CASE 1

Submitted by: John M. Hardman, Major, MC, USA, and Kenneth M. Earle, M.D., Armed Forces Institute of Pathology, Washington, D.C. 20305

Ref. No. AFIP Accession 1212387

This 27-year-old American Soldier was found dead in bed near Pleiku, Viet Nam. The only available history indicated that he seemed to be well before going to bed on 20 April 1966. He was found dead in bed the following morning. The examining physician noted that he was "yellow as a pumpkin."

Autopsy revealed marked yellowish discoloration of the skin and sclera. The right lung weiged 900 gm., left 850 gm. Both lungs were hyperemic. The heart weight 250 gm. with no abnormalities. The spleen weighed 850 gm. and was reddish-brown in color. The liver weighed 2100 gm. with a tan-brown color. The kidneys weighed 150 gm. each and were not remarkable. The brain weighed 1500 gm. and was slightly congested. Examination of the blood 33 hours postmortem revealed total serum bilirubin 8.5 mg%, direct acting bilirubin 3.5mg%. Wright and Romanowsky stained smears of cardiac blood demonstrated many chromatin-like dots and cytoplasmic rings compatible with plasmodium falciparum malaria.

Stain: Hematoxylin and eosin section of cerebral cortex.

Points for discussion:
1) Diagnosis
2) Reason for rapid demise.

CASE 2

Submitted by R. N. Baker and U. Tomiyasu, V.A. Center, Los Angeles, California.

Ref. No. A-401-64

Nineteen months prior to his death this 48-year old white man began to have clonic movements of his left leg. This gradually became worse accompanied by a "drawing up" of the left leg. He also began to have jerking movements of the left arm and drawing up of the left arm over his head. Ten months after onset of these symptoms he was hospitalized. A mild left hemiparesis was found, but initial skull and chest X-rays, EEG, brain scan, spinal fluid and right carotid angiogram were normal. At that time, he was found to be anemic with a hemoglobin of 7.4 gm. %, a hematocrit of 24% with 15% nucleated red blood cells and immature circulating leukocytes. There was enlargement of the spleen to three fingers' breadth. Bone marrow aspiration was unsuccessful on several attempts. The bone biopsy showed small fibrous fragments with scattered abnormal cells. The patient was treated with transfusions, Dilantin and depo-testosterone. Bilateral femoral neck radiolucent areas were found on X-ray. The hemiparesis became more severe and papilledema developed. Repeat brain scan and angiogram now showed a right fronto-parietal mass. Craniotomy was performed and a malignant, cystic, glial tumor was found. He subsequently was treated with 5100 rads of deep cobalt therapy. Four months after the craniotomy, a rib biopsy was performed because of a painful mass in the right anterior chest wall. Microscopically, this tissue was similar to that seen in the brain biopsy material. The patient developed pneumonia, became stuporous and died.

Autopsy revealed widespread bone marrow and lymph node involvement with tumor, in addition to a large mass in the right fronto-parietal region of the cerebral hemisphere.

Points of interest and for discussion: Glioma producing extracranial metastases before craniotomy? Frequency of this?

CASE 3

Submitted by Dr. Ursula T. Slager, Orange County Hospital, Orange, Calif.

Ref. No. 66-0485.

FAMILY HISTORY: The patient was born in 1955, the last of four children, to parents 34 and 33 respectively. There was a half-brother, born to the same mother in 1941, and three sisters born in 1946, 1948 and 1951 respectively. The parents were of Dutch and Danish-Irish extraction, without known Jewish contributions.

The sister born in 1948 developed normally until she was hospitalized for convulsions and mental retardation at age 3. Skull films, electroencephalograms, urinalysis, blood sugar, calcium, phosphorus and lumbar puncture were normal. Deterioration progressed, and she died at age 6 without autopsy.

The other two sisters, half-brother and parents are living and well. Blood samples were obtained from each on March 4, 1967 for chromosome studies.

CLINICAL HISTORY: The patient developed normally until he had a convulsion at the age of 3. At that time, pneumoencephalograms showed only enlarged ventricles. At age 4 he had an occipital craniotomy with division of the tentorium. No biopsy was taken.

