

**40th ANNUAL DIAGNOSTIC SLIDE SESSION  
1999  
REFERENCES AND DIAGNOSES**

**Moderated by E. Tessa Hedley-Whyte, M.D.  
Edited by Leroy R. Sharer, M.D.**

**Case 1999-1**

**Submitted by:** Aryn Rojiani, M.D., Ph.D., Jason Francey, M.D., and Edward Haller, University of South Florida College of Medicine, Tampa, and University of Florida College of Medicine, Gainesville, FL

**Diagnosis:** Melanosis of the dentate nucleus

**Comment:** The material in the dentate in this case was Fontana positive, and it bleached with potassium permanganate. The material is not autofluorescent, unlike lipofuscin, and the particles have been found to be composed largely of sulfur.

**References:**

1. Singer PA, Cate J, Ross DG, Netsky M. Melanosis of the dentate nucleus. *Neurology* 1974; 24:156-161.
2. Best PV, Bojsen-Moller M, Janota I, Kristensen IB. Melanosis of the dentate nucleus: a widespread disorder of protoplasmic astrocytes. *Acta Neuropathol* 1981; 55:29-33.
3. Bianchi C, Grandi G, Berti N, Di Bonito L. Melanosis Cerebelli. *Acta Neuropathol* 1981; Suppl 7:400-402.
4. Fan KJ, Kovi J, Duhaney SD. Melanosis of the dentate nucleus: fine structure and histochemistry. *Acta Neuropathol* 1978; 41:249-251.

**Case 1999-2**

**Submitted by:** Juan Bilbao, M.D., and Dr. Gary Moddel, University of Toronto, Toronto, Ontario, CANADA

**Diagnosis:** Autophagic-vacuolar myopathy induced by omeprazole.

**Comment:** On EM there were myelin bodies and extruded lysosomes, as well as glycogen granules which however were not incorporated into the lysosomes. No curvilinear bodies were found. Congo red stain exhibited threads in the affected fibers. Some people thought that the picture was that of inclusion body myositis, but it was pointed out that in Japan, Congo red positive material has been described in muscle fibers

in chloroquine myopathy, which this case resembles. The patient's symptoms subsided following cessation of omeprazole treatment, and they recurred after rechallenge, with elevation of serum CK.

**References:**

1. Mastaglia FL. Toxic myopathies. In: Rowland LP, DiMauro S, eds. Handbook of Clinical Neurology, vol 18(62): Myopathies. Elsevier, 1992, pp 595-622.
2. Garotte FJ, Lacambra C, Del Ser T, Garcia Diaz B, Obeso G, Solis J. Subacute myopathy during omeprazole therapy. Lancet 1992; 340: 672.

**Case 1999-3**

**Submitted by:** Martha Simmons, M.D., Ph.D., and Richard L. Davis, M.D., University of California San Francisco, San Francisco, CA

**Diagnosis:** Central Neurocytoma.

**Comment:** The tumor cells were positive for synaptophysin, and there was also focal positivity for GFAP, on immunocytochemistry. Neurofilament protein was negative.

**References:**

1. Hassoun J, Gambarelli D, Grisoli F, Pellet W, Salamon G, Pellisier JF, Toga M. Central Neurocytoma. An electron microscopic study of two cases. Acta Neuropathol 1982; 56:151-156.
2. Hassoun J, Soylemezoglu F, Gambarelli D, Figarella Branger D, von Ammon K, Kleihues P. Central neurocytoma: a synopsis of clinical and histological features. Brain Pathol 1993; 3:297-306.

**Case 1999-4**

**Submitted by:** Eun-Sook Cho, M.D., and Meera Hameed, M.D., New Jersey Medical School, Newark, NJ

**Diagnosis:** Endolymphatic sac tumor (low grade adenocarcinoma of probable endolymphatic sac origin)

**Comment:** At surgery, the tumor was extradural. On immunocytochemistry it was positive for cytokeratin, EMA and vimentin, and it was focally positive for GFAP. It was negative for S-100. Patients with this tumor should be investigated for expression of the Von Hippel-Lindau (VHL) gene.

