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Cerebrospinal Fluid Guanase Activity in Multiple Sclerosis

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ABSTRACT Thirty-eight CSF specimens obtained from 33 patients with multiple sclerosis (MS) (20 definite, 18 probable; 20 active, 18 inactive) were subjected to the measurement of guanase activity, cell count and concentrations of total protein and Ig G. There was no difference in cell count and total protein concentration between MS and normal controls ($n=14$). The guanase activity, however, was significantly higher in MS as compared with normal controls ($p<0.05$). In addition, active MS revealed significantly elevated guanase activity, total protein and Ig G as compared with inactive MS ($p<0.05$). Serial guanase determinations together with Kurtzke's expanded disability status scales in 5 MS patients supported the idea that CSF guanase activity reflects the disease activity more appropriately than other parameters in CSF. (Received May 16, 1989 and accepted May 30, 1989)

Key Words: Multiple sclerosis, Guanase, Ig G, CSF

1. Introduction

Guanase is a deaminating enzyme which was identified by Schmidt *et al*¹⁾ from extracts of homogenized rabbit liver tissues. The biochemical role of this enzyme is to catalyze the transformation from guanine to xanthine in the purine salvage pathway. The measurement of serum guanase activity has been used clinically to assess liver function. The characteristics of the distribution of guanase activity in human tissue was reported by Levine *et al*²⁾ who found high guanase activity only in the liver, the kidney and the brain. As regards the brain tissue, Mansoor *et al*³⁾ demonstrated the regional distribution of guanase activity of the monkey brain; namely, the highest activity was in the thalamus, fairly abundant activity in most of the cerebral cortical regions, very low activity in the corpus callosum, and no activity in the cerebellum and the optic nerve. We have not been able to find any report concerning the clinical value of guanase activity in cerebrospinal fluid (CSF) obtained from patients with neurological diseases. The present study, therefore, was undertaken to determine the possible value of measuring CSF guanase activity in multiple sclerosis (MS) with special reference to the disease activity.

2. Patients and Method

CSF specimens were collected from 33 patients with clinically definite MS or probable MS (9 male, 24 female, mean age; 38.5 years old) and 14 normal controls (9 male, 5 female, mean age; 37.0 years old). Serial guanase activity was determined in 5 cases in order to find any correlation between guanase activity and neurological impairment of the patients assessed by Kurtzke's expanded disability status scale (EDSS)⁴⁾. CSF, obtained by lumbar puncture, was subjected to cell count and total protein determination by the method of Meulemans⁵⁾, and the rest of the CSF was stored at -80°C until use. Guanase activity in CSF was measured by the method described by Itoh *et al*⁶⁾ which indirectly quantitated the amount of

indophenol released from ammonia by adding phenol and hypochlorous acid. In MS patients, CSF Ig G was measured by Laser nephelometry. Lastly, all the parameters were evaluated with reference to mutual correlations and EDSS.

3. Results

Table 1 shows cell count, total protein concentration and guanase activity in CSF. Although there was no difference in the values of cell count and total protein between MS and normal controls, it was of interest that guanase activity in MS was significantly elevated as compared with that of normal controls. Subsequently, cell count, total protein concentration and guanase activity were examined to find any difference between clinically definite Ms and probable MS. None of the above items was statistically different between the two groups. However, the guanase activity of clinically definite MS tended to be higher than that of probable MS (Fig. 1).

Table 1 Cell count, total protein concentration and guanase activity in CSF

	Cell count (/mm ³)	Total protein (mg/dl)	Guanase (IU/L)
Multiple sclerosis (n=38)	1.5±1.6	26.4±18.3	0.96±0.50*
Normal control (n=14)	3.6±2.1	24.5±11.7	0.46±0.28*

