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Short report

The early risk of multiple sclerosis after optic neuritis

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SUMMARY Serial brain MRI was performed in 53 patients with clinically isolated optic neuritis. Using clinical and imaging evidence for relapse, multiple sclerosis developed within a mean of 12 months in 19 of 34 cases (56%) with brain lesions at presentation, and in only 3 of 19 cases (16%) without (Relative Risk = 6·8, $p < 0·005$).

In the United Kingdom, over 50% of adults presenting with optic neuritis later develop multiple sclerosis.[1–4] The risk of progression from optic neuritis to multiple sclerosis has been correlated with age,[5–8] sex,[5] CSF oligoclonal bands,[7] HLA antigens,[8] and recurrent attacks,[5 8] but with longer follow up, some of these associations disappear as more and more patients convert to multiple sclerosis.[4]

Magnetic resonance imaging (MRI) of the brain reveals multifocal white matter lesions indistinguishable from those in multiple sclerosis in 50–70% of adults with clinically isolated optic neuritis.[9–11] However, multiple sclerosis cannot be diagnosed at presentation as the criterion of dissemination in time is not fulfilled:[12] such multifocal lesions could represent a monophasic illness, that is, acute disseminated encephalomyelitis, in which the MRI appearances are similar.[13 14] New brain lesions at follow up MRI or the development of new non-ocular symptoms and signs, would indicate a multiphasic disease process and allow a diagnosis of clinically probable multiple sclerosis in the former case and clinically definite multiple sclerosis in the latter.[12] We report here a combined clinical and serial MRI study to determine whether the presence of brain lesions at presentation of optic neuritis is a prognostic indicator for the subsequent development of multiple sclerosis. Since in multiple sclerosis the MRI abnormalities correspond with plaques,[10] the difference between the clinical and MRI criteria is determined simply by the chance location of the new lesion in a region in which damage leads to symptoms. We have therefore considered the results together.

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Methods

Optic neuritis was diagnosed using accepted clinical criteria.[8] Patients aged more than 50 years were excluded as multifocal white matter lesions are not infrequent in normal individuals in this age group.[15 16] Sixty nine patients with clinically isolated optic neuritis had brain MRI performed at presentation on a Picker 0·5T MR imager (a few initial scans were performed at 0·25T). Fifty three of 61 tracable patients agreed to be rescanned.

At presentation, 46 patients had had a single episode of optic neuritis, 41 unilateral, five bilateral simultaneous (within 2 weeks); seven patients had had recurrent optic neuritis involving both eyes.

Patients were carefully repositioned and identical MRI sequences (always including $SE_{2000/60}$) were used at the first and second scan. The scans were reported by three neuroradiologists who were unaware of the clinical details. New lesions were recorded only when they were unequivocal.

Patients were re-examined when they attended for the follow up scan. Multiple sclerosis was diagnosed clinically when a relapse involved the central nervous system beyond the optic nerve, provided there was an interval of more than 3 months from the presenting episode.

The results were analysed in two groups: (A) patients with disseminated brain lesions at presentation; (B) those with normal MRI of the brain at presentation. There were no differences between the groups in terms of age, sex or clinical features except that bilateral simultaneous optic neuritis was seen more often in group B (four cases) than in group A (1 case).

The significance of differences between groups A and B was tested by chi-square analysis. The relative risk (RR) of multiple sclerosis was calculated.[17]

Results (table)

Group A: abnormal MRI at presentation
Thirty four patients (64%) had multifocal lesions. Clinical follow up from presentation was 6 to 23 (mean 12·3) months. Twelve of 34 had clinical relapses, implicating the spinal cord in 10 and the brain stem in two. On clinical grounds alone, these cases could be classified as clinically definite (9) or probable (3) multiple sclerosis, depending on the presence or absence of neurological signs accompanying the symptomatic relapse.[12] However, as MRI had already shown disseminated lesions, these patients could all be classified as clinically definite.

