The analysis of mirror pattern bands synthesized in patients with neurological disorder during Oligoclonal immunoglobulin isoelectric focusing electrophoresis

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Research article

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Abstract

Background The analysis of oligoclonal band (OCB) of cerebrospinal fluid is of vital importance for the clinical diagnosis and differential diagnosis of neurological disease. However, there still exists limited knowledge about the interpretation of the mirror pattern bands (one of OCB results) for the neurological disorders during the clinical courses. In this study, we thoroughly analyzed the 12 patients with mirror pattern bands combined with laboratory and clinical information in order to explore the clinical implications of mirror bands as much as possible. **Methods** Matched CSF and serum specimens were obtained from 5892 patients with various neurological disorders who were required to undergo lumbar puncture for OCB analysis over the past four years in the Neurological Special Examination Laboratory of XuanWu Hospital. A total of 12 patients with mirror pattern bands were screened out from the 5892 patients. Serum immunofixation electrophoresis (IFE) was then performed on the 12 patients respectively in order to tentatively explore the correlation with M protein. We also collected the clinical and laboratory information of the 12 patients in great detail. **Results** All three types of mirror patterns are closely connected with M protein from peripheral serum. However, not all patients with the mirror patterns present positive M protein. 7 out of 12 patients (58.3%) were finally diagnosed as blood system-related diseases. None of the 12 patients were diagnosed with Multiple Sclerosis (MS). **Conclusions** Great emphasis should be taken on the mirror pattern bands during the isoelectric focusing electrophoresis (IEF). The mirror pattern bands combined with the result of M protein will greatly contribute to the differential diagnosis of neurological disorder.

Introduction

Oligoclonal Bands (OCB) is the most consistent and characteristic features of Multiple Sclerosis (MS)[1]. Intrathecal oligoclonal band synthesis occurs in over 90% of patients with clinically definite MS but may also occur in the context of CNS infection and other inflammatory conditions[2]. The isoelectric focusing (IEF) on agarose gels followed by immunoblotting has been universally recognized as the “gold standard” for detecting the presence of oligoclonal bands.[3-5] OCB serves as not only an especially valuable tool for differential diagnosis but also for prognosis[6], and even for predicting the conversion of optic neuritis and clinically isolated syndromes (CIS) to MS[7]. For such a qualitative and clinically significant technique, the correct recognition and interpretation of CSF oligoclonal band patterns are utmost crucial. A general consensus is that there are five typical types of band patterns[8], of which the presence of oligoclonal bands in CSF but not in serum means local synthesis of immunoglobins in the central nervous system, this band pattern is most likely observed in patients with MS[8, 9]. Relatively little attention has been paid, however, to the mirror pattern bands, which are quite uncommon and the clinical significances of which are still rarely clarified. There are three types of abnormal mirror patterns, the first type is termed “type 3”, which performs both identical bands in CSF and serum and additional CSF restricted oligoclonal bands. The second is so-called “type 4”, which presents identical oligoclonal bands (irregularly spaced bands) in CSF and serum, and which may indicate a systemic instead of intrathecal immune reaction[4]. The third type is “type 5”, which symmetrically displays monoclonal bands both in

the CSF and serum sample[10]. The monoclonal proteins form clusters and are more prominent, with higher concentrations and stronger immunoreaction, which have the characteristic of space in symmetric steps among bands and tend to be evenly distributed [11-13]. This identical multiple bands in both CSF and serum (mirror pattern) may be relative to the following disorders, such as the systemic inflammation, probable MS, systemic lupus erythematosus, paraneoplastic syndrome, vascular disease, peripheral neuropathies and so on[2, 11, 14]. However, in clinical practice, there are still many discrepancies among different research institutions in interpreting the above three CSF/serum mirror pattern bands, which is to a large extent attribute to the very rare occurrence[15]. Quite a few neurologists usually unreasonably downplayed the clinical significance of mirror patterns when the paired CSF and serum samples were analyzed for OCB, instead played more emphasis on the classical pattern 2 which to a large extent indicates MS.

