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The prevalence and characteristics of epilepsy in patients with multiple sclerosis in Nordland county, Norway

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ABSTRACT

Purpose: The prevalence of epilepsy among patients with multiple sclerosis (MS) has been found higher than in the general population. Although cortical pathology may be involved, the causal link between MS and epileptic seizures is still unclear. We aimed to identify and describe the patients with active epilepsy in a previously described population based MS-cohort.
Methods: Medical records of all patients with MS in Nordland County on January 1, 2010, were scrutinizing for evidence of comorbid seizures and epilepsy.
Results: Among 431 patients with MS, we identified 19 (4.4%) with a history of seizures or epilepsy. Fourteen (3.2%) of these had active epilepsy defined as use of antiepileptic drugs or seizures within the last 5 years. One patient got epilepsy before other signs of MS. In patients with relapsing-remitting MS (RRMS) at onset and active epilepsy (n = 10), 70% had converted to secondary progressive (SPMS) at prevalence date, compared to only 35% of those without active epilepsy (p = 0.02). 43% had converted to SPMS before they got epilepsy. Attack semiology or electroencephalogram recordings indicated a focal onset of seizures in 12 of 14 (86%) with active epilepsy.
Conclusion: The frequency of active epilepsy among MS patients in Nordland was 3.2%, approximately 4.5 times higher than in the general Norwegian population. RRMS patients with active epilepsy had more likely converted to SPMS than patients without active epilepsy. With a high frequency of focal epilepsy, the study supports that focal MS brain pathology is the cause of the comorbid epilepsy.

1. Introduction

Multiple sclerosis is a chronic inflammatory disease of the central nervous system, characterized by focal white matter lesions, but both deep and cortical grey matter is also involved [1–3].

A review of 29 previously published clinical series found the mean prevalence of epilepsy among MS patient to be 2.3%, 3–6 times that in the general adult population [4]. In the general Norwegian population the prevalence of epilepsy is about 0.7% [5–7]. Epilepsy has previously been reported in 3.2 to 3.6% of the Norwegian MS patients [8,9]. The cause of the increased occurrence of epilepsy among patients with MS is unknown [4], but it is reasonable to assume an epileptogenic role of cortical lesions [10].

The aim of the study was to identify and describe the patients with epilepsy in a well-defined MS-population [11] of northern Norway at prevalence date January 1, 2010.

2. Methods

This was a retrospective cross-sectional epidemiological study based on patient records of all known MS patients living in Nordland County, Northern Norway at prevalence point.

Nordland County is situated between latitude 64°56′ N and 69°20′ N, and is covering a total area of 38456 km^2. The population was 236 271 (118537 men, 117734 women) at January 1, 2010.

There is only one neurological department in the county, at the Nordland Hospital in Bodø, serving the majority of the population, but there are also two neurological outpatient services at the hospitals in Mosjøen (Helgeland) and Stokmarknes (Vesterålen). We had full access to the MS-patients medical files. The medical records were consecutively written as electronic files from 1992, and older documents are scanned and added to the electronic files.

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In a previous population study [11] we identified 431 persons (294 women and 137 men) with MS according to the diagnostic criteria of Poser or McDonalds [12,13] living in Nordland County at January 1, 2010, giving a prevalence of 182 per 100 000 inhabitants. At that time point, we classified the initial disease course to be RRMS for 345 (80.0%) of the patients, 80 (18.6%) had primary progressive MS (PPMS), and six (1.4%) with unknown disease course. In the present study, we were able to classify these six patients as having RRMS at onset. In the present study we also ascertained the transformation from RRMS at onset to secondary progressive MS (SPMS).

The medical files were scrutinized to identify seizures and epilepsy. The diagnosis of epilepsy was set in accordance with the 1989 criteria of the International League Against Epilepsy [14]. Active epilepsy was defined as use of antiepileptic drugs at prevalence point or seizures within the last 5 years [15]. Seizures were classified according to the criteria of the International League Against Epilepsy from 1981 [16]. We classified the epilepsy as focal or not, based on the described seizure semiology and electroencephalogram (EEG) findings. In addition, age, sex and treatment for MS and epilepsy were recorded.

Statistical analyses were performed by the use of Microsoft Office Excel for Windows 7. Normally distributed continuous variables were presented as means with standard deviations (SD). Independent-sample T-test was used to compare age and disease duration. Categorical variables were presented as numbers with percentages, and compared by using chi square test. All tests were two-sided. Statistical significance was set at $p < 0.05$. To estimate confidence interval for the sample proportion of patients with EP, Wilson's method was applied [17].

2.1. Ethical approval

The study was approved by the Regional Committee for Medical and Health Research Ethics (REK Nord).