Table *Clinical and MRI follow up in clinically isolated optic neuritis*

	Group A	*Group B*
No of patients	34 (64%)	19 (36%)
Female	21	12
Male	13	7
Mean age (first attack optic neuritis)	33·2 (21–48)	32·1 (16–44)
Clinical presentation:		
Acute unilateral	29	12
Bilateral simultaneous	1	4
Bilateral consecutive	4	3
Mean clinical follow up (months)	12·3	12·1
Clinical relapse (multiple sclerosis)	12*	0
Mean MRI follow up (months)	9·9	10·3
New MRI lesions	12*	3

*Five patients had both clinical and MRI relapses, while clinical relapse only was seen in seven, and MRI relapse only in seven.

MRI follow up was performed after 4–23 (mean 9·9) months. New lesions were seen in 12 patients (fig), of whom five relapsed clinically.

Group B: normal MRI at presentation
Nineteen patients (36%) had normal MRI studies of the brain at presentation. Clinical follow up was 5–30 (mean 12·1) months. There were no relapses attributable to lesions outside the optic nerves. MRI follow up was at 5–24 (mean 10·3) months. New lesions were seen in three patients.

Combining both clinical and MRI criteria, multiple sclerosis developed within a mean of 12 months in 19 of 34 patients (56%) in group A and 3 of 19 (16%) in group B (RR = 6·8, $p < 0·005$). Clinical relapses were seen only in Group A (12 of 34; 33%).

Relationship of outcome to clinical presentation
Acute unilateral optic neuritis: 15 of 29 (52%) in group A developed clinical and/or imaging evidence of multiple sclerosis, as did 2 of 12 (17%) in group B (RR = 5·4, $p < 0·05$). Clinical relapses were confined to group A (9 of 29; 31%). *Bilateral simultaneous optic neuritis:* 2 of 5 patients (one in group A, one in group B), developed new brain lesions. None had clinical relapses. *Bilateral consecutive optic neuritis:* 3 of 4 in group A and 0 of 3 in group B developed clinical and/or MRI evidence of multiple sclerosis.

Discussion

Using combined clinical and imaging criteria, 56% of patients with disseminated MRI lesions at presenta-

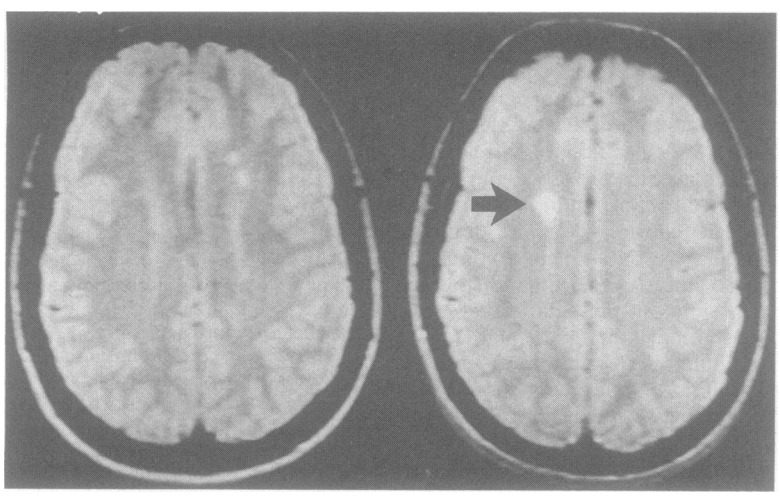

Fig *Spin echo images two weeks (left), and eight months (right) after an attack of acute unilateral optic neuritis. A new lesion is seen at follow up adjacent to the right frontal horn (arrowed). Two small left frontal lesions on the first scan are not present at follow up. There was no clinical relapse during the follow up period.*

tion developed multiple sclerosis during a relatively short follow up period (mean = 12 months), though determination of the true frequency of multiple sclerosis will require much longer follow up. The presence of brain lesions was associated with a relative risk of 6·8 for developing the disseminated disease.

The risk was even high (RR = 7·8, $p < 0·01$) when the four patients with bilateral simultaneous optic neuritis were removed.

At present, an early diagnosis of multiple sclerosis in the monosymptomatic patient carries no therapeutic implications and until such time as it does we do not routinely advise serial MRI in optic neuritis.

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