At the age of 5 peripheral blood was cultured for chromosomes. Three abnormal marker chromosomes with secondary constrictions in their long arms were found. They were postulated due to a translocation derived from elements of groups 1-3 and 6-12. (See Lancet, Sept. 19, 1961 pp 627-30).

The child became progressively more lethargic, unable to sit or stand, opisthotonic, unresponsive and finally deaf and blind. Grand mal as well as petit mal seizures developed. Eventually coma ensued. He died at the age of 11 years with a diagnosis of progressive leukodystrophy.

PATHOLOGIC FINDINGS: At autopsy, only a non-specific colitis was seen.

The skull and dura revealed evidence of healed bilateral craniotomy. The brain weighed 600 grams. The gyri over both cerebral hemispheres were shrunken. In some areas throughout the cortex, the atrophy had progressed to laminar necrosis. The white matter appeared very firm and showed no gross focal lesions. The septum pellucidum was intact. The corpus callosum appeared attenuated. The ventricles were uniformly dilated. The basal ganglia and brain stem were somewhat small, but the substantia nigra was normally pigmented. The spinal cord was grossly normal. Both cerebellar hemispheres were shrunken, more so in the midline and on the caudal surface.

H & E sections of cortex and midbrain are submitted. Similar changes were present throughout the cortex, basal ganglia, brain stem and spinal cord. The material in the neurones stained with PAS was acid fast but not metachromatic or birefringent. Both frozen and paraffin sections stained red-orange with Sudan IV. The inclusions seen in the midbrain stained orange with Congo-red.

The cerebellum showed extensive necrosis of the granular layer of the cortex. Purkinje cells were scant, and those present contained similar storage material.

Diagnosis: Juvenile familial amaurotic idiocy.

Point of Interest: Chromosomal abnormality.

Points for discussion: 1. Significance of chromosomal changes in this case?
2. Any other cases with this association?

CASE 4

Submitted by Dr. Jans Muller, Indiana University Medical Center, Indiana.

Ref. No. NP66-66

This white female, first-born infant, was delivered two months prematurely (wt 1900 gm.) Family history negative. The first year of life was uneventful, although in retrospect the veins of the left forehead always were rather prominent. Fever and the first of several 30-minute episodes of deep lethargy led to hospitalization at 13 months of age. OFC then was 48 cm, and there were somewhat large, non-pulsating veins in the optic fundi; otherwise the child was normal. At 17 months the left eye had become prominent; OFC was unchanged, and psychomotor retardation was now obvious. Irregular calcifications of the frontal lobes of a peculiar, punctate, and serpiginous type were first seen at 19 months. The left superior orbital fissure was widened. Air study revealed normal ventricles; angiography was not helpful. Cerebrospinal fluid protein: 73 mgm, slight increase in globulin. Chemical studies, including Ca and P, revealed no changes. The further course was one of steady retrogression with increase in calcifications. A serum test for toxoplasmosis was negative. The child died early in 1966, 3 years old.

Autopsy findings: The left eye was protuberant and enlarged veins, normal in distribution, were noted in the left orbit. The brain was small (700 gm) but normal in shape. There were large and abnormal veins over the surface and two frank small hemangiomas in the right uncus and in the cerebellum. The basal ganglia contained many enlarged veins. There were cavities of the white matter, mostly in the frontal lobes with white slivers of calcium. Small specks of calcific material were also visible, especially under slight magnification, at or slightly below the corticomedullary junction -- a finding confirmed in low KV x-rays of the specimen. The remainder of the autopsy was non-contributory.

Diagnostically, we consider the possibility of a widespread, transcortical arteriovenous shunting with calcifications in and around the abnormal vessels.

Dr Muller's diagnosis

2 sections are submitted, one stained with H & E, the other with a modified reticulin method.

CASE 5

Submitted by Raymond A. Clasen, Presbyterian-St. Luke Hospital, Chicago, Illinois

Ref. No. 66-A240

The patient, a 7 year old white female, was admitted to Evanston Hospital on 10-10-66 in a comatose state. On 9-27-66, she developed what was diagnosed as an upper respiratory infection. Two days prior to admission she began vomiting dark brown material and on the day of admission her rectal temperature rose to 107°. Positive physical findings at the time of admission included a bilaterally positive Babinski sign, hyperactive knee jerks, absent abdominal reflexes, and extensor spasticity of the legs. The pharynx showed hemorrhagic areas with petechial-like lesions. A spinal tap was traumatic. The child was given antibiotics, Cortisone, and treated symptomatically but she remained in a comatose state. She developed what appeared to be renal failure and peritoneal dialysis was begun on 10-13-66. On 10-15, she went into shock and on 10-16 upper gastrointestinal bleeding was noted. This persisted until her death on 10-18-66 following a period of respiratory distress.

At autopsy the brain was not swollen. No focal lesions were found in the cerebral hemispheres or brain stem. The cerebellum showed bilateral hemorrhagic areas in the mid-potion of the hemispheres involving both grey and white matter. A virus was isolated from the stool and spinal fluid during life and from the brain at autopsy. This has been identified as Coxsackie B4.

Points for discussion:

1. Changes related to viral infection or to generalized anoxia?
2. If viral-related, due to primary encephalitis or to secondary "immune" reaction?

CASE 6

Submitted by Dr. Ellsworth C. Alvord, Jr., University of Washington, Seattle, Washington

Ref. No. NP-1113

This patient, a 76-year-old white female, was initially seen by her private physician February 23, 1965 for a painful eruption of the right upper face of approximately four days duration. Examination revealed it to be herpes zoster involving the supraorbital branch of the trigeminal nerve. She was placed on ACTH and protamine; however, her symptoms progressed with increasing pain and spread of the eruption to involve the middle portion of the right face and the right eye.

She was hospitalized for a short time and then followed as an out-patient, but, because of continued episodes of pain and the fact that she lived alone, she was readmitted. Examination was as before, revealing a crusting lesion over the right forehead (sharply demarcated at the midline) down to the level of the nose. The right periorbital region was swollen and the right eye closed.

She rested comfortably until the morning of March 24 when she developed sudden respiratory distress and cyanosis. She became hypotensive and expired later that day, about 5 weeks after onset of herpes zoster ophthalmicus.

At autopsy massive pulmonary thrombo-embolism was discovered as the immediate cause of death.

Microscopically the lesion involving the Gasserian ganglion and adjacent nerve was quite characteristic of herpes zoster. Of interest was the continuation of the inflammatory response to involve the trigeminal nerve as it entered the pons and to involve the spinal nucleus of the 5th nerve throughout the medulla and upper cervical cord. The lesion is necrotizing with microglial proliferation, focal demyelination, loss of neurons, as well as perivascular cuffing. A mild leptomeningitis was present throughout the brainstem and slight perivascular cuffing was also seen in the hippocampus and hypothalamus.

The stain is Luxol fast blue, periodic acid Schiff, and hematoxylin. Points for consideration are the frequency with which central lesions occur in herpes zoster and whether they may contribute to the pain.

CASE 7

Submitted by Dr. J. H. Sung, University of Minnesota, Minneapolis.

Ref. No. OC-64-12

History: This 3-year-old child developed clinical symptoms and signs of a mass in the posterior fossa two months prior to death. Ventriculographic examinations revealed changes consistent with a space-occpying lesion extending into the 4th ventricle. An occipital craniotomy disclosed a large tumor in the midline of the cerebellum extending to the 4th ventricle. It was not possible to remove the tumor entirely and a biopsy was done. The patient died about 1-1/2 months after the operation.

Gross Findings on the Brain: There was a massive tumor in the midline of the cerebellum which had protruded into and distended the 4th ventricle. The tumor was grayish-white, firm and had many scattered dark gray or black patches or spots. The tumor had also invaded diffusely the cerebellar leptomeninges, often distending the interfolial sulci. The cerebellar cortex in many areas was invaded and destroyed by the neoplasm, but the folial white matter appeared relatively preserved. The tumor also massively filled the basal cistern and cisterna ambiens. The leptomeninges over the cerebrum and brain stem, practically everywhere, except for those over the anterior portions of the frontal lobes, were diffusely infiltrated by the neoplastic tissue. The tumor frequently extended into the sulci distending them. Other findings of note were changes related to obstruction of the 4th ventricle and increased intracranial pressure.

General Organs: Not remarkable.

Histological Diagnosis: "Pigmented medulloblastoma" or

"Melanotic progonoma"

Points of Discussion:

1. Relationship between this tumor and "melanotic progonoma" in other parts of the body.
2. Nosology of this tumor.

Submitted by F. H. Gilles, M.D. and E. T. Hedley-Whyte, Children's Hospital Medical Center, Boston, Mass.

Ref. No. A65-3I.

This patient was the product of an unremarkable full term pregnancy in a gravida 3 mother. She appeared entirely normal at birth. Early developmental milestones were within normal limits. She sat alone at 8 months. From then on she progressed somewhat more slowly, crawling at 14 months, and walking with support at 18 months. She never walked alone, and she developed no speech. After age 18 months there was gradual regression in motor performance. By age 28 months she no longer stood or crawled, and she could sit only with support. She had lost the ability to feed hereself. There had been no seizures.

Physical examination at age 28 months showed a well-nourished, fair-skinned child, who was in the 25th percentile for height and weight. Head circumference was 45.8 cm. Visual fixation and following were present, and the pupils reacted briskly to light. A right convergent strabismus was noted. A constant, fine pendular nystagmus was present at rest, and was replaced by a jerk nystagmus on lateral gaze. Fundoscopic examination showed a small cataract on the right, and questionable optic atrophy bilaterally. The child reached for objects presented to her, but grasping movements were clumsy. She appeared generally hypotonic. Little spontaneous movement was seen in the feet. Tendon reflexes were normally active in the upper extremities, brisk at knees, and diminished at ankles. Plantar responses were extensor. There was little response to pin prick over the extremities or trunk, but a normal response was noted over the face.

Re-examination at age 31 months showed absence of ankle jerks, but no other obvious change. The child was subsequently admitted to a school for the retarded.

At age 5-1/2 years the child showed further evidence of worsening in neurologic state. She now was emaciated, weighing only 12 kg., height being 107.5 cm. The head circumference still was only 45.8 cm. Liver and spleen were not palpable. There was a blink response to light, but no visual following, and the pupils responded only sluggishly to light. No movements of the eyes could be elicited on doll's head maneuver. Fundoscopic examination showed pallor of optic discs bilaterally. Corneal reflexes were sluggish. Facial movements were weak bilaterally, and eye closure was incomplete during sleep. The child turned toward loud noise. When undisturbed, she was lying quiently, with elbows and wrists flexed, and legs extended. There were no voluntary movements of the legs. Tendon reflexes were hyperactive in the upper extremities, but knee and ankle jerks were absent. Plantar responses were extensor.

The subsequent course was one of gradual deterioration. She became unable to swallow and required tube feedings. Death occurred at age 9 years.

At autopsy, the visceral pathology was not contributory. Widespread griseal involvement was present.

Diagnosis: Cortical deposits in infantile neuroaxonal dystrophy.

Main Point for Discussion: Locus of the extraneuronal small bodies.

1 H and E slide submitted.

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CASE 9

Submitted by Dr. George Margolis, Dartmouth College, Hanover, N. H.

Ref. No.

This dog comes from a closely inbred strain of West Highland Terriers in which a genetically dominated neurological disease has appeared in approximately one out of four offspring of a brother-sister or a mother-son mating. The affected pups appear normal at birth, but very quickly show a progressive disability manifested by weakness and finally paralysis of the rear extremities and a coarse tremor affecting the head as well as the trunk and limbs. Throughout this relentless progressing deterioration, the animal appears alert and responsive. It has been necessary to sacrifice these animals at 4 to 5 months of life because of decubitus ulcers and inanition.

Diagnosis: Globoid-body leukodystrophy.

Stain: Luxol fast blue-periodic acid Schiff-hematoxylin.