* : p<0.05

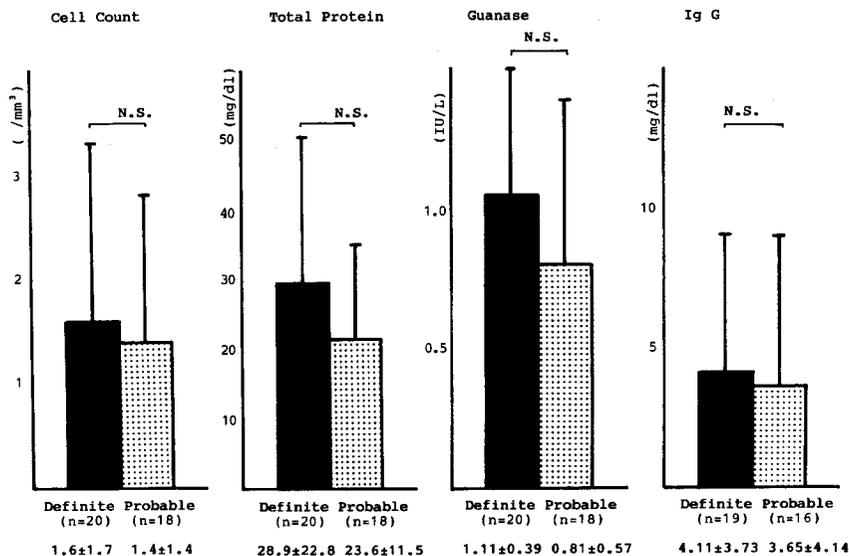


Fig. 1 CSF parameters in clinically definite MS and probable MS

In order to obtain more information on the disease activity, we divided all MS patients into active and inactive cases, where "active" was defined as a patient who had acute exacerbation within one month prior to lumbar puncture. Guanase activity, concentrations of total protein and Ig G were all significantly higher in active MS than in inactive MS ($p<0.05$) (Fig. 2). In MS as a whole, guanase activity and Ig G concentration showed a gross correlation without statistical significance (Fig. 3), whereas no relationship was present between guanase activity and total protein concentration.

Five cases, in whom serial determination of guanase activity and concentrations of total protein and

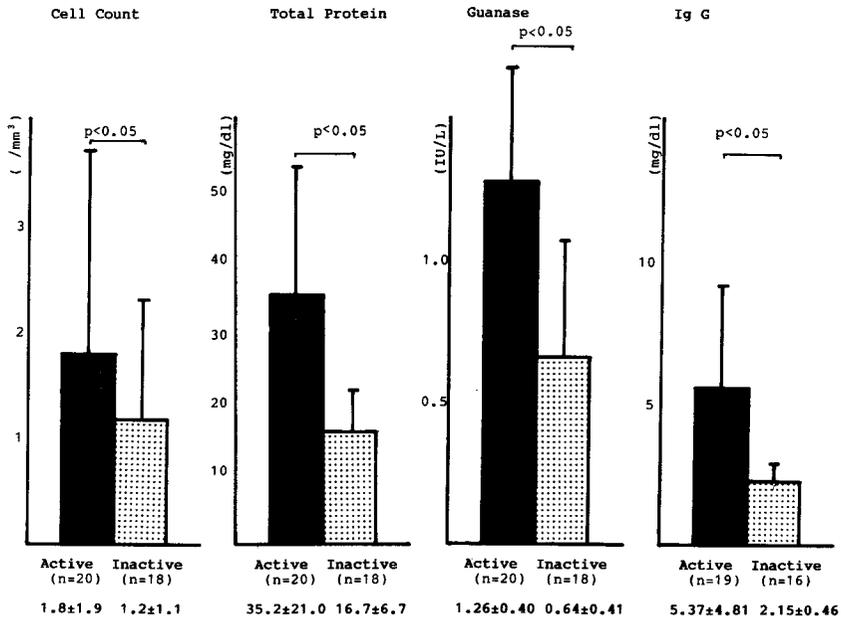


Fig. 2 CSF parameters in active MS and inactive MS

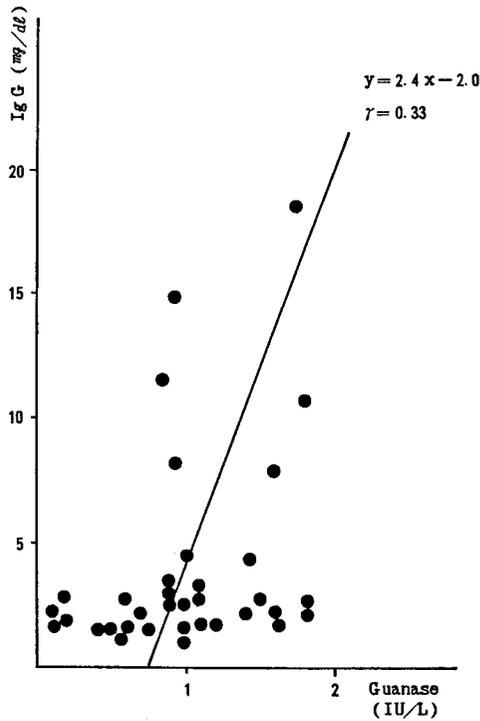


Fig. 3 Correlation between guanase and Ig G in CSF in MS (definite and probable)

Fig. 3 Correlation between guanase and Ig G in CSF in MS (definite and probable)

Table 2 Serial changes of CSF parameters and neurological impairments in 5 cases with multiple sclerosis

Case No.	Age/Sex	Date	Guanase (IU/L)	Ig G (mg/dl)	EDSS*
1	55/F	12/4, '86	1.4	4.7	3.5
		5/1, '87	1.7	1.8	6.0
2	32/F	5/23, '87	1.8	2.4	6.0
		8/3, '87	1.6	2.0	5.5
3	37/M	12/8, '86	0.9	8.3	3.0
		2/16, '87	0.9	15.0	3.0
4	36/M	2/4, '86	0.6	1.8	2.0
		8/13, '87	0.7	1.8	3.5
5	19/F	9/11, '86	0.1	1.8	1.5
		3/9, '87	0.6	1.8	3.6

* expanded disability status scale (Kurtzke)

Ig G were done, are shown together with EDSS in Table 2. Judging from the serial determinations of guanase, Ig G and EDSS in these cases, it was concluded that guanase activity reflected more appropriately the disease activity of MS rather than Ig G concentration in CSF.

4. Discussion

It has been generally accepted that Ig G in CSF reflects the disease activity of MS. In addition, Caroscio *et al*⁷⁾ reported that CSF Ig G was the most sensitive parameter revealing the disease activity of MS. Since we could not find any report dealing with guanase activity in patients with neurological diseases, including MS, we evaluated the clinical significance of CSF guanase activity in MS, and found a significantly higher activity of CSF guanase in clinically definite MS and probable MS as compared with normal controls. Interestingly enough, there was a significant elevation of CSF guanase activity in active MS as compared with inactive MS. It is assumed to be important that a gross correlation was observed between guanase activity and Ig G level in the present study. The repeated serial results of CSF guanase activity and Ig G level, together with neurological impairments quantitated by EDSS, supports the idea that guanase activity reflects the disease activity more appropriately than Ig G concentration.

The patho-physiological mechanism by which guanase activity in CSF is elevated may probably be the release of this enzyme from the central nervous system into the subarachnoid space, and therefore, may be different from that of the increased Ig G levels in CSF. In any case, it could be reasonably supported that the measurement of guanase activity in CSF can be used as one of the parameters to monitor the disease activity of MS.

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多発性硬化症における髄液中 Guanase 活性

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多発性硬化症 33 例から総計 38 検体(definite 20 例, probable 18 例; 活動期群 20 例, 非活動期群 18 例)の髄液を採取し, guanase 活性, 細胞数, 総蛋白濃度および Ig G を測定し検討した.

細胞数, 総蛋白濃度は正常群 (14 例) と多発性硬化症群では差異を認めなかった. しかし guanase 活性は多発性硬化症群で正常群に比較し有意の高値を示した

($p < 0.05$). さらに活動期群の多発性硬化症では非活動期群に比較し guanase 活性, 総蛋白濃度および Ig G は有意の高値を示した ($p < 0.05$).

多発性硬化症 5 例について, guanase 活性と同時に Kurtzke による全般障害度スケールを反復して検討したところ, guanase 活性は他の髄液の指標よりもより鋭敏に病態の活動性を反映した.