

42nd ANNUAL DIAGNOSTIC SLIDE SESSION, 2001
REFERENCES AND DIAGNOSES

MODERATOR: E. Tessa Hedley-Whyte, M.D.

EDITOR: Leroy R. Sharer, M.D.

Case 2001-1

Submitted by: Bernardino Ghetti, M.D., Indiana University School of Medicine, Indianapolis, IN

Diagnosis: Neuroserpin body disease (progressive myoclonus epilepsy associated with the S52R mutation in the *Neuroserpin* gene)

Comment: Neuroserpin is a serine protease inhibitor. Mutated neuroserpin accumulates in neurons in this disorder. The inclusions are separated by a space, representing dilated endoplasmic reticulum, in which the inclusions reside. Another family has been described in Syracuse, NY, with a different mutation in the neuroserpin gene.

References:

Davis RL, Holohan PD, Shrimpton AE, et al. Familial encephalopathy with neuroserpin inclusion bodies. *Am J Pathol* 1999; 155:1901-13.

Davis RL, Shrimpton AE, Holohan PD, et al. Familial dementia caused by polymerization of mutant neuroserpin. *Nature* 1999; 401(6751):376-9.

Takao M, Benson MD, Murrell JR, et al. Neuroserpin mutation S52R causes neuroserpin accumulation in neurons and is associated with progressive myoclonus epilepsy. *J Neuropathol Exp Neurol* 2000; 59:1070-86.

Yazaki M, Liepnieks JJ, Murrell JR, et al. Biochemical characterization of a neuroserpin variant associated with hereditary dementia. *Am J Pathol* 2001; 158:227-33.

Case 2001-2

Submitted by: Dr. B. Lach, S. Bohlega, and E. Cupler, King Faisal Specialist Hospital and Research Centre, Riyadh, SAUDI ARABIA

Diagnosis: Hyaline body myopathy

Comment: Every type 1 fiber in the biopsy was involved by hyaline bodies, as demonstrated on myofibrillar ATPase at low pH. On electron microscopy, the bodies

were not membrane bound, and they were faintly fibrillar and granular, with occasional thicker filaments. On immunocytochemistry, they were positive for myosin but negative for slow heavy chain myosin. Biopsy of the patient's mother revealed bodies that were desmin positive and also positive for slow myosin.

References:

Barohn RJ, Brumback RA, Mendell JR. Hyaline body myopathy. *Neuromuscul Disord* 1994; 4: 257-262.

Isozumi K, DeLong R, Kaplan J, et al. Linkage of scapulo-peroneal spinal muscular atrophy to chromosome 12q24.1-q24.31. *Hum Mol Genet* 1996; 5:1377-1382.

Masuzugawa S, Kuzunhara S, Narita Y, Taniguchi A, Ibi T. Autosomal dominant hyaline body myopathy presenting as scapulo-peroneal syndrome: clinical features and muscle pathology. *Neurology* 1997; 48: 253-257.

Wilhelmsen KC, Blake SM, Lynch T, et al. Chromosome 12-linked autosomal dominant scapulo-peroneal muscular dystrophy. *Ann Neurol* 1996; 39: 507-520.

Case 2001-3

Submitted by: Dr. Juan M. Bilbao, Dr. Felix Tyndell, Sandra Cohen, Dr. John Acker, and Dr. Lev Goldfarb, Department of Pathology, University of Toronto, and St. Michael's Hospital, Toronto, CANADA, and National Institutes of Health, Bethesda, MD

Diagnosis: Cytoplasmic body myopathy, ?Desminopathy

Comment: On myofibrillar ATPase, both type 1 and type 2 fibers were affected. The rimmed vacuoles were negative on Congo red, but they were positive for calcium. The bodies exhibited some staining for desmin, on immunocytochemistry. Electron microscopy demonstrated rod-like structures and myofibrillar disarray, as well as cytoplasmic bodies. Blood from this patient was sent to Dr. Lev Goldfarb's laboratory at the National Institutes of Health. There were no mutations in the coding regions of the desmin and alpha-B-crystallin genes, but there is an abnormality in intron four of the desmin gene that cannot be further characterized. A cell culture to evaluate the pathogenic effects of this defect was attempted but was unsuccessful.
Follow-up: The patient has remained respirator dependent, in a chronic care facility. There has been a slight variation in the serum CK levels.

