.

Coronal sections revealed congestion with mild herniation of the right uncus and of both cerebellar tonsils. No other significant changes were present.

Material submitted: H&E and unstained sections of hippocampus and cerebellum

Points for discussion: 1. Basic Diagnosis

2. Unusual Aspects of the History and Clinico-Pathologic Correlation

3. Preventive Medicine Implications for the Hospital and Community

CASE 1997-9

Submitted by: Dr.'s Brian Summers and Alexander de Lahunta, College of Veterinary Medicine, Cornell University, Ithaca, New York 14850 and Dr. John Speciale, Specialist Veterinary Practice, Rochester, New York, 14618.

Case reference number: E96-526

Clinical history: This 2-year-old female domestic short haired cat was seen in late July 1996 for an episode of sneezing. Approximately 10 days later she presented febrile (103.8, normal 101), was reported to be inactive and to "stare at uninteresting objects" and was found to have dilated pupils. Some improvement was afforded by dexamethasone but the cat was returned 10 days later; she was dull and also had become propulsive, persistently walking in circles to the left. Examination at this time also revealed anisocoria with the left pupil smaller than the right. Prolonged corticosteroid therapy over approximately 8 weeks resulted in improvement and was tapered. However, the cat subsequently deteriorated and met its demise after a total clinical course of 4.5 months.
Examination of the brain at necropsy showed the left pyriform lobe to be small, depressed and slightly yellow. There was a significant depression of the left cerebrum in the area of distribution of the left middle cerebral artery (frontal/temporal). On transverse section, this extended deeply into the left internal capsule and caudate nucleus.

Material submitted: (a) H&E stained transverse section of the brain at the level of the septal nuclei (most sections) or an adjacent block, and (b) one kodachrome taken at the ventral midline of the section.

Points for discussion: Diagnosis, etiology and pathogenesis.

CASE 1997-10

Submitted by: Hans H. Goebel, M.D. and J.K. Mellies, M.D.
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Case reference number: N 1662/96

Clinical History:

This 59-year-old housewife was referred for further investigation of cognitive decline. She reported progressive forgetfulness especially with problems naming. She had started to make frequent notes, complained about poor concentration and being easily overcharged. Since her mid-thirties she had unilateral, throbbing headache of alternating sides about once a week. In recent years this headache has become rare. During the migraine attacks, numbness spreads from the right hand all over her right hemibody, and she has an expressive type of aphasia. Headache and neurologic deficits usually subside within half an hour. She experienced one similar event at the age of 19 years, buth has been headache-free thereafter for almost 20 years. She reported urinary urge and incontinence for one year, which had not been alleviated by vesical neck surgery in January 1996. There were no history of stroke or TIA, no mood disorder and no vascular risk factors, beside obesity and hyperlipidaemia.

Neurological exam was normal. Results of further investigation were as follows: The blood pressure was normotensive during 24-h monitoring. Echocardiogram and CW-Doppler ultrasound of the neck vessels were normal. By Holter-monitoring sinus rhythm, but no arrhythmias were encounterd. Electrocardiomyography showed sinus rhythm and a left anterior hemiblock. Chest X-rays were normal. Electroencephalography showed 9 Hz alpha activity with intermittent generalized 3-6 Hz slowing and left parieto-occipital intermittent rhythmic delta activity. Laboratory results were normal except for cholesterol of 255 mg/dl, triglycerides of 280 mg/dl, alkaline phosphatase of 217 U/L and (-glutamic transaminase of 37 U/L, reflecting steatosis and obesity. Homocysteine was 15.2 nmol/ml, fibrinogen 667 mg/dl. Vitamin B12, folic acid, HDL- and LDL-cholesterol, thyroid hormones, lues serology, antinuclear-antibodies, c-Anca, p-Anca, anti-phospholipid-antibodies, rheumatic factors, and C-reactive protein were within normal limits. Erythrocyte sedimentation rates were 13/31 over the first two hours. Cerebrospinal-fluid examination was normal.

The patient's sister, a niece, one daughter, and one son have the same disease, another daughter is genetically affected, but without clinical symptoms, and a third daughter has migraine with aura, but is genetically unaffected.

Material submitted: 1 plastic-embedded section, Richardson stain
1 electron micrograph

Points for discussion: 1. Diagnosis
2. Nature of the lesion