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Lyme neuroborreliosis disguised as normal pressure hydrocephalus

Article abstract—A 74-year-old woman presented with gait impairment, urinary incontinence, and dementia. She showed lymphocytic CSF pleocytosis and pronounced intrathecal *Borrelia burgdorferi* antibody production, indicating active Lyme neuroborreliosis. The syndrome of normal-pressure hydrocephalus (NPH) fully remitted after ceftriaxone treatment. Lyme neuroborreliosis may cause NPH by interfering with subarachnoid CSF flow.

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The syndrome of normal-pressure hydrocephalus (NPH), with the clinical triad of impaired cognition, gait, and micturition, may be present in up to 6% of patients with dementia.[1] Ventricles that are enlarged out of proportion to external CSF space on neuroimaging, as well as subependymal resorption areas, help distinguish NPH from other types of dementia. The syndrome may fully remit after ventricular shunting, but optimal patient management has not been established. We would like to draw attention to *Borrelia burgdorferi* infection as a differential diagnosis in suspected NPH.

Case report. A 74-year-old retired opera singer presented in October 1993 with a disorder of gait that was progressive since February 1993. She also complained of general weakness upon exertion, increasing memory problems, and urge incontinence with involuntary losses of small amounts of urine. She was unable to do her household work, cook, or shop and had become completely dependent on her husband. Her history was remarkable only for familial restless legs and cholecystectomy. There was no history of previous tick bites, erythema migrans, or distant journeys.

On examination, the right-handed patient showed a hesitant, broad-based gait with leftward drift, an inability to perform tandem gait or stand on one leg, and reduced attention and memory, but her neurologic findings were otherwise normal. The night nurse repeatedly found her bed wet and described the patient's confused state of mind with wandering about the ward, sitting on the floor, or attempting to enter her neighbor's bed. On the Mini-Mental Status Examination (MMSE) the patient scored 20/30, compatible with dementia, and she obtained a score of 3 (normal: 10 ± 3) in the digit–symbol subtest of the Wechsler Adult Intelligence Scale (WAIS). In computerized alertness tests,[2] her reaction times of "phasic" and "tonic alertness" were at least one standard deviation below controls (table). Brain imaging, which showed ventricular dilatation not matched by an equal increase of the subarachnoid space, together with patches of subependymal signal abnormality (figure), was compatible with the clinical diagnosis of NPH.

The patient did not improve after a test spinal tap of 40 ml. CSF leukocytes were increased (98/μl; 82% lymphocytes, 10% lymphoid cells, 4% monocytes, 3% plasma cells, and 1% granulocytes). CSF protein was 191 mg/dl, and isoelectric focusing showed oligoclonal bands.

Antibodies to *B. burgdorferi* were determined using an indirect immunofluorescence test (IFT) after absorption with *Treponema phagedenis,* as well as ELISA.[3] Serum immunoglobulin G (IgG) and IgM IFT titers of ≥1:64 and CSF IgG and IgM titers of ≥1:4 were considered significantly elevated. In the patient, serum IgG showed a titer of 1:256, CSF IgG of 1:64, and CSF IgM of 1:4. Intrathecal production of antibodies to *B. burgdorferi* was assessed by

Table *Psychometry and CSF findings before and after ceftriaxone treatment (November 16 to 29, 1993)*

Date	Phasic alertness*		Tonic alertness*		CSF cells (WBC/μl)	CSF protein (mg/dl)
	msec†	T value	msec†	T value		
Nov 4, 1993	320	37	382	31	98	191
Nov 5, 1993	391	29	465	26	ND	ND
Nov 11, 1993	ND	ND	ND	ND	88	190
Nov 29, 1993	306‡	40	288‡	47	ND	ND
Jan 11, 1994	254‡	51	281	49	23	43
May 24, 1994	ND	ND	ND	ND	6	31
March 9, 1995	229‡	62	217‡	74	2	29

* Phasic alertness was determined as mean reaction time in response to a visual stimulus preceded by an alerting tone, and tonic alertness in response to the visual stimulus alone.

† The normal range (T value, 40 to 60) of age-matched control subjects is 307 to 233 msec for phasic alertness and 320 to 243 msec for tonic alertness.[2]

‡ Significantly different at 0.05% when compared with previous examination.

ND = not done.

comparing the CSF/serum ratio of ELISA IgG values with the CSF/serum ratio of total IgG (CSF/serum index) and an index of ≥4 was considered elevated.[3] The CSF/serum index in the patient was 12.6, indicating specific intrathecal antibody production. In addition, IgM antibodies against *B. burgdorferi* were detected in the CSF both by ELISA and IFT, but not in serum. *Treponema pallidum* hemagglutination (TPHA) was negative in CSF and in serum. We made the additional diagnosis of active Lyme disease and postponed the decision about neurosurgical treatment of NPH until after antibiotic therapy.