References:

Dalakas MC, Park K-Y, Semino-Mora C, Lee HS, Sivakumar K, Goldfarb L. Desmin myopathy, a skeletal myopathy with cardiomyopathy caused by mutations in the desmin gene. *New Engl J Med* 2000; 342:770-80.

Edstrom L, Thronell LE, Albo J, Landin S, Samuelsson M. Myopathy with respiratory failure and typical myofibrillar lesions. *J Neurol Sci* 1990; 96:211-228.

Case 2001-4

Submitted by: Anat Stemmer-Rachamimov, M.D., and E. Tessa Hedley-Whyte, M.D., Massachusetts General Hospital, Boston, MA

Diagnosis: Acute hemorrhagic leukoencephalitis

Comment: Special stains for infectious agents were negative, including Gomori methenamine silver for fungi, PAS stain, Gram stain, and Steiner stain. Immunocytochemistry was negative for varicella-zoster virus (VZV), herpes simplex virus, and *Toxoplasma gondii*. Immunofluorescence studies performed at the CDC were negative for rabies virus and *Acanthamoeba*. The pathology consists of perivascular demyelination, as well as hemorrhage and necrosis of vessels.

References:

Adams RD, Cammermeyer J, Denny-Brown D. Acute necrotizing hemorrhagic encephalopathy. *J Neuropathol Exp Neurol* 1949; 8:1-29.

Case Records of the Massachusetts General Hospital. *New Engl J Med* 1999; 340:127-135.

Hurst W. Acute Hemorrhagic Leukoencephalitis: a previously undefined entity. *Med J Australia* 1941; 2:1-6.

Posey K, Alpert JN, Langford LA, Yeakley JW. Acute hemorrhagic leukoencephalitis: A cause of acute brainstem dysfunction. *Southern Med J* 1994; 87:851-854.

Case 2001-5

Submitted by: Mônica da Silva Nunes, M.D., Massachusetts General Hospital, Boston, MA, and Luciano S. Queirós, M.D., Ph.D., Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Campinas, SP, BRAZIL

Diagnosis: Histoplasmosis of the central nervous system, involving mainly the spinal cord

Comment: The lungs at postmortem exhibited parenchymal nodules containing yeast forms, and there was also involvement of lymph nodes and the adrenals. The brain exhibited chronic ependymitis with hydrocephalus. The main involvement by histoplasmosis was in the spinal cord.

References:

Cooper, RA, Goldstein E. Histoplasmosis of the central nervous system: report of two cases and review of literature. Am J Med 1963; 35:45-57.

Goodwin, RA, Shapiro JL, Thurman GH, Thurman SS, Des Prez M. Disseminated histoplasmosis: clinical and pathologic correlations. Medicine 1980; 59:1-52.

Livas IC, Nechay PS, Nauseef WM. Clinical evidence of spinal and cerebral histoplasmosis twenty years after renal transplantation. Clin Infect Dis 1995; 20:692-695.

Vos MJ, Debets-Ossenkopp YJ, Claessen FAP, Hazenberg GJ, Heimans JJ. Cerebellar and medullary histoplasmosis. Neurology 2000; 54:1441.

Case 2001-6

Submitted by: Philip J. Boyer, M.D., Ph.D., Justin Cates, M.D., Ph.D., Julia A. Castle, M.D., Peter A. Merkel, M.D., and E. Tessa Hedley-Whyte, M.D. Penn State University, Hershey, PA, and Massachusetts General Hospital, Boston, MA

Diagnosis: Rheumatoid meningitis

Comment: The patient had severe rheumatoid arthritis with rheumatoid skin lesions, and she had been treated with methotrexate, cyclophosphamide, and gold.

References:

Karam NE, et al. Rheumatoid nodulosis of the meninges. J Rheumatol 1994 21:1960-1963.

Neamtu L, Belmont M, Miller DC, Leroux P, Weinberg H, Zagzag D. Rheumatoid disease of the CNS with meningeal vasculitis presenting with a seizure. Neurology 2001; 56:814-5.

Spurlock RG, Richman AV. Rheumatoid meningitis: a case report and review of the literature. Arch Pathol Lab Med 1983; 107:129-131.