**References:**

1. Gaffey MJ, Mills SE, Fechner RE, Intemann SR, Wick M. Aggressive papillary middle ear tumor: A clinicopathologic entity distinct from middle ear adenoma. *Am J Surg Pathol* 1988; 12:790-797.
2. Heffner DK. Low grade adenocarcinoma of probable endolymphatic sac origin: A clinicopathologic study of 20 cases. *Cancer* 1989; 64:2292-2302.
3. Meyer JR, Gebarski SS, Blaivas M. Cerebellopontine angle invasive papillary cystadenoma of endolymphatic sac origin with temporal bone involvement. *AJNR* 1993; 14:1319-1321.
4. Reinneveld J, Hanlo P, Groenewoud, Gjansen G, Overbeeke KV, Tulleken C. Endolymphatic sac tumor: A case report and review of literature. *Surg Neurol* 1997; 48:368-373.

#### Case 1999-5

**Submitted by:** Chris Ingram, Diane Armao, Scott Kilpatrick and Kinuko Suzuki, University of North Carolina, Chapel Hill, NC

**Diagnosis:** Malignant neoplasm, favor sarcomatoid carcinoma

**Comment:** The members of the audience suggested several differential diagnoses for this case, including a fibrohistiocytic lesion (such as malignant fibrohistiocytoma, or MFH), an inflammatory or reactive condition, or a desmoplastic mesothelioma. On immunocytochemistry, the tumor was positive for EMA and, unlike MFH, was strongly positive for cytokeratin. Electron microscopy did not reveal long microvilli, which are characteristic of mesothelioma, but nevertheless at least one outside consultant electron microscopist thought that it was a desmoplastic tumor of this type. The primary has not been discovered. The patient has been treated with chemotherapy and radiation, but he is not doing well and is currently wheel-chair bound.

**References:**

1. Guarino M, Tricomi P, Giordano F, Cristofori E: Sarcomatoid carcinomas: pathological and histopathologic considerations. *Pathology* 1996; 28:298-305.
2. Wick MR, Ritter JH, Humphrey PA: Sarcomatoid carcinoma of the lung: a clinicopathologic review. *Am J Clin Pathol* 1997; 108:40-53.
3. Ro JY, Chen JL, Lee JS, Sahin AA, Ordonez NG, Ayala AG. Sarcomatoid carcinoma of the lung. Immunohistochemical and ultrastructural studies of 14 cases. *Cancer* 1992; 15:376-386.
4. Balercia G, Bhan AK, Dickersin GR. Sarcomatoid carcinoma: an ultrastructural study with light microscopic and immunohistochemical correlation of 10 cases from various

anatomic sites. *Ultrastruct Pathol* 1995; 19:249-263.

5. Mentzel T, Dry S, Katenkamp D, Fletcher CDM: Low grade myofibroblastic sarcoma: Analysis of 18 cases in the spectrum of myofibroblastic tumors. *Am J Surg Pathol* 1998; 22:1228-1238.

#### **Case 1999-6**

**Submitted by:** Hans Klunemann, M.D., and William Pendlebury, M.D., University of Vermont, Burlington, VT; and John Woulfe, M.D., and David G. Munoz, M.D., University of Western Ontario, London, Ontario, CANADA

**Diagnosis: Niemann-Pick disease type C**

**Comment:** The material was PAS positive, and the neurofibrillary tangles were positive for ubiquitin and tau. Histiocytes were also present in the bone marrow. This disease is due to a deficiency of cholesterol transport; the gene for the disorder, which is located on Chromosome 18, has recently been cloned. Records from the patient's family are available back to Normandy and the year 1488, with involvement of many individuals.

#### **References:**

1. Love S, Bridges LR, Case P. Neurofibrillary tangles in Niemann-Pick disease type C. *Brain* 1995; 118:119-129.
2. Suzuki K, Parker CC, Pentchev PG, et al. Neurofibrillary tangles in Niemann-Pick disease type C. *Acta Neuropathol* 1995; 89:227-238.
3. Horoupian DS, Yang SS. Paired helical filaments in neurovisceral lipidosis (juvenile dystonic lipidosis). *Ann Neurol* 1978; 4:404-411.

#### **Case 1999-7**

**Submitted by:** Shigeo Murayama, M.D., Tokyo Metropolitan Institute of Gerontology, Tokyo, JAPAN

**Diagnosis: Gaucher's disease, neonatal lethal form**

**Comment:** The electron micrograph demonstrates angulate lysosomes with linear structures. The brain was very small, and neither stainable myelin nor axons were demonstrable in the frontal lobes. The tangles in neurons were ubiquitin positive. Many Gaucher cells were present in the brain.