Undoubtedly, CSF OCB analysis is an important tool to auxiliarily diagnose the some causes of neurological disorders[17, 18]. Analysis of paired CSF/serum for OCB has been a conventional method in our laboratory for the patients with neurological disfunction but without clear pathogeny. In the past four years, among 5892 patients with various neurological disorders who received OCB detection in our hospital, just only 12 cases presented the mirror patterns. In view of the potential correlation between mirror pattern bands and M proteins, we next analyzed the M protein of the 12 cases by means of immunofixation electrophoresis(IFE), which was a standard method for the detection of immunotyping of M protein[16]. M protein can be further immunotyped for immunoglobulin (Ig) G, IgA, IgM, and total light chains κ and λ with IFE. Subsequently, we focused on the 12 patients with comprehensive clinical and laboratory information in order to further evaluate the potential value of OCB mirror patterns and explore to what extent do the OCB mirror patterns results contribute to the final diagnosis.

Results

1. The demographical and immunological data of the 12 patients with mirror patterns are summarized in Table 1. Oligoclonal IgG band results of all the 12 patients accompanied with immunofixation electrophoresis respectively are shown in the Figure 1. Five patients were female and seven patients were male. The mean age were 59.5 years (range 42-72). A quantitative measured increased intrathecal synthesis of IgG was present in 5 patients (No. 1,3,5,11,12) and was always accompanied by the increased QALB. Expect for three patients (No.4,5,9), the other nine patients were positive for M protein. Besides, among 12 cases with mirror patterns, only one patient (No. 5) presented pattern 3 (a mirror plus pattern), two patients displayed pattern 4 (equal number of matched bands in CSF and serum) and nine patients presented pattern 5 (monoclonal bands).

2. The clinical characteristics of all the 12 patients are presented in Table 2 including the first clinical symptoms and the final diagnosis. 8 out of 12 cases (patient No.1,2,3,4,5,7,8,11) were at the onset of atypical demyelinating lesion of peripheral nervous system. 7 patients (No.1,2,3,7,8,11,12) were finally diagnosed as blood system-related diseases including Multiple myeloma (MM), POEMS syndrome, and monoclonal gammopathy of undetermined significance (MGUS).

Table 1. The primary laboratory parameters of the 12 patients with mirror patterns

Table 2. Overview of the clinical characteristics of 12 patients

Discussion

In clinical practice, OCB are often investigated in the diagnostic work-up of inflammatory CNS disorders, in particular MS and especially in the earlier stage of MS according to the McDonald criteria[12, 23]. Therefore, IgG isoelectric focusing followed by immunofixation electrophoresis is increasingly employed to be a routine laboratory technique for those patients with neuropathy to perform oligoclonal band analysis in order mainly to aid early differential diagnosis of multiple sclerosis. The mirror patterns are usually an incidental finding during CSF OCB analysis[24]. Due to the rarity, the laboratory interpretation to the mirror patterns is still often ambiguous[13], not to mention most neurologists involuntarily weaken the clinical significance of this patterns[4]. In this retrospective study, we spent more than four years focusing on the value of OCB analysis in the neurological diseases, ultimately only 12 patients who presented mirror patterns were screened out from 5892 patients. The very low detection rate of just only 0.2% indeed made the possible clinical implications overlooked. Subsequently, the 12 specimens were thoroughly analyzed combined with various clinical information.

First of all, 12 cases covered all types of the mirror patterns, among which only patient No.5 displayed the “type 3”, patient No.6 and 11 were “type 4”, the remaining were “type 5”. For any equivocal bands, IFE is the definitive method to evaluate. The immunofixation electrophoresis demonstrated that three types of mirror patterns tightly linked with M protein. In our study, both the two type 4 cases (patient No.6 and 11) are positive for M protein; 7 out of 9 cases with the mirror pattern 5 were related to M protein; well, only one patient with type 3 (patient No.5) are negative in M protein. Whereas, only one case of mirror pattern of type 3 cannot rule out the possibility of M protein positive, case report by Chen had revealed that the same mirror bands of type 3 coexisted with IgG-κ monoclonal protein[10]. Our findings, beyond the previous recognition that the pattern 4 mainly resulted from the systemic inflammation and pattern 5 implied the monoclonal gammopathy [8], suggested that 3 types of mirror pattern bands were all closely associated with M protein. In addition, the significantly elevated intrathecal synthesis of 5 cases (No. 1,3,5,11,12) were in accordance with the QALB, which meant more active immune reactions originate from perivascular infiltrates of B-lymphocytes through damaged blood-brain barrier. Consequently, the OCB results of 5 cases indeed presented relatively more prominent bands than other cases. Nevertheless, whether it’s prominent or subtle bands had nothing to do with M protein, which means the prominent bands didn’t necessarily indicate the positive M protein and the subtle bands should also be alert to the presence of M protein. Our results demonstrated that mirror pattern bands primarily originated from peripheral serum M protein and also highlighted the valuable clinical implications of all the three types of mirror patterns.