Case 2001-7

Submitted by: Edward S. Johnson, M.D., Alfons L. Kroll, M.D., and Richard J. Fox, M.D., University of Alberta, Edmonton, Alberta, CANADA

Diagnosis: Spinal tumor, showing xanthomatous histiocytic infiltrate with desmoplasia, consistent with xanthoma disseminatum

Comment: The osteosarcoma that was resected at age 12 was considered cured, with no evidence of recurrence. MRI demonstrated lesions in the pineal, the pons, and the optic chiasm, among other regions. The skin biopsy disclosed a dermal infiltrate of multinucleated giant cells and polygonal cells, with a xanthomatous reaction and chronic inflammation, with a few eosinophils. The cells in the skin were CD68 positive, S-100 negative, and CD1a negative, and no Birbeck granules were detected on electron microscopy. Similar cells were seen in the dural mass, although they were S-100 positive.

References:

Ferrando J, et al. Systemic xanthohistiocytoma: a variant of xanthoma disseminatum? Br J Dermatol 1998; 138:155-160.

Hammond RR, MacKenzie IRA. Xanthoma disseminatum with massive intracranial involvement. Clin Neuropathol 1995; 14:314-321.

Knobler RM, et al. Xanthoma disseminatum with progressive involvement of the central nervous and hepatobiliary systems. J Am Acad Dermatol 1990; 23:341-346.

Case 2001-8

Submitted by: Caterina Giannini, M.D., and Bernd W. Scheithauer, M.D., Mayo Clinic, Rochester, MN

Diagnosis: Optic nerve choristoma

Comment: The specimen is from the intracranial portion of the optic nerve, and it contains adipose tissue, which is not normally present in this region. There are also myoid (smooth muscle) elements in this lesion that were positive for actin, on immunocytochemistry. In addition, there is severe atrophy of the optic nerve itself, with almost no axons remaining. There have only been six cases, including this one, of optic nerve lipoma and choristoma.

References:

Daxer A, Sailer U, Ettl A, Bleckenwegner G, Felber S. Choristoma of the optic nerve: neuroimaging characteristics and association with spinal cord lipoma. Ophthalmologica 1998; 212:180-3.

Zimmerman LE, Arkfeld DL, Schenken JB, Arkfeld DE, Maris PJ. A rare choristoma of the optic nerve and chiasm. Arch Ophthalmol 1983; 10:766-70.

Case 2001-9

Submitted by: Sandra L. Cottingham, M.D., Ph.D., Spectrum Health-Butterworth/Blodgett, Grand Rapids, MI

Diagnosis: Primary (granulomatous) angiitis of the central nervous system

Comment: There was transmural granulomatous inflammation of the central nervous system vessels in this case, including involvement of the media and the elastica. Workup included special stains for fungi, acid fast bacilli and spirochetes, all of which were negative. There was also no obvious involvement by VZV.

Reference:

Lie JT. Primary (granulomatous) angiitis of the central nervous system: a clinicopathologic analysis of 15 new cases and review of the literature. *Hum Pathol* 1992; 23:164-171.

Case 2001-10

Submitted by: Jane H. Uyehara-Lock, M.D. and Martha Simmons, M.D., Ph.D., University of California, San Francisco, CA

Diagnosis: Glioblastoma multiforme of the spinal cord (T10-T12) and nerve roots

Comment: The tumor cells were positive for glial fibrillary acidic protein (GFAP), by immunocytochemistry. This was a cordectomy specimen, and the rostral and distal resection margins were both positive for tumor. It was noted that patients with this type of involvement by glioblastoma tend to do very poorly, despite heroic surgical resection, since the tumor tends to spread through the subarachnoid space and the leptomeninges. Indeed, this patient succumbed four months after surgery.

References:

Brotchi J. Intramedullary spinal cord astrocytomas: diagnosis and treatment. *Critical Rev Neurosurg* 1997; 7:83-88.

Innocenzi G, Salvati M, Cervoni L, Delfini R, Cantore G. Prognostic factors in intramedullary astrocytomas. *Clin Neurol Neurosurg* 1997; 99:1-5.

Linstadt DE, Wara WM, Leibel SA, Gutin PH, Wilson CB, Sheline GE. Postoperative radiotherapy of primary spinal cord tumors. *Int J Radiation Oncol Biol Phys* 1989; 16:1397-403.

Nishio S, Morioka T, Fujii K, Inamura T, Fukui M. Spinal cord gliomas: management and outcome with reference to adjuvant therapy. *J Clin Neurosci* 2000; 7:20-23.