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What is the prognosis of optic neuritis? How often does it lead to multiple sclerosis?

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Clinical question

What is the chance of developing multiple sclerosis following the first episode of optic neuritis in a nineteen-year-old male?

This question was asked of us at the Centre for General Practice, University of Queensland, Australia, where we were providing a literature-search service in collaboration with the Department of Primary Health Care at the University of Newcastle funded through the NHS Northern and Yorkshire Regional Library Advisory Service, for local GPs. The service was based on an Australian model (1).

We present our response to one of the questions asked, updating the original search July 2005.

Search question

First, the clinical question was reformatted into a 'searchable question' (2).

What is the risk of developing clinically apparent multiple sclerosis following a first episode of optic neuritis in a young male?

The ideal study to answer this question would be an inception cohort study of adults experiencing a first episode of optic neuritis over several years, with minimal loss to follow-up, and the development of clinically apparent multiple sclerosis (MS) as the outcome.

Rapid search

We searched Medline (on SilverPlatter via WebSpirs) for articles published in English using the following terms optic neuritis (MeSH and text) AND multiple sclerosis (MeSH and text) combined with a sensitive search filter for detecting clinically sound prognostic studies (3).

Summary of findings

There were many studies evaluating the risk of developing multiple sclerosis after a single episode of optic neuritis. Their quality was good, although there may have been differential measurement causing bias (people with positive brain MRIs may have been less likely to have been lost to follow up, for example), Table.

The risk of developing MS after an episode of optic neuritis ranged from 13% to 58%. Even with brain lesions identified at baseline, only slightly more than half of patients later developed clinical MS, although their absence did not eliminate the risk (0-22%).

Abnormal brain MRI were a strong predictor of MS in the largest study (Optic neuritis trial), with 87% complete follow-up, the presence of one or more white matter lesions on baseline MRI brain scan more than doubled the 10-year risk of MS.

Comment

The variation in results may be attributable to differences in study design, variation in criteria for the diagnosis of MS and optic neuritis, and length of follow-up. The studies give a reasonably robust indication of the prognosis. The prognosis seems to be better than expected, and raises questions about whether optic neuritis may have other causes than the demyelination of MS, or that MS has a wide spectrum of expression, often little or never interfering with patients' lives.(15)

Applying the results to the patient

Apart from offering an overall prognosis, the literature suggests that this can be improved onby testing with MRI for other lesions on diagnosis of optic neuritis.

It also raises the question of treatment. The CHAMPS trial compared interferon β-1a and placebo on developing MS after a single demyelinating event among 192 patients (16). After three years, the adjusted rate ratios clinically definite MS between the two trial arms was 0.58, (95% CI 0.34 to 1.00). Similarly, in a second randomised placebo controlled trial of interferon β-1a among 309 patients with a first neurologic episode consistent with MS (although in only 35% was this from optic neuritis), clinically apparent MS developed in 34% intervention patients compared with 45% controls (17). But this is a different question…

Table: Relevant prospective cohort studies

Study first author and year	N	Follow up	Loss to follow-up (%)	Probability of developing apparent clinical MS (%)	Prognostic factors
Beck 2003 (4)	388	5 year risk 10 year risk	 13	30 38 (95% CI 33 -43)	Presence of ≥1 lesions on the baseline brain MRI in 160 patients had a risk of 56%; In 191 patients with no lesions the risk was 22% (the risk of multiple lesions was not significantly higher than of a single lesion, 58% vs 51%; P = 0.22). There was increased risk (70%) with a history of non-specific neurological symptoms, or optic neuritis in the opposite eye, compared to neither (50%), p = 0.005. If there were no baseline MRI brain lesions, the risk was lower in males than females (hazard ratio, 0.35: 95% CI 0.12-0.98) Swelling of the optic disc was associated with reduced probability of developing MS (hazard ratio 0.41; 95% CI 0.20-0.84).
Ghezzi 2000 (5)	102	2 year risk 4 year risk 6 year risk 8-10 year risk	Unclear	13 30 38 49	59% of patients (42/71) with lesions at baseline brain MRI developed MS compared to 0% patients with a normal MRI.
Jin 2003 (6)	147	2.1years (mean)	Unclear	36	The presence of 3 or more MS-like MRI lesions as well as the presence of oligoclonal IGG bands was strongly associated with the development of MS (p<0.001). In multivariate analysis, age and season of clinical onset were also significant predictors
Nilsson 2005 (7)	86	15 year risk	8	40 (95% CI 31 - 52)	60% of MS cases occurred with three years of the first incident of ON. CSF with mononuclear pleocytosis and/or oligoclonal Ig increased the risk for subsequent MS, 49% (95% CI 38% - 65%) vs 23% (95% CI 12% - 44 %) for those with normal CSF
Druschky 1999 (8)	29	8 year risk	10	54	64% of MS cases developed within 2 years after ON episode. No significant correlation (p = 0.09) was observed between the presence of abnormal MRI and conversion to CDMS.
Rizzo 1988 (9)	60	14.9 years (mean)	35	58	Life table analysis suggested a greater risk of developing MS for women (3.4 times greater) than men
Frith 2000 (10)	82	15 year risk	13	52	Significantly greater risk of developing multiple sclerosis for patients in the 21-30 year age group
Francis 1987 (11)	101	15 year risk	31	75	Patients with optic neuritis who were HLA-DR3 positive had an increased risk for the development of multiple sclerosis (RR = 2.8) and this risk was further enhanced when DR3 occurred in combination with DR2 (RR = 6.7)
Amirzargar 2005 (12)	56	Mean follow-up unclear	Unclear	27	
Tintore 2005 (13)	123	3.3	Unclear	Unable to extract or obtain data.	Optic neuritis had a smaller risk for conversion to MS than other clinically isolated syndromes

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