#### **References:**

1. Suzuki K, Proia RL, Suzuki K: Mouse models of human lysosomal diseases. *Brain*

Pathol 1998; 8:195-215.

2. Sidransky E, Sherer DM, Ginns EI: Gaucher disease in the neonate: a distinct Gaucher phenotype is analogous to a mouse model created by targeted disruption of the glucocerebrosidase gene. *Pediatr Res* 1992; 32:494-498.

[1999-8: case not submitted]

#### Case 1999-9

**Submitted by:** J. Barron and D. Munoz, London Health Sciences Centre, London, Ontario, CANADA

**Diagnosis:** Diffuse hereditary leukoencephalopathy with axonal spheroids

**Comment:** The changes were confined to the white matter, with no involvement of the gray matter. The pathology appeared to have three stages, with axonal swellings first, progressing to loss of axons and vacuolation of white matter, with complete loss of axons, myelin and oligodendrocytes as the end stage. The white matter changes were restricted to the dorsal cerebral hemispheres and the corpus callosum. Similar conditions mentioned by members of the audience included solvent abuse leukoencephalopathy and Nasu-Hakola disease, in which there are also bone lesions.

#### **References:**

1. Axelsson et al. Hereditary diffuse leukoencephalopathy with spheroids. *Acta Psych Scand (Suppl)* 1984; 314:1-65.

#### Case 1999-10

**Submitted by:** Saroja Ilangovan, M.D., Rajeswari Chandran, M.D., Reuben Cuison, M.D., Elena Kloes, M.D., and Marc G. Reyes, M.D., Cook County Hospital, Chicago, IL

**Comment:** Tests for herpes I & II, PCR for were all negative, as well as cultures for bacteria, fungi and TB.

**Diagnosis:** Neurosarcoidosis, meningoencephalitic type

**Comment:** All ante- and postmortem cultures, isolations and PCR studies were negative, including for bacteria, fungi, HSV-1, HSV-2, CMV, herpes zoster, syphilis, Lyme disease, toxoplasmosis, HIV-1, M. tuberculosis, and the prion protein. There were no skin or bone lesions, although granulomas were found in the uterus. Audience members suggested several alternative diagnoses, including granulomatous meningoencephalitis, visceral larva migrans (in which the parasites are notoriously difficult to find), HHV-6 infection, and HIV-2 involvement of the brain. Regarding the last, the patient was from Mexico, which has not

been an endemic region for HIV-2.

**References:**

1. Ericson TC, Odom G, Stern K. Boeck's disease (sarcoid) of the central nervous system. *Arch Neurol Psych* 1942; 48:613-620.
2. Colover J. Sarcoidosis with involvement of the nervous system. *Brain* 1948; 71:451-453.
3. Silberg D. Sarcoidosis of the nervous system. *Neurology and General Medicine*. Aminoff M., ed. Churchill Livingstone, 1995, pp 847-858.

**Case 1999-11**

**Submitted by:** Rebecca D. Folkerth, M.D., Boston VA medical Center, Boston, MA

**Diagnosis:** Herpes simplex rhombencephalitis in acquired immunodeficiency syndrome

**Comment:** Some observers thought that they recognized intranuclear inclusions, while others reported that they could not find any. PCR on CSF obtained during life revealed HSV-1. In addition, immunocytochemistry was positive for HSV in the pontine sections. Demyelination has been reported in the brainstem in this acute disorder, similar to that seen with VZV. The patient also had HIV leukoencephalopathy in the cerebral hemispheres.

**References:**

1. Nakajima H, Furutama D, Kimura F, Shinoda K, Nakagawa T, Shimizu A, Ohsawa N. Herpes simplex virus type 2 infections presenting as brainstem encephalitis and recurrent myelitis. *Int Med* 1995; 34:839-842.
2. Hamilton RL, Achim C, Grafe MR, Fremont JC, Miners D, Wiley CA. Herpes simplex virus brainstem encephalitis in an AIDS patient. *Clin Neuropathol* 1995; 14:45-50.
3. Ayuso-Blanco T, Gimenez-Mas JA, Omenaca-Teres M, Campello-Morer I, Marta-Moreno ME, Martinez-Lanao D. [Brain stem encephalitis due to Herpes simplex]. *Neurologia* 1994; 9:112-114.