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Commentary

Radiation Myelopathy

Timothy E. Schultheiss[1,3] and L. Clifton Stephens[2]

Because of the low frequency of radiation-induced myelopathy, few reports of magnetic resonance (MR) imaging studies of this condition have been published. The article by Wang et al (1) is the only study of a series of such cases of which we are aware. In this study, the authors make several useful points, not all of which are easily explained within the current understanding of the pathogenesis of radiation myelopathy. Briefly, they found reduced intensity in T1-weighted images and increased intensity in T2- or T2*-weighted images in patients who were imaged 2 to 8 months after the onset of symptoms. These findings are characteristic of edema, and swelling of the cord was commonly observed in these patients. Also noted in these patients was focal enhancement using Gd-DTPA. In two patients imaged 36 and 52 months after the onset of symptoms, atrophy of the cord was the only change noted. Contrast was not administered in either of these latter two cases.

The diagnosis of radiation myelopathy is always made by a process of exclusion. The most common alternative diagnosis is recurrent or metastatic tumor. However, even when myelograms, CT scans, MR scans, and plain films are negative for tumor or other etiology, both the symptomatic presentation and the spinal cord dose must still be consistent with radiation myelopathy before this diagnosis is accepted. Unexplained myelopathy should remain in the differential diagnosis if no other reason is found to explain the patient's symptoms and the radiation dose regimen or the symptomatology is not consistent with radiation myelopathy (2, 3).

A negative myelogram is almost a requirement for a diagnosis of radiation myelopathy, except that diffuse spinal cord enlargement has been reported (4–7). Wang et al (1) reported swelling in six of eight cases examined 2 to 8 months after onset of symptoms, but did not see this in the two cases with long latencies. Swelling of the spinal cord can produce a complete myelographic block and has been associated with particularly poor prognosis in the cases in which it has been reported (7). Lymphocytes and moderately elevated total protein are commonly found in the cerebrospinal fluid of radiation myelopathy cases, but Wang et al did not find elevated protein levels. Elevated myelin basic protein is a less consistent finding. Measurements of nerve conduction velocities show slowed spinal conduction or complete blocks (8, 9).

In the absence of tumor or other obvious etiology, the differential diagnosis for a patient with suspected radiation myelopathy may also include necrotizing carcinomatous myelopathy (10). This condition is found most frequently in patients with lung carcinoma or lymphoma, but is rare nonetheless. One should also consider myelopathy secondary to chemotherapy. Because the spinal cord can respond to injury in only a limited number of ways, it is unlikely that an MR image of a myelopathic spinal cord will uniquely identify the cause of the myelopathy. Moreover, with an interdisciplinary approach to cancer treatment, it may not be possible to ascribe a single causative agent to a treatment-related myelopathy.

It is by histopathologic examination that radiation myelopathy is confirmed and best characterized. However, because pathologic studies of the irradiated spinal cord are generally restricted to autopsy cases that were symptomatic with neurologic dysfunction, the available clinical material represents only the more advanced expressions of damage. Animal studies have provided a

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broader picture of the lesions by affording the opportunity to view milder degrees of injury and lesions that are fresher.

The typical histopathologic diagnosis associated with radiation myelopathy is leukomalacia. Rarely is the gray matter involved, and never is it involved to the exclusion of the white matter. The literature on radiation myelopathy typically emphasizes the interval between radiotherapy and the development of symptoms. It is this interval that correlates with the morphology of the lesions. In general, shorter latent periods in (less than about 17–18 months) are associated with white matter histopathology that may or may not be accompanied by various degrees of morphologic vascular changes. Lesions in cases with longer latencies until the onset of signs have been attributed most often to significant vascular pathology, including necrosis and thrombosis (11). Although morphologic changes correlate with the latency, no correlation was apparent between MR findings and the duration of the latent period before the onset of symptoms. Perhaps this can be explained on the basis that 1) correlation between latency and pathology of lesions is not perfect and, 2) the sample size in the study by Wang et al (1) was small. It is also difficult to understand their frequent finding of edema months after the onset of symptoms since this is often a transient response in recently developed lesions and is not observed as frequently in myelography of radiation myelopathy as Wang et al have reported for MR.

The findings of Wang et al are consistent with both the edematous changes seen in their patients and also with the inflammatory responses that often are seen in radiation myelopathy (sometimes called radiation myelitis). Enhancement with Gd-DTPA is consistent with increased vascular permeability and breakdown of the blood-brain barrier. Disruption of the blood-brain barrier has been seen in experimental models of radiation myelopathy prior to the development of signs and has been interpreted by some as being contributory to the later development of demyelination and malacia.

Wang et al seem to attribute the focal contrast enhancement at least in part to "vascular factors, such as venous drainage." We believe that the venous side of the vasculature is more likely to be the region of vascular changes than the arterial side because of the propensity of lesions to have a lateral location (as also noted by these authors), the greater susceptibility of white matter to edema, and the rarity of gray matter changes that would be characteristic of impaired arterial supply.

Any disease process that has potential CNS effects may be regarded as a candidate for increasing the spinal cord's radiation sensitivity. Among the possibilities are several infectious diseases as well as diseases that affect the mechanical integrity of the spine. Of the 800 cases of cancers of the head and neck reviewed by Marcus and Million (12), one of the two cases of radiation myelopathy was in a patient who was severely deformed, having had rickets as a child (13). We are aware of a case of low-dose radiation myelopathy in a woman with a previously undiagnosed Arnold-Chiari malformation. Diabetes, hypertension, hypotension, vascular diseases, and possibly some infectious diseases may potentiate radiation damage to the spinal cord (14).

No treatment of radiation myelopathy has shown impressive results. The use of steroids has ameliorated symptoms in some patients. Presumably these patients are those that have an edematous or inflammatory reaction. Given the common finding of edema by Wang et al, it may be that more patients than previously thought could benefit from the use of steroids. Unfortunately, by the time symptoms of radiation myelopathy appear, the lesions are probably so advanced that recovery is not possible. The occurrence of radiation myelopathy is highly idiosyncratic. If patients who are more likely to develop this complication could be identified, then perhaps earlier intervention would result in improved treatment for this condition, similar to recent improvements in the treatment of traumatic myelopathy.

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