corresponding to existing differentiation models is not an uncommon finding.[10] We believe that the S-100 positivity in our case represents one such example of aberrant marker expression. However, the existence of a very minor population of normal S-100+, T4+ lymphocytes not yet detected by current techniques cannot be entirely excluded. Whether cases of T-cell lymphoma expressing S-100 protein will behave in a more aggressive fashion, as in our case, remains to be clarified.

ADDENDUM

Since acceptance of our article for publication, a similar case report has appeared.[11] The authors describe a case of S-100–positive T-cell lymphoma (T11+, T3+, T4−, T8+) that ran a rapidly fatal course in a 16-year-old girl. The morphologic features of the lymphoma cells were also similar to those of our case. They postulate that this represented a poorly defined group of neoplasia with features intermediate between T-cell lymphoma and malignant histiocytosis.

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CONCURRENT NEOCORTICAL BORRELIOSIS AND ALZHEIMER'S DISEASE

ALAN B. MACDONALD, MD,* AND JOSEPH M. MIRANDA, MD†

Borrelia spirochetes were directly visualized in autopsy brain tissue from a patient with Alzheimer's disease and were cultured from cerebral cortex in artificial media. The authors propose that, as occurs in tertiary neurosyphilis and general paresis of the insane, Borrelia species may invade the brain, remain in a latent state for many years, and cause dementia in the absence of other focal neurologic deficits. An undetermined fraction of patients with Alzheimer's disease may be shown to have late tertiary neuroborreliosis. HUM PATHOL 18:759–761, 1987.

Diseases of the central nervous system including cranial neuropathies, meningoencephalitis, chronic meningitis, and progressive encephalomyelitis have recently been described in patients showing serologic evidence of infection with the spirochete *Borrelia burgdorferi*.[1–6] Months or years of clinical latency may pass between primary infection with *B. burgdorferi* and the onset of central nervous system disease. The possibility that late tertiary borreliosis might be manifest as dementia without other associated neurologic abnormalities led the authors to undertake this clinicopathologic investigation.

REPORT OF A CASE

A 74-year-old white woman died suddenly at home. Approximately one week previously, she had been evaluated in the hospital for a mild organic mental syndrome of recent onset. After a detailed neuropsychiatric evaluation by an internist, a neurologist, and a psychiatrist, a computed tomogram of the brain was obtained, and a battery of tests excluded biochemical, metabolic, and infectious causes for mental impairment. She was discharged from the hospital with a diagnosis of probable early Alzheimer's disease. After her death, an autopsy was requested by the family and her physicians to determine the neuropathologic basis for her memory disorder. The autopsy was performed by the medical examiner 24 hours after her death to determine that trauma or accident was not a proximate contributing factor in her sudden death.

METHODS

The previous complete neurologic examination had disclosed no deficits in the cranial nerves, sensory or motor function, reflexes, or cerebellar function. Tests of the patient's mental status revealed that she was disoriented as to place and date. Deficits in abstract reasoning were apparent on testing. Her thoughts were vague, and she was unable to concentrate on reading or while watching television.

Laboratory evaluation showed the serum vitamin B_{12} level was 321 ng/l (normal, 200 to 900); thyroxine, 6.0 μg/dl (5 to 12); and triiodothyronine, 2.4 μg/dl (1.5 to 4.8). The VDRL serology was nonreactive.

A standard autopsy disclosed the cause of death was a ruptured abdominal aortic aneurysm. At the request of one of us (ABM), a portion of fresh cerebral cortex (frontal lobe) was placed in sterile phosphate-buffered saline solution and stored at 4°C for special studies.

Under sterile conditions, cubes of fresh washed cerebral cortex gray matter were trimmed to approximately 0.5 cm in size, and these were transferred to sterile Barbour-Stonner-Kelly medium. The cultures were maintained at

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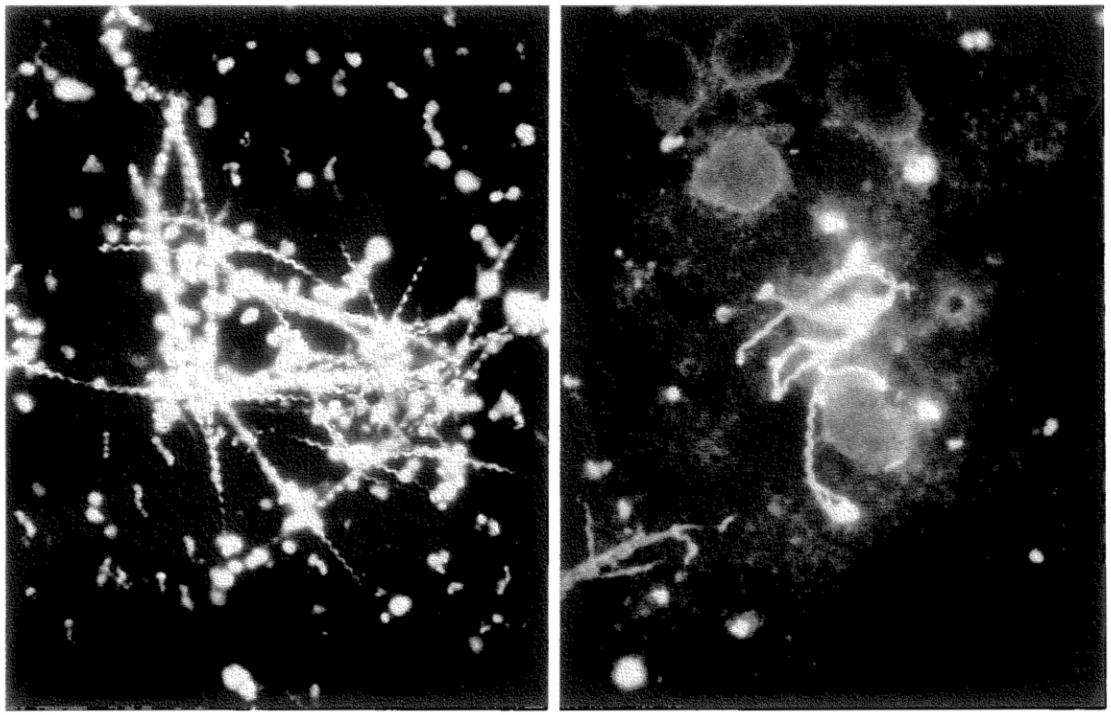

FIGURE 1. Borrelia spirochetes. **Left,** Subculture of frontal lobe of brain in Barbour-Stonner-Kelly medium. (Darkfield microscope image. × 500.) **Right,** Cytologic preparations from fresh frontal lobe cortex (touch preparations) stained with mouse monoclonal antibody H5332, IgG (outer envelope epitope). (Indirect immunofluorescence microscope image. × 1000.)

24°C. Subcultures were prepared from aliquots of the original material two months later.

The Krajian, Warthin-Starry, and Dieterle silver stains were performed on tissue imprints and paraffin sections. Control materials consisted of autopsy tissues from a patient with fetal borreliosis (positive control), autopsy brain from a 74-year-old man with no evidence of dementia (negative control), and the B 31 strain of *B. burgdorferi* obtained from the American Type Culture Collection.

An indirect immunofluorescent assay for detection of *B. burgdorferi* in tissue sections and in imprint preparations used serial incubations of the monoclonal antibody H5332 followed by incubations with staphylococcal protein A conjugated to fluorescein isothionate (Cappel Laboratories, Cochranville, Pennsylvania). Tissue controls for these studies were the same materials as used in the silver staining procedures.

RESULTS

Spirochetes were demonstrated with the H5332 monoclonal antibody in the tissue imprints in a bandlike distribution that corresponded to the gray matter region of the cortex. More than 100 spirochetes were photographed in aggregates, small clusters, and solitarily in various microscopic fields in the cortex imprints. Fragments of spirochetes were photographed in frozen tissue sections from the cortex using the H5332 monoclonal antibody–fluorescent method. Spirochetes were also demonstrated with the Krajian silver stain in tissue sections.

Cultures of brain tissue yielded spirochetes after two months of incubation at room temperature, but excessive contamination with other bacterial flora has so far prevented us from obtaining a pure culture of the spirochete. The subcultures have yielded corkscrew-shaped spirochetes that react with the monoclonal antibody H5332 on indirect immunofluorescence (fig. 1). Silver impregnation of the frontal lobe cortex demonstrated neurofibrillary change in neurons and an excess of argyrophilic plaques consistent with a pathologic diagnosis of Alzheimer's disease.

DISCUSSION

This report describes the discovery of *Borrelia burgdorferi* in brain tissue preparations from a patient with dementia. Although previous clinical studies using serologic tests have linked *B. burgdorferi* with various categories of neurologic illness, this is the first report of direct visualization of the spirochete in the brain. The immunofluorescent method is more specific than traditional histochemical methods using silver stains to demonstrate spirochetes in tissue. All of the previous reports that have demonstrated *B. burgdorferi* in various human tissues have relied on silver impregnation methods (Dieterle stain or Warthin-Starry stain). In only rare instances have *Borrelia* spirochetes been cultured from the tissues in which the spirochete has been seen in tissue sections.

Dr. Hideyo Noguchi established the link between the presence of the spirochete *Treponema pallidum* in the brain and the clinical illness general paresis of the insane. Noguchi's 1913 report described spirochetes in 12 of 70 cases of general paresis and ended the dispute between those who believed that general paresis was a type of late tertiary neurosyphilis and those who asserted that the association between the two diseases was only coincidental. A prolonged period of clinical latency and the gradual development of impairment of higher cognitive functions in the patient with general paresis parallel the developmental stages of pathologic processes in other organ sytems in tertiary syphilis and late tertiary borrelia infection.

Evidence accumulated from a novel approach to the

pathologic examination of the frontal lobe cortex from one extremely carefully documented case of senile dementia of the Alzheimer's type has provided circumstantial evidence that the spirochete *B. burgdorferi* was present in the neocortex, where higher cognitive functions are resident and where neuropathologic evidence of Alzheimer's disease is virtually always present. Further work is needed to determine whether the presence of the *Borrelia* spirochete in the neocortex and the development of dementia in the human host are linked.

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CORRESPONDENCE

Prostatic Tissue Sampling

To the Editor:—May I have the last word regarding Dr. Mandell's letter[1] on prostatic chips? Flawed statistics aside, what should be of prime consideration is what is in the best interest of the patient. Using Dr. Mandell's logic, the dermatologist would be justified in discarding excised nevi and the otolaryngologist in discarding all nasal polyps, because malignant melanoma in nevi and squamous cell carcinoma in polyps are rare.

The rule at this institution is that all prostatic chips, all curettages, and all biopsy samples are to be submitted in toto. If only one patient benefits from our small added effort, the expense and effort are well worthwhile.

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Proliferation of Laboratory Subspeciality Certifications

To the Editor:—In October 1986, the American Board of Allergy and Immunology (ABAI) offered its first examination for special qualification in Diagnostic Laboratory Immunology. The ABAI states that "the certification process was developed to ensure that clinical immunology laboratories are directed by those most knowledgeable about the conduct of such tests, their proper applications . . . and the interpretation of the results. . . ." Are immunology laboratories in such disarray that a new certification is necessary? No less than three boards (American Board of Pathology, American Board of Microbiology, and American Board of Allergy) were compelled to establish certification for special qualification in this field. This "plethora" of certifications in a laboratory field is perplexing.

What is most disturbing is that some boards drastically restrict those eligible for certification. For example, the ABAI requires prior certification by the American Board of Internal Medicine or American Board of Pediatrics; i.e., to qualify in laboratory immunology, one has to be an internist or pediatrician! As recently written by the Executive Secretary of ABAI, it is irrelevant that one is an immunologist with much experience; what matters is that this candidate already be certified in internal medicine or pediatrics. This requirement certainly is not needed to ascertain that "clinical immunology laboratories are directed by those most knowledgeable about the conduct of such tests." Should the American Board of Surgery offer an examination for special competence in surgical pathology, open only to those already certified in surgery? Does one have to be a surgeon to interpret biopsy findings? Does one have to be a pediatrician to perform and interpret immunologic tests?

The proliferation of the subspeciality boards, each with its own arbitrary requirements, has no proven value and therefore cannot be justified.

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Medullary Carcinoma of the Breast with Granulomatous Stroma

To the Editor:—In a review of 144 cases coded as "medullary carcinoma" of the breast from the Charity Hospital of Lousiana Tumor Registry over the last 30 years, three cases were identified that had a granulomatous stromal component (figs. 1 and 2). This component was marked and diffuse in one case and relatively minimal and focal in the two others. Whereas Moore and Foote[1] in their classic descriptive article on medullary carcinoma of the breast made reference to a stroma which "at times . . . almost assumes the character of a granulomatous bed," there is no reference to a granulomatous stromal component in subsequent major references on medullary carcinoma.[2-7] Interestingly, Moore and Foote noted that "the whole pattern may be such that one would consider the possibility of the lesion being an ovarian dysgerminoma metastatic to a node." The presence of a granulomatous stromal component in the present cases extends that analogy.

The significance of the lymphoplasmacytic stroma in medullary carcinoma of the breast has been debated; however, a host response to tumor would seem to be a plausible explanation in view of the relatively good prognosis for this variant of breast carcinoma. The finding of a granulomatous stromal component in the present three cases might offer additional support for that hypothesis. The stromal lymphoid and granulomatous reaction seen in seminoma or germinoma has also been postulated to represent a host