3. Results

The cohort consisted of 431 patients, 351 (81.4%) with RRMS and 80 (18.6%) with PPMS at onset. At prevalence day of January 1 2010, 226 (64.4%) of those with an initial RRMS course still had a RRMS disease course, 122 (34.8%) had converted from RRMS to a secondary progressive MS (SPMS), and three had an unclassified disease course.

We identified 19 patients (age 53.3 ± 14.6 years), 14 women (age 53.3 ± 16.2 years) and 5 men (age 53.2 ± 11.0 years), with a history of epilepsy, accounting for 4.4% (95% CI 2.8–6.8) of the cohort. Three patients (two women and one man) with childhood epilepsy, and two patients (one woman and one man) who were diagnosed with epilepsy as adults, had not had any seizures during the last five years. Hence, 14 (3.2%, 95% CI 1.9–5.4), 11 women and three men, were classified to have an active epilepsy. Table 1 shows demographics and clinical characteristics of these patients.

Simple partial seizure was noted in four patients, and in one of these there was also evidence of complex partial seizures. In total, we classified three patients with complex partial seizures. In addition, one patient was reported to have slurred speech prior to a generalized seizure, and another reported feeling "strange" prior to generalized convulsions. Generalized seizures were reported in 11 patients, of which 10 had convulsive and one had nonconvulsive seizures. In two patients, eye deviation was noted during a generalized seizure. One of these patients also had a post-ictal transient hemiparesis (Todd's paresis) ipsilateral to the eye deviation.

All patients with MS and epilepsy had at least one electroencephalogram (EEG), and in total 69 EEG-recordings were registered. There were epileptiform discharges in 17 (Fig. 1), focal slow activity without epileptiform discharges in 20, diffuse slow activity without epileptiform discharges in 14, and 18 recordings were normal.

With the reported seizure semiology and the EEG findings combined, focal epilepsy was registered on at least one occasion in 12 of the 14 patients (86%) with active epilepsy.

Status epilepticus was reported in five (36%) of the patients. Four had generalized clonic seizures. Gaze deviation was noted in two of these. One patient had a simple partial status epilepticus with prolonged convulsions in the right part of her body. There were no fatal cases of status epilepticus.

One patient experienced a seizure before other symptoms of MS. Another patient was registered with a seizure as the onset symptom, and a third patient experienced her first seizure the same year as the first symptom of MS, but 10 years prior to the MS diagnosis. The remaining 11 patients got their first epileptic seizure after other symptoms of MS.

Table 1
Multiple sclerosis patients with active epilepsy in Nordland County, Northern Norway.

Sex	*Age (yrs)	Age (yrs) at 1. symptom of MS	Age (yrs) at diagnosis of MS	Disease course	*EDSS	Age (yrs) at diagnosis of EP	SPS	CPS	Generalized seizure	Status	Focal EEG	Focal EP	*Antiepileptic medication
f	47	19	21	RRMS → SPMS	9.5	23	-	-	+	-	-	-	CBZ
m	58	22	31	RRMS	3.0	54	-	-	+ (focal start)	+	+	+	CBZ
f	30	23	23	RRMS	0	29	-	+	+ (focal start)	-	+	+	LTG
f	39	23	37	RRMS → SPMS	4.0	30	-	-	+	-	+	+	VPA, LTG
m	53	24	28	RRMS → SPMS	9.0	43	+	+	+	+	-	+	CBZ
f	77	25	41	RRMS → SPMS	6.5	71	-	-	+ (eye deviation, Todd's paresis)	+	-	+	CBZ
f	41	27	27	RRMS → SPMS	5.5	27	+	-	+	-	-	+	-**
f	54	35	45	PPMS	6.5	35	+	-	-	+ (focal)	+	+	OXC, PGB
m	66	36	57	RRMS → SPMS	3.0	53	-	+	-	-	+	+	CBZ
f	70	39	44	RRMS → SPMS	8.5	65	-	-	+ (eye deviation)	+	+	+	PHT
f	55	48	50	PPMS	7.0	53	-	-	+	-	+	+	OXC
f	83	46	62	PPMS	7.5	77	-	-	+(non-convulsive)	-	+	+	-
f	63	51	57	PPMS	4.0	34	+	-	-	-	+	+	CBZ
f	55	54	54	RRMS	4.0	54	-	-	+	-	-	-	LTG

*At prevalence point January 1, 2010. **No treatment due to patient's choice.
CPS = complex partial seizure; EEG = electroencephalogram; EP = epilepsy; PPMS = primary progressive multiple sclerosis, RRMS = relapsing-remitting multiple sclerosis; SPS = simple partial seizure; SPMS = secondary progressive multiple sclerosis.
CBZ = Carbamazepine; LTG = Lamotrigine; OXC = Oxcarbazepine; PHT = Phenytoin; PGB = Pregabalin; VPA = Valproate.