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Prevalence and Patterns of Cranial Nerve Involvement in CIDP, Autoimmune Nodopathy, MMN, and Anti-MAG Neuropathy: A Multicenter Korea/UK Study of 582 Patients

Young Gi Min[1,2] | Hyunjin Kim[3] | Hee Jo Han[2] | Byeol-A Yoon[4] | Jong Kuk Kim[4] | Woohee Ju[5] | Seok-Jin Choi[6] | Sung-Min Kim[6] | Ki Hoon Kim[2] | Young Nam Kwon[2] | Seung Woo Kim[2] | Eun-Jae Lee[3] | Young-Min Lim[3] | Kabir K. Nazeer[7] | Yusuf A. Rajabally[7,8] | Ha Young Shin[2,9,10] | Jung-Joon Sung[1,6]

[1]Department of Neurology, Seoul National University College of Medicine, Seoul, Korea | [2]Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea | [3]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea | [4]Department of Neurology, Dong-A University Hospital, Dong-A University College of Medicine, Busan, Republic of Korea | [5]Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, Republic of Korea | [6]Department of Neurology, Seoul National University Hospital, Seoul, Korea | [7]Aston Medical School, Aston University, Birmingham, UK | [8]Inflammatory Neuropathy Service, Neurology, Queen Elizabeth Hospital Birmingham, Birmingham, UK | [9]Brain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea | [10]Graduate Program of Biomedical Engineering, Yonsei University College of Medicine, Seoul, Republic of Korea

Correspondence: Yusuf A. Rajabally (y.rajabally@aston.ac.uk) | Ha Young Shin (hayshin@yuhs.ac) | Jung-Joon Sung (jjsaint@snu.ac.kr)

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ABSTRACT

Background: Cranial nerve involvement is a well-recognized feature in Guillain–Barré syndrome (GBS) but remains less well understood in chronic forms of autoimmune neuropathies. Earlier studies of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) were conducted before updated diagnostic criteria and the recognition of autoimmune nodopathy (AN), which may limit the interpretation of their findings.

Methods: We retrospectively analyzed 582 patients with chronic autoimmune neuropathies—CIDP ($n = 431$), multifocal motor neuropathy (MMN) ($n = 64$), anti-myelin-associated glycoprotein (MAG) neuropathy ($n = 54$), and AN ($n = 33$)—from 4 Korean and 1 UK centers. Patients with cranial nerve involvement were identified and described. CIDP patients with cranial nerve involvement (cranial+ CIDP) were compared with those without (cranial− CIDP).

Results: Cranial nerve involvement was observed in 8.8% (38/431) of CIDP and 24.2% (8/33) of AN patients but was absent in MMN (0/64) and anti-MAG neuropathy (0/54). Facial palsy was overall the most common manifestation (CIDP: 45%, AN: 50%). Patients with AN more frequently exhibited bilateral optic neuropathy (50%) and facial diplegia (38%), while CIDP patients more often showed trigeminal neuropathy and oculomotor nerve palsy (both 32%). Compared with cranial− CIDP, cranial+ CIDP patients were more often younger, of variant subtypes (especially multifocal), presented (sub)acutely with preceding infection/vaccination, followed by relapsing–remitting rather than progressive courses, and achieved greater improvement despite greater pre-treatment disability.

Conclusions: Cranial nerve involvement serves as a diagnostic clue in chronic autoimmune neuropathies, particularly in identifying AN and CIDP. Cranial+ CIDP appears to represent a distinct subset with partial overlap to GBS, suggesting unique underlying mechanisms.

Young Gi Min and Hyunjin Kim contributed equally as co-first authors.

1 | