Idiopathic Transverse Myelitis

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Reports in the medical literature of “acute myelitis” date back to 1882 and are credited to H. C. Bastain, MD Lond, FRS, a consulting physician to what was then called University College Hospital and the National Hospital for the Paralysed and Epileptic (London, England). He described several cases of acute myelitis resulting in “softening of the spinal cord.” He presented the pathologic findings of several autopsies from patients who died of the myelitis and divided the cases into those that he thought were due to “blood changes and toxins, often associated with feeble cardiac action, which may well act as causes of thrombosis in vessels of the spinal cord” and those that were due to acute inflammation. The “inflammatory” cases were postulated to be due to an infectious or an allergic mechanism.

William Spiller, MD, at the University of Pennsylvania, Philadelphia, published a report in 1909 detailing thrombosis of the cervical anterior spinal artery and proposed that virtually all cases of acute myelitis were due to thromboses, not inflammation. His patient in that report (named John W) was an employee of the Philadelphia General Hospital who was required one morning to lift 100-lb blocks of ice with the assistance of another man. These blocks were then transported to each patient’s room as “air conditioning” and to provide cool washcloths. Shortly after lifting the fourth ice block, John W “began to have a sensation of coldness and pain between the shoulders.” Spiller then noted “hands began to grow stiff... ten or fifteen minutes later the lower limbs began to be numb and stiff. He lost power in the upper limbs within a very short time.” John W became paralyzed by the next day, and despite use of an iron lung ventilator, he died shortly thereafter. Autopsy of his spinal cord showed a blood clot in the cervical anterior spinal artery, and it was proposed that the lifting had caused the clot to form.

In 1922 and 1923, physicians in England and Holland became aware of a rare complication of smallpox vaccination: inflammation of the spinal cord and brain. Given the term postvaccinal encephalomyelitis, more than 200 cases were reported in those 2 years alone. Pathologic analyses of fatal cases revealed inflammatory cells and demyelination rather than the vascular pathologic findings noted by Spiller. The ratio of cases to vaccination was 1:50,000 in England and 1:5,000 in Holland. England carried out all its smallpox inoculations in children younger than 1 year, giving rise to the notion that “infants under 1 year of age are relatively insusceptible to postvaccinal encephalitis.” What was perplexing then and continues to be perplexing today is that family members received an identical vaccine but only 1 member of the family developed encephalomyelitis. In response to these data, in 1929 T. M. Rivers, MD, queried whether “a new virus made its appearance or mutant virus appeared?” in 1 of the children or alternatively that “constitutional changes occurred... that

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gic mechanisms are contributory.

In 1928, Frank Ford, MD, reported his hypothesis that many cases of acute myelitis are postinfectious rather than infectious in cause. His reasoning was that in many cases of acute myelitis associated with mumps, the patients’ fever had fallen and the rash had begun to fade when the myelitis symptoms began. He proposed the idea, therefore, that it was an allergic response to the virus rather than the virus itself that caused the spinal cord damage. Ford also noted that “neuroparalytic” accidents had been noted even dating back to 1887. Specifically, many patients had become paralyzed following regular virus vaccination. The paralysis was not found to be due to the rabies virus itself, but rather to the repeated inoculation of patients with brain tissue carrying the virus. Ford was not aware of the functions of the immune system but this “human model” of experimental allergic encephalomyelitis was likely caused by activation of autoreactive T and B lymphocytes, migration into the central nervous system, and inflammation and demyelination. Several cases were then reported during the next 2 decades, showing that several infectious agents can directly cause acute myelitis—notably measles and rubella viruses.

In 1948, A. I. Suchett-Kaye, MD, an English neurologist at St Charles Hospital in London, England, used the term acute transverse myelitis in reporting a case of paralysis following pneumonia. Since that time, the syndrome of progressive paralysis due to spinal cord inflammation has been known as transverse myelopathy or transverse myelitis (TM). The term transverse myelopathy, first introduced by Paine and Byers, is a broader term than TM, meant to indicate that clinical definitions do not prove the presence of spinal cord inflammation. Several authors then adopted this term and established various diagnostic criteria. Ropper and Poskanzer defined transverse myelopathy as development of bilateral spinal cord dysfunction across a 4-week period or less with a well-defined upper level, no antecedent illness, and exclusion of compressive etiologies. Berman et al excluded patients with only patchy sensory deficit or hemicond syndrome, as well as those individuals with other known neurologic disease including syphilis, severe back trauma, and malignant disease with metastases and encephalitis. Chris- tensen et al emphasized temporal progression and considered that patients with transverse myelopathies progress to maximum deficit across 14 days in contrast to hereditary and toxic disorders, which typically progress over several weeks to months. Jeffery et al also excluded other known diseases including arteriogenous malformations of the spinal cord, human T cell lymphotropic virus-1 infection, and sarcoidosis. Using these criteria, 46% of patients were felt to be parainfectious (as defined by a preceding illness within 1 month of the neurologic symptoms), 21% ultimately met criteria for multiple sclerosis, 12% met criteria for an anterior spinal artery syndrome, and 21% were felt to be idiopathic.

Acute noncompressive myelopathies were recently classified according to an etiologic scheme: (1) those associated with multiple sclerosis, (2) those related to systemic disease (systemic lupus erythemato- sis, antiphospholipid syndrome, Sjögren disease), (3) parainfectious, (4) delayed radiation myelopathy, (5) spinal cord infarct, and (6) idiopathic myelopathy.

We proposed a definition for TM that incorporates both cerebrospinal fluid sampling and gadolinium-enhanced magnetic resonance imaging of the spinal cord as a way to establish whether there is inflamma-
tion within the central nervous system. We proposed that abnormal gadolinium enhancement of the spinal cord or cerebrospinal fluid pleocytosis or elevated cerebrospinal fluid IgG index is required for a diagnosis of TM. If none of the inflammatory criteria are met at symptom onset, magnetic resonance imaging and lumbar puncture evaluation should be repeated between 2 and 7 days following symptom onset to determine if these inflammatory criteria are met. Vascular myelopathies and hereditary myelopathies can be differentiated from TM by temporal progression of symptoms and the lack of inflammation as defined earlier. We have also emphasized the need to distinguish TM from multiphasic and multifocal disorders of the central nervous system (eg, acute disseminating encephalomyelitis and multiple sclerosis) and idiopathic TM from TM associated with systemic inflammatory disorders (eg, sarcoidosis, systemic lupus erythematosus). We believe these criteria establish a framework both for immunologic studies aimed at defining critical abnormalities in TM and for clinical trials.

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REFERENCES