leukodystrophies and may eliminate the need for brain biopsy in premortem diagnosis.

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Prognostic Indicators in Optic Neuritis

Terry A. Cox, MD

The paper by Nikoskelainen and associates on prognosis of optic neuritis (Nikoskelainen E, Frey H, Salmi A: Prognosis of optic neuritis with special reference to cerebrospinal fluid immunoglobulins and measles virus antibodies. Ann Neurol 9:545–550, 1981) is an important contribution, but I had difficulty understanding a few points.

How many patients presenting with optic neuritis had no history of other neurological symptoms or previous optic neuritis? The paper states that 28 patients had isolated optic neuritis, but the context implies that some had had previous symptoms. In order to verify the theory that patients with truly isolated optic neuritis are no different from patients who had optic neuritis and a history of neurological symptoms, the two groups must be compared in terms of prognosis, cerebrospinal fluid findings, and similar factors. The authors undoubtedly have the data to establish this point.

There is some mathematical confusion in the Results section. Fifty affected eyes with normal vision cannot be 69% if 12 affected eyes with normal fundi is 25%. How many affected eyes were there? Did the 3 eyes with subclinical involvement enter into these calculations?

What criteria were used to establish subclinical involvement of the optic nerve?

How many patients had one or more abnormal cerebrospinal fluid findings? I tried to calculate this number from the data given but could not get the totals to agree.

Does classification of patients on the basis of normal versus abnormal cerebrospinal fluid predict the development of multiple sclerosis?

The inclusion of 3 patients with other diagnoses (polyneuropathy and Leber's optic neuropathy) is confusing. Did any of these patients have abnormal cerebrospinal fluid?

I hope the authors do not mind answering these questions. I think their work is too important to allow ambiguities to stand in presentation of the results.

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Reply

Eeva Nikoskelainen, MD

The points raised by Dr Cox are important. Some of the ambiguities occurred because three tables from the original article had to be deleted from the final manuscript. We have reanalyzed our data according to the suggestions made, and our answers to the specific questions are as follows.

As given in the text of our article, 28 patients had isolated optic neuritis when the cerebrospinal fluid specimens were taken. These patients had no history of previous neurological symptoms or earlier episodes of optic neuritis. Their neurological examinations during optic neuritis were normal. For discussion of prognosis they are treated as a separate group in our article. All but 8 patients later developed multiple sclerosis.

Seventeen patients with optic neuritis had had previous neurological symptoms (the initial diagnosis was viral meningitis in 1, Guillain-Barré syndrome in 2, and unknown in 14). All but 1 of these patients later developed multiple sclerosis. We could not find any prognostic markers which would distinguish these patients from the 28 with isolated optic neuritis.

At the end of the follow-up period there were 73 subjectively and objectively affected eyes (not including the 3 with subclinical involvement). These eyes had all suffered from one or more attacks of optic neuritis that caused visual symptoms to the patients. The numbers given in the article for various ophthalmological findings in these eyes are correct, but there are two errors in percentage calculations. Thus, 50 affected eyes (69%) had normal vision and 34 (46%) normal visual fields, but only 18 (25%) had normal color vision. The optic fundus was normal in only 12 (16%) of the affected eyes.

At the end of the follow-up period 23 eyes were subjectively healthy. The patients had never experienced any visual trouble in these eyes. However, the opthalmological reexamination showed that 3 of these subjectively healthy eyes had suffered from subclinical involvement, manifested by abnormal function tests associated with pallor of the optic disc and thinning of the retinal nerve fiber layer in an eye which had not suffered visual symptoms.

Many tests were performed on the cerebrospinal fluid specimens. The most important were leukocyte count, relative IgG, cellulose acetate electrophoresis, and measles antibody titer. Table 1 in this communication gives the frequencies of specimens with one or more abnormalities on these tests in relation to the final diagnosis of the patients. Except for 2 cases, all the patients who had two or more abnormalities later developed multiple sclerosis. The other patient with all these abnormalities has suffered a recurrent attack of optic neuritis but otherwise has been symptomless, and her neurological reexamination is normal.

In clinical work, the most important tests of cerebrospinal fluid in patients suspected of having multiple sclerosis are leukocyte count, relative IgG, and electrophoresis. Table 2 shows the various combinations of abnormalities found on these three tests. Except for 2 patients, all those who had two or all three abnormalities in these tests later developed multiple sclerosis. However, as shown in both our article and Table 1 of this letter, several patients who had normal cerebrospinal fluid during the course of optic neuritis also later developed multiple sclerosis.

I agree with Dr Cox that the inclusion of 3 patients with other diagnoses (polyneuropathy and Leber's hereditary

Table 1. Combined Abnormalities in CSF Leukocyte Count, Relative IgG (% of total protein), Gelatinized Cellulose Acetate Electrophoresis, and Serum/CSF Measles Antibody Ratio in Relation to Total Patients Tested

	Isolated Optic Neuritis		Total Material	
Result	Patients with MS	Other Patients	Patients with MS	Other Patients
All tests abnormal	1	2	3	2
Three tests abnormal	4	0	9	0
Two tests abnormal	3	0	7	0
One test abnormal	8	1	10	1
No test abnormal	4	5	7	9
Total patients	20	8	36	12

Table 2. Patients with Combined Abnormalities of Leukocyte Count, Relative IgG (% of total protein), and Electrophoresis

	Isolated Optic Neuritis		Total Material	
Result	Patients with MS	Other Patients	Patients with MS	Other Patients
All 3 tests abnormal	2	2	5	2
IgG and electrophoresis abnormal	1	0	8	0
IgG and leukocyte count abnormal	1	0	1	0
Electrophoresis and leukocyte count abnormal	2	0	2	0

optic neuropathy) is confusing. They should have been left out of the material. Two of these patients had normal cerebrospinal fluid. The third, who was afflicted with Leber's disease, had slightly elevated total protein (56 mg/dl) but all other tests were normal.

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