

Necrotizing Myelopathy

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The preceding paper by Mirich et al. [1] describes the MR findings in four subjects with biopsy-proved necrotizing myelopathy. In the first three patients, the clinical course was characterized by progressive motor and sensory dysfunction in the lower extremities, evolving over periods ranging from 3 months to 2 years. In the fourth case, the clinical course was characterized by a Brown-Séquard syndrome with a C4 sensory level that developed over a 3-week period. All four patients had abrupt worsening of their signs and symptoms. In each instance, initial MR imaging showed focal intramedullary expansion of the spinal cord, and histologic examination of the specimen obtained at surgery showed parenchymal coagulative necrosis and thickening and hyalinization of the vascular walls. A definite etiologic diagnosis could not be made.

The development of clinically progressive necrosis of the spinal cord not related to traumatic injury, an infectious or a primary inflammatory process, or infiltration or compression by neoplasm, though not particularly common, may pose difficulties in diagnosis. The purpose of this discussion is to review briefly some of the disorders that might be considered.

Among the circulatory disorders, the most frequently discussed are those that are related to impairment of spinal venous outflow. Clinically, nonhemorrhagic venous infarction of the spinal cord tends to evolve over a period of weeks to months and is typically accompanied by extensive thrombosis within leptomeningeal veins [2]. The longitudinal extent of the damage is variable but may be considerable. Factors that predispose its development include hypercoagulability (e.g., migratory thrombophlebitis or polycythemia rubra vera) or spinal venous hypertension (such as that seen in the presence

of a spinal dural arteriovenous fistula [AVF]. The existence of AVFs draining into the spinal leptomeningeal venous system was recognized only relatively recently, with the aid of selective spinal angiography [3] and angiotomography [4, 5], but these AVFs are now thought to be the commonest type of spinal vascular malformation [6–9]. Although the feeding arteries may be situated outside the spinal canal [4, 10], in most instances the vascular nidus is embedded within or is adjacent to the dura ensheathing the proximal spinal nerve root [7], thus giving rise to the term *spinal dural AVF*. Most of these lesions are found at or below midthoracic levels [4, 6–8]. Despite the absence in the literature of any descriptions of the pathologic findings within the spinal cord of *angiographically or pathologically confirmed* spinal dural AVFs, it is widely thought that the alterations correspond to those described initially by Foix and Alajouanine [11] and subsequently by others [12–15]. These were given a variety of names, including subacute necrotic myelitis, Foix-Alajouanine syndrome, angioma racemosum venosum, angiodysgenic necrotizing myelopathy, type I spinal arteriovenous malformation (AVM), thrombosing spinal AVM, and spinal AVM with acute neurologic deterioration [11, 13, 16–19]. The general belief is that shunting of arterial blood into spinal leptomeningeal veins results in venous hypertension, which in turn leads to interference with venous outflow from the spinal cord, progressive intramedullary congestion, mural thickening and hyalinization within the venocapillary network, and hypoxic parenchymal atrophy [4, 7, 15].

Necrotizing myelopathy is also a feature of the condition referred to as neuromyelitis optica or Devic's syndrome. Although the symptom complex classically consists of a com-

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bination of blindness and paraplegia, there is no reason why the many disorders that have been associated with it, including multiple sclerosis [20, 21], acute disseminated encephalomyelitis [21], varicella-zoster infection [22, 23], mumps [23], rubeola [23], infectious mononucleosis [24], systemic lupus erythematosus (SLE) [25, 26], pulmonary tuberculosis [27–29], and cloquinal intoxication [30–32], could not lead to the development of myelopathy alone. It has been repeatedly emphasized, for example, that the spinal cord lesions in Japanese patients with multiple sclerosis tend to be more necrotic than the lesions in other patients [33, 34]. Additionally, of the three cases of noninflammatory necrotizing myelopathy described by Hughes and Mair [27] in patients with pulmonary tuberculosis, only one had evidence of involvement of the optic nerve. Finally, lupus myelopathy in the absence of optic neuropathy has been recognized for many years [35–38].

The subject of lupus myelopathy deserves further comment. Although myelopathy usually appears within a few years of the time at which a diagnosis of SLE is made, in a minority (15–20%) it is the presenting feature [38]. Typically, the course of illness is one of fairly rapid progression, but at times it is characterized by remissions and relapses. In most instances, the spinal cord is affected at or below thoracic levels, but approximately one quarter of the cases have involved the cervical region. Pathologically the lesion consists of one or more foci of subtotal coagulative or liquefactive necrosis [35, 37, 39, 40], although, occasionally, circumferentially distributed pallor of the white matter with ballooning degeneration of myelin sheaths and disruption of axons has been described [36, 40]. The pathogenesis of the myelopathy has not been determined, but at least two groups of investigators have recently suggested a relationship to the presence of antiphospholipid antibodies [41, 42].

The existence of a malignancy-associated or paraneoplastic necrotizing myelopathy not associated with radiation therapy or with compression or infiltration by tumor was first suggested by Mancall and Rosales in 1964 [43]. The subject has been reviewed periodically since then [44–48]. The typical clinical course is one of fairly rapidly progressive neurologic dysfunction that reflects involvement of the spinal cord at any level. The condition, which has been described in association with a variety of neoplasms (most notably bronchopulmonary and lymphoreticular malignancies), is characterized by massive or patchy multifocal coagulative necrosis affecting both gray and white matter, with a paucity of inflammatory cells. The pathogenesis of the disorder is unknown. Recently, however, Iwamasa et al. [49] have described two cases of malignancy-associated necrotizing myelopathy in which, despite the relative scarcity of inflammatory cells, the presence of herpes simplex virus type 2 was demonstrated both immunohistochemically and by electron microscopy. This raises the possibility that the cause of some of the other noninflammatory necrotizing myelopaths that have been included in this discussion may, at times, be viral.

The last major form of noninflammatory necrotizing myelopathy is not associated with any other pathologic disorder. This condition, which was called "acute necrotic myelopathy" by Hoffman [50] and "progressive necrotic myelopathy" by

Folliss and Netsky [51], is entirely idiopathic. The pathologic findings, which may vary in their extent, are those of coagulative or liquefactive necrosis in the absence of striking infiltration by inflammatory cells. It is likely that, as knowledge advances, this form of myelopathy will be shown to be etiologically heterogeneous.

The confusion caused by the noninflammatory necrotizing myelopaths is attributable to our lack of knowledge of the pathogenesis of most of these disorders, the difficulty of access to adequate amounts of tissue for diagnostic purposes, the relatively small number of persons with expertise in spinal angiography, the lack of suitable radiologic methods for the study of the spinal parenchymal and spinal leptomeningeal venous systems, and the relatively low frequency with which the spinal cord is examined at autopsy.

In the patients described by Mirich et al. [1], we can only speculate about the cause of the necrotizing myelopathy. Although selective spinal angiography was not done, it is certainly possible that some of them may have had spinal dural AVFs. The finding of thickening and hyalinization of vascular walls is not specific, however, and may have been caused by the spinal cord necrosis [51]. More suggestive would have been the presence of marked thickening of the walls of leptomeningeal veins. Moreover, involvement of the cervical spinal cord, as was seen in case 4, is most unusual, and the development of a Brown-Séquard syndrome has not, to my knowledge, previously been described in association with a spinal dural AVF. It is likely, therefore, that more than one disorder is represented in this interesting group of patients, and I hope that MR imaging studies of the type described by Mirich et al. will be beneficial to our understanding of this mystifying form of spinal cord disease.

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