Multiple Sclerosis Risk After Optic Neuritis Final Optic Neuritis Treatment Trial Follow-up.

Arch Neurol. 2008. doi 65(6):727-732. doi:10.1001/archneur.65.6.727

This article included the results of the final follow-up study to the landmark Optic Neuritis Treatment Trial (ONTT) from 1992. If you recall, the original trial in 1992 showed that treatment with IV methylprednisolone followed by an oral prednisone taper in acute isolated optic neuritis (ON) accelerates the recovery of vision but does not improve the eventual visual outcome. Later, a 1997 follow-up study reported the 5-year risk of multiple sclerosis (MS) in these same ONTT patient cohorts, showing a 5-year cumulative probability of 30% regardless of treatment. Even later, this 2008 follow-up study was conducted to provide the final results for the risk of developing MS in the ONTT cohorts, after following them for up to 15 years.

Experimental design and statistical analysis: The original ONTT was a multicenter, randomized controlled trial that first enrolled 457 patients aged 18-46 years with acute unilateral ON and then randomized them into 3 treatment groups: IV methylprednisolone, oral prednisone, and oral placebo (see prior summary of the original ONTT for more details). Standardized, unenhanced baseline brain MRIs were performed at enrollment. Because this follow-up study examined the risk of MS development, they excluded the enrolled ONTT patients who were diagnosed as having either probable or definite MS at the time of trial entry. As such, for this follow-up study there were 389 eligible patients with acute unilateral ON without an initial diagnosis of probable or definite MS. Data was complete for only 300 patients (77%) at 15-year follow-up, but a few patients who were unable to be examined had details verified over telephone.

Results: Overall, the results of this follow-up study found that the aggregate, cumulative probability of developing MS by the 15-year follow up time point (after an episode of acute ON) was 50%. In patients with 1 or more lesions on a baseline brain MRI, the probability was 72% as opposed to only 25% in patients with no brain lesions. Notably, there were no significant differences in the risk of developing MS among the 3 original ONTT treatment groups (e.g. treatment with IV steroids or not). Of note, the time interval to developing MS also seemed to differ based on the number of baseline MRI lesions, and the risk of developing MS was highest in the first 5 years. For instance, the probability of developing MS was 42% in the first 5 years in patients with 1+ brain lesions vs. 16% in patients with no brain lesions. At 6-10yrs, the probability of developing MS in patients with 1+ baseline MRI brain lesions was 30%, and it was 32% at 10 to 15 years after the initial optic neuritis event. This is compared to 9% and 2% respectively in patients without brain lesions. Among patients without lesions on MRI, baseline factors associated with a LOWER risk for MS development included male sex (women had a 3x higher risk), optic disc swelling at the onset of visual loss, and atypical features of ON including disc or peripapillary hemorrhages, retinal macular exudates, absence of pain, and reduction of vision to no light perception. Among patients with MS who completed the 15-year examination, the degree of disability as assessed by the EDSS score was not related to the number of brain lesions on baseline MRI. The authors also noted that the use of disease modifying therapy among these patients with and without lesions on baseline MRI brain was similar.

Conclusion: In summary, the overall 15-year risk of developing MS after an episode of acute, unilateral ON was 50% and strongly correlated to the presence of demyelinating lesions on baseline MRI scan. The risk appeared to be much higher if there was at least 1 lesion present on a baseline brain MRI (72% versus 25% without lesions). The risk of developing MS in patients with at least 1 lesion on baseline brain MRIs appears to be relatively consistent throughout the 15 years of examination, though in patients without any brain lesions, the risk of developing MS is greatest within the first 5 years and then sharply declines. This longitudinal study of MS risk in patients who presented with ON is clinically useful when risk-stratifying and counseling patients.

Summary created by Amy Li Safadi, M.D.