

RADIOLOGICALLY ISOLATED SYNDROME (RIS) PATIENTS ARE AT HIGH RISK OF DEVELOPING MS AND WARRANT TREATMENT WITH DMD – YES

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Most neurologists have encountered patients with RIS only a few times during their professional lives. In the 2005 edition of McAlpine's Multiple Sclerosis there is no mention of it. But with the increasing use of imaging, patients with RIS will become more common and RIS will become an issue that more and more neurologists will have to deal with.

RIS refers to MRI findings typical of multiple sclerosis in an individual with a normal neurological examination who had an MRI for some reason completely unrelated to anything that could be interpreted as MS – bad headache, minor trauma – and the MRI findings are truly surprising. The MRI findings are typical of demyelinating lesions and satisfy the criteria for dissemination in space and dissemination in time either by a single scan demonstrating both non-enhancing and enhancing lesions or by serial scans.

Can we be certain that the patient has RIS and is at high risk of developing MS?

We must, of course, exclude MS mimics. But relatively few things look absolutely identical to MS. Paraclinical screening can demonstrate surrogate markers of inflammatory disease. There is evidence that their presence reduces the time to the first clinical event. Oligoclonal bands in the cerebrospinal fluid should be present in the vast majority of people with RIS. An MRI lesion in the cervical spinal cord in addition to those in the brain narrows the differential diagnoses and increases the likelihood of MS. Older people get lesions in the brain but not in the spinal cord. Abnormal latencies on visual evoked potentials point to a silent lesion in the optic nerve.

Why should we treat patients with RIS?

Every mm³ CNS (central nervous system) tissue that is demyelinated will have about 10,000 axons transected, and once transected they do not recover, they will die. Every relapse counts and around 50% leave some residual deficit. Most MRI lesions in people with MS are asymptomatic and it makes no scientific sense to consider symptomatic lesions more relevant than asymptomatic. Rather, patients with RIS should be considered lucky that they have no symptomatic lesions, and therapy is equally justified in patients with RIS as in patients with symptomatic lesions and clinically definite MS.

This view point is backed by follow up of patients with RIS. In a retrospective review of 71 subjects with RIS, 25 had findings in the cervical spinal cord highly suggestive of demyelinating disease. Of these, 21 (84%) progressed to CIS (clinically isolated syndrome) or PPMS (primary progressive MS) over a median time of only 1.6 years from the date when RIS was diagnosed. The odds ratio of clinical progression was 75.3 (95% CI 16.1-350.0, $p < 0.0001$). In a prospective cohort, clinical conversion occurred in 23 (33%) of 70 patients after a mean time of 2.3 years (range 0.8-5.0 years). In another prospective study, cognitive performance in patients with RIS ($n=26$) and MS ($n=26$) was compared to performance in healthy subjects ($n=26$). Individuals with RIS and MS performed significantly worse than healthy subjects in all seven tests, and the MS group performed worse than the RIS group in three of the tests.

All our treatments to date are anti-inflammatory, and although we lack definite proof most believe that neurodegeneration is secondary to neuroinflammation. Therefore, it makes sense to quench the inflammation and treat patients with RIS in order to avoid or delay the occurrence of neurological dysfunction.

References:

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