Secondly, all the 12 cases started with neurological symptoms and subsequently admitted to the neurology department. But, eventually none of the 12 patients were diagnosed with MS. 8 out of 12 cases

(patient No.1,2,3,4,5,7,8,11) were at the onset of atypical demyelinating lesion of peripheral nervous system. 6 out of 8 cases (patient No.1,2,3,7,8,11) were positive with M protein. All the above 6 patients except the patient No.7 were ultimately diagnosed with blood system disease after admission to the hospital, who benefited from timely detection of OCB and reasonable analysis without any delay. Moreover, the patient No.7 was diagnosed as MM after three-year follow-up since discharged from hospital. It makes sense that there exists a likely causal relationship between the M protein and peripheral neuropathy. The pathogenesis is thought to be a direct effect of M proteins on the peripheral nerve, resulting in a demyelinating process, which causes a series of clinical symptoms. Whereas, clinically, it's very hard to distinguish monoclonal gammopathy-associated peripheral neuropathy from other cases of neuropathy due to the complexity of pathogeny. The precise diagnosis is of vital importance, because the early treatments considerably improve the outcome. Besides, it's noteworthy that there were three patients (No.4,5,9) presenting mirror patterns with negative M protein. The three patients were respectively diagnosed with Amyotrophic lateral sclerosis, Inflammatory mediated demyelination and Dementia with Lewy body. However, unfortunately, so far it was still poorly understood why the mirror patterns appeared in the above three diseases.

Among the 12 patients included in our study, a total of 7 patients were diagnosed with blood system related diseases. Two cases (No.2 and 11) were diagnosed POEMS syndrome, three cases (No.3,7 and 8) were monoclonal gammopathy of undermined significance (MGUS) and two cases (No.1 and 12) were multiple myeloma (MM). Admittedly, the 58.3% positive rate (7/12) was conservative, because some patients with mirror patterns who didn't diagnosed with blood system disorder in the short time were highly likely to be diagnosed maybe a few years later. The presence of mirror patterns was though almost excluded the possibility of MS, provided an additional and powerful evidence to the diagnose of blood system diseases. Amounts of researches concluded that MGUS was present in more than 3% to 4% of population older than age 50 years[25] and was regarded as a premalignant precursor of MM and often categorized as low-tumor-burden diseases as well[26], almost all cases of the MM was preceded by MGUS[27, 28]. Based on the researches, it's very necessary to closely follow up on those patients (such as the No.6 and 10 in our study) with mirror pattern bands and positive M protein but who were still not diagnosed as blood system disorder yet in the short term. In the following study, we still need to shed light on whether all the positive M protein can lead to the occurrence of mirror patterns no matter what types of or it just happens on the patients with neurologic disability. In addition, we also need next to figure it out what does it means that mirror patterns accompanied by negative M protein.

Conclusions

The analysis of OCB is very helpful for differential diagnoses. Any abnormal OCB bands could convey valuable diagnostic implications. In this study, we firstly highlight the clinical significance of mirror patterns during cerebrospinal fluid oligoclonal band analysis, which absolutely cannot be underestimated, although our results are to certain degree limited by the relatively small sample size. Furthermore, we figure it out that all three mirror pattern bands closely connected with M protein. It's

necessary for the patients with results of mirror pattern bands to perform immunofixation electrophoresis timely.

Method

1. Patients and Routine blood and CSF analysis

5892 patients with various neurological symptoms in the department of neurology in our hospital received CSF OCB analysis, of which the results of only just 12 patients displayed mirror pattern. Lumbar puncture and all specimens (CSF and serum) of these 12 patients were obtained for routine determination of IgG and albumin quantitation both in CSF and serum, evidence of intrathecal immunoglobulin synthesis (IgG-Syn) was based on the calculation according to the method of Reiber-Felgenhauer[19]. IgG-Syn demonstrates an immunologic reaction in the CNS, the upper limit of reference >9 is thought to have immune response[20]. CSF/serum albumin quotients ($QALB = \text{CSF albumin} / \text{serum albumin}$) is to assess the integrity of blood-CSF barrier. The upper reference limit of $QALB \times 10^3 > 8$ for the patients over 40 years predicts blood-CSF barrier disfunction[21]. In addition to laboratory parameters, we also analyzed the 12 patients in great detail with clinical characteristics including first clinical manifestations and suspected or confirmed diagnosis.

2. Oligoclonal band determination and Immunofixation electrophoresis

IgG and albumin in CSF and serum were quantified respectively by kinetic nephelometry (Beckman Coulter IMMAGE800). Paired serum/CSF samples were used to analyze the IgG-specific OCB performed with IgG-isoelectric focusing on agarose gel followed by immunofixation (HYDRASYS FOCUSING, Sebia, France)[22]. Before IEF, serum samples were diluted in deionized water to reach the same IgG concentration as that of parallel CSF samples. Serum samples are run in parallel to CSF samples. The patterns were interpreted qualitatively by comparing the presence or absence of OCB in CSF and serum. The present of two or more bands in the electrophoresis lanes are considered to be positive reaction[12].

Immunofixation electrophoresis was performed on a commercial hydrogel kit with a Sebia HYDRASYS 2 automated electrophoresis system (Sebia, Evry, France). The IFE method used polyclonal antihuman serum samples for identifying IgG, IgA, IgM, and total light chains κ and λ .

Abbreviations

NO.: patient number, Age: patient age in years, CSF: cerebrospinal fluid, TP: total protein, OCB: oligoclonal bands, QALB: CSF/serum albumin quotient, IgG-Syn: intrathecal IgG synthesis, C-IgG: CSF IgG, S-IgG: Serum IgG, MS: multiple sclerosis, SIE: serum immunofixation electrophoresis, P3: pattern 3, P4: pattern 4, P5: pattern 5, ND: not detected; MGUS: monoclonal gammopathy of undermined significance; MM: Multiple myeloma, POEMS: POEMS syndrome, MGAPU: monoclonal gammopathy-associated peripheral neuropathy; ALS: Amyotrophic lateral sclerosis DLB: Dementia with Lewy body, IMD: Inflammatory mediated demyelination.

Declarations

Ethics approval and consent to the participate

This study was approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University (Beijing, China), and written informed consent were obtained from all participants.

Consent for publication

All the authors have read and approved the paper for publication.

Availability of data and materials

All data generated or analyzed this study are included in the article.

Competing interests

The authors declare no conflicts of interest.

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Author's contributions

Jinling Wang designed the study, collected and analyzed the data, and then wrote the manuscript. Peichang Wang made the critical revision of the manuscript. All authors have given final approval of the version to the published.

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References

1. Andlovic A, Babic M, Accetto S, Rot U: Comparison of two methods for the detection of oligoclonal bands in a large number of clinically isolated syndrome and multiple sclerosis patients. *Clin Neurol*

Neurosurg 2012, 114(6):659-662.

2. Davies G, Keir G, Thompson EJ, Giovannoni G: The clinical significance of an intrathecal monoclonal immunoglobulin band: a follow-up study. *Neurology* 2003, 60(7):1163-1166.
3. Villar LM, Masterman T, Casanova B, Gomez-Rial J, Espino M, Sadaba MC, Gonzalez-Porque P, Coret F, Alvarez-Cermeno JC: CSF oligoclonal band patterns reveal disease heterogeneity in multiple sclerosis. *Journal of neuroimmunology* 2009, 211(1-2):101-104.
4. Link H, Huang YM: Oligoclonal bands in multiple sclerosis cerebrospinal fluid: an update on methodology and clinical usefulness. *Journal of neuroimmunology* 2006, 180(1-2):17-28.
5. Abaira V, Alvarez-Cermeno JC, Arroyo R, Camara C, Casanova B, Cubillo S, de Andres C, Espejo C, Fernandez O, Ferrer J *et al*: Utility of oligoclonal IgG band detection for MS diagnosis in daily clinical practice. *J Immunol Methods* 2011, 371(1-2):170-173.
6. Lechner-Scott J, Spencer B, de Malmanche T, Attia J, Fitzgerald M, Trojano M, Grand'Maison F, Gomez JA, Izquierdo G, Duquette P *et al*: The frequency of CSF oligoclonal banding in multiple sclerosis increases with latitude. *Mult Scler* 2012, 18(7):974-982.
7. Masjuan J, Alvarez-Cermeno JC, Garcia-Barragan N, Diaz-Sanchez M, Espino M, Sadaba MC, Gonzalez-Porque P, Martinez San Millan J, Villar LM: Clinically isolated syndromes: a new oligoclonal band test accurately predicts conversion to MS. *Neurology* 2006, 66(4):576-578.
8. Andersson M, Alvarez-Cermeno J, Bernardi G, Cogato I, Fredman P, Frederiksen J, Fredrikson S, Gallo P, Grimaldi LM, Gronning M *et al*: Cerebrospinal fluid in the diagnosis of multiple sclerosis: a consensus report. *J Neurol Neurosurg Psychiatry* 1994, 57(8):897-902.
9. von Glehn F, Farias AS, de Oliveira AC, Damasceno A, Longhini AL, Oliveira EC, Damasceno BP, Santos LM, Brandao CO: Disappearance of cerebrospinal fluid oligoclonal bands after natalizumab treatment of multiple sclerosis patients. *Mult Scler* 2012, 18(7):1038-1041.
10. Chen Y: Multiple cerebrospinal fluid bands with accompanying serum bands. *Clin Chem* 2014, 60(12):1582-1583.
11. Petzold A: Intrathecal oligoclonal IgG synthesis in multiple sclerosis. *Journal of neuroimmunology* 2013, 262(1-2):1-10.
12. Freedman MS, Thompson EJ, Deisenhammer F, Giovannoni G, Grimsley G, Keir G, Ohman S, Racke MK, Sharief M, Sindic CJ *et al*: Recommended standard of cerebrospinal fluid analysis in the diagnosis of multiple sclerosis: a consensus statement. *Arch Neurol* 2005, 62(6):865-870.
13. Chen Y, Watts G: Systemic inflammation or monoclonal gammopathy? *Arch Pathol Lab Med* 2011, 135(12):1527-1529.

14. Franciotta D, Zardini E, Lolli F: The clinical significance of an intrathecal monoclonal immunoglobulin band: a follow-up study. *Neurology* 2004, 62(4):675; author reply 675-676.
15. Reiber H, Thompson EJ, Grimsley G, Bernardi G, Adam P, Monteiro de Almeida S, Fredman P, Keir G, Lammers M, Liblau R *et al*: Quality assurance for cerebrospinal fluid protein analysis: international consensus by an Internet-based group discussion. *Clin Chem Lab Med* 2003, 41(3):331-337.
16. Wu Y, Yang X, Wang T, Wang H, Li Z: Identification of M protein from filter paper using serum protein and immunofixation electrophoresis. *Am J Clin Pathol* 2012, 138(4):604-608.
17. Haertle M, Kallweit U, Weller M, Linnebank M: The presence of oligoclonal IgG bands in human CSF during the course of neurological diseases. *J Neurol* 2014, 261(3):554-560.
18. Reiber H, Peter JB: Cerebrospinal fluid analysis: disease-related data patterns and evaluation programs. *J Neurol Sci* 2001, 184(2):101-122.
19. Reiber H: Cerebrospinal fluid–physiology, analysis and interpretation of protein patterns for diagnosis of neurological diseases. *Mult Scler* 1998, 4(3):99-107.
20. McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD, McFarland HF, Paty DW, Polman CH, Reingold SC *et al*: Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Ann Neurol* 2001, 50(1):121-127.
21. Blennow K, Fredman P, Wallin A, Gottfries CG, Karlsson I, Langstrom G, Skoog I, Svennerholm L, Wikkelso C: Protein analysis in cerebrospinal fluid. II. Reference values derived from healthy individuals 18-88 years of age. *Eur Neurol* 1993, 33(2):129-133.
22. Sadaba MC, Gonzalez Porque P, Masjuan J, Alvarez-Cermeno JC, Bootello A, Villar LM: An ultrasensitive method for the detection of oligoclonal IgG bands. *J Immunol Methods* 2004, 284(1-2):141-145.
23. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, Fujihara K, Havrdova E, Hutchinson M, Kappos L *et al*: Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011, 69(2):292-302.
24. Chen Y: Laboratory Performance on Reporting Monoclonal Gammopathy During Cerebrospinal Fluid Oligoclonal Banding Analysis from External Quality Assessment Surveys. *the Journal of APPLIED LABORATORY MEDICINE* 2018, 3(2):261-266.
25. Go RS, Swanson KM, Sangaralingham LR, Habermann EB, Shah ND: Clinical prevalence (diagnosed cases) of monoclonal gammopathy of undetermined significance in the US: estimating the burden on health care. *Leukemia* 2016, 30(6):1443-1446.

26. Willrich MAV, Murray DL, Kyle RA: Laboratory testing for monoclonal gammopathies: Focus on monoclonal gammopathy of undetermined significance and smoldering multiple myeloma. *Clin Biochem* 2018, 51:38-47.
27. Chaudhry HM, Mauermann ML, Rajkumar SV: Monoclonal Gammopathy-Associated Peripheral Neuropathy: Diagnosis and Management. *Mayo Clin Proc* 2017, 92(5):838-850.
28. Dhodapkar MV: MGUS to myeloma: a mysterious gammopathy of underexplored significance. *Blood* 2016, 128(23):2599-2606.

Tables

Table 1. The primary laboratory parameters of the 12 patients with mirror patterns

No.	Gender	Age	CSF TP (mg/dl)	QALB ($\times 10^3$)	C-IgG(mg/dl)	S-IgG (mg/dl)	OCB patterns	IgG-syn	SIE (+/-)
1	Female	62	141	20.9	37.9	3160	P5	45.6	+IgG- κ
2	Male	53	56	9.1	4.95	1040	P5	5	+IgG- κ
3	Female	62	181	37	35.2	1200	P5	84.7	+IgG- λ
4	Male	55	39	7	7.53	1260	P5	7.9	ND
5	Male	68	123	24	13.9	1040	P3	14.22	ND
6	Female	53	64	9.8	7.06	1860	P4	0	+IgG- λ
7	Female	42	21	3.3	2.66	1160	P5	2.85	+IgG- λ
8	Male	69	30	4.2	2.78	1300	P5	1.55	+IgG- λ
9	Male	72	41	6.4	4.33	1280	P5	3.37	ND
10	Male	65	49	6.5	4.46	1450	P5	1.18	+IgG- λ
11	Male	59	173	38	45.1	1990	P4	61.5	+IgG- λ
12	Female	54	94	12.6	18.3	2130	P5	32.5	+IgG- λ

NO.: patient number, Age: patient age in years, CSF: cerebrospinal fluid, TP: total protein, OCB: oligoclonal bands, QALB: CSF/serum albumin quotient, IgG-Syn: intrathecal IgG synthesis, C-IgG: CSF IgG, S-IgG: Serum IgG, MS: multiple sclerosis, SIE: serum immunofixation electrophoresis, P3: pattern 3, P4: pattern 4, P5: pattern 5, ND: not detected

Table 2. Overview of the clinical characteristics of 12 patients

No.	First and primary clinical manifestation	Confirmed diagnosis
1	Numbness and weakness of both lower limbs for 2 years	MM
2	Burning sensation on both feet for half a year	POEMS
3	Numbness and weakness of both lower limbs for two years, walking unsteadily for a month	MGUS
4	Progressive muscle weakness of lower limbs for 2 years	ALS
5	Numbness and weakness of both lower limbs for 53 days	IMD
6	Paroxysmal consciousness disorder with limb stiffness for 18 days	Viral encephalitis?
7	Numbness and weakness of both lower limbs for 5 months	1Demyelinating myelopathy 2MGAPU 3MGUS
8	Cold sensation on both lower limbs for 3 years, walking unsteadily for 1.5 years	MGUS
9	Memory loss for half a year	DLB
10	Narcolepsy for 29 years and paroxysmal falls for 1 year	Narcolepsy
11	Numbness of two feet for 1 month, weakness of both lower limbs for 25 days	POEMS
12	Fever for 5 days, clouding of consciousness for 3 days	1Epstein-Barr viral encephalitis 2MM

MM: Multiple myeloma, POEMS: POEMS syndrome, MGAPU: monoclonal gammopathy-associated peripheral neuropathy, MGUS: monoclonal gammopathy of undetermined significance, ALS: Amyotrophic lateral sclerosis DLB: Dementia with Lewy body, IMD: Inflammatory mediated demyelination

Figures

Figure 1

Results of isoelectric focusing electrophoresis and immunofixation electrophoresis in 12 cases with mirror patterns. (A) Isoelectric focusing of the patient's CSF and Serum samples. C lane: CSF sample. S lane: corresponding serum sample. (B) Results of serum immunofixation electrophoresis in the corresponding patient.