Clinical examination at the end of 14 days of intravenous ceftriaxone (2 g/day from November 16 to 29, 1993) showed that gait and mental status had improved. Episodes of nocturnal incontinence or abnormal behavior had ceased. Two months later, the patient reported gait, micturition, and memory as normal. Tandem gait was still difficult, and there was a tendency to fall backwards on Romberg testing. Alertness results differed significantly from those obtained before treatment. Gradual normalization of CSF data was evident during the follow-up period of 18 months (see table).

In March 1995, she managed her household completely independently. On examination, only tandem gait with eyes closed was slightly impaired. The MMSE and WAIS digit–symbol subtest were normal (scores of 29 and 11, respectively). Mean reaction times of "phasic" and "tonic alertness" differed significantly from all previous values and were at least one standard deviation above the mean of controls. A decrease in subependymal signal changes and ventricular dilatation 18 months after ceftriaxone treatment was equivocal. In contrast, CSF cell and protein content was within normal limits (see table). Oligoclonal IgG bands, however, were still present in the CSF. Serum IgG antibodies to *B. burgdorferi* had fallen to 1:128, CSF IgG to 1:16, and CSF IgM to <1:2. The CSF/serum index had remained positive (>12.4). *B. burgdorferi* cultures from each CSF sample taken using modified Kelly's medium yielded negative results.

Discussion. Our patient provides an unusual example of a treatable dementia. Antibiotic therapy directed against *B. burgdorferi* led to resolution of

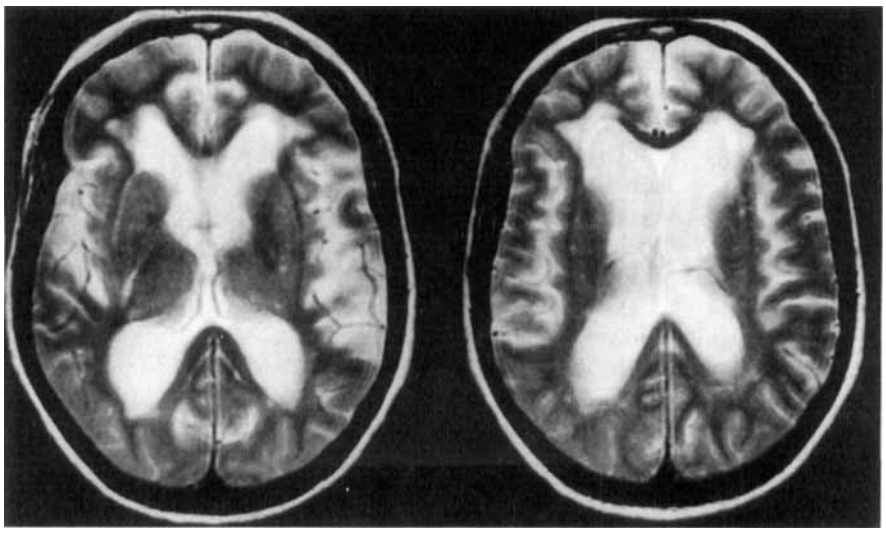

Figure. Magnetic resonance brain imaging (T_2-weighted, TR/TE = 2300/85) showed ventricular dilatation and subependymal signal increase in this 74-year-old woman presenting with gait impairment, urinary incontinence, and dementia.

meningeal inflammation, as well as complete remission of dementia, gait, and micturition disorder. Thus, the syndrome was secondary to infection with *B. burgdorferi,* a spirochete transmitted by ticks, which causes Lyme borreliosis.[4] Our patient's habit of forest walks in Upper Bavaria points to the geographic region where she was most likely infected.

Cerebral disease in Lyme borreliosis shows great variety,[5] and cognitive disorders in association with *B. burgdorferi* infection respond to antibiotic treatment.[6] However, there is no previous report of an NPH syndrome caused by the "new great imitator."[7]

The mechanism of CNS involvement in Lyme disease has not been firmly established. Thus, we can only speculate about the pathophysiology of the NPH syndrome in our patient. The association of NPH with meningeal inflammation[1] and documentation of basal meningovasculitis in *B. burgdorferi* infection[8] would be compatible with impairment of subarachnoid CSF flow. Lyme disease can interfere with CSF flow, as evident from papilledema and pseudotumor cerebri in affected children.[9]

Absence of clear-cut improvement on magnetic resonance brain scans taken before treatment and 2, 7, and 18 months after treatment could indicate a considerable delay of structural as compared with clinical recovery. Similarly, CSF cell count and protein content had normalized after treatment with ceftriaxone, whereas oligoclonal IgG bands and intrathecal *B. burgdorferi* antibody production were still present. Persistence of oligoclonal IgG and specific antibodies within the CSF for years after the acute stage occurs in CNS infections such as herpes encephalitis and neurosyphilis as well as in Lyme neuroborreliosis.[10] As an isolated finding, this does not indicate active disease or necessitate repeat treatment.

We stress the need to fully investigate patients with suspected NPH for causes that can be treated nonsurgically, such as *B. burgdorferi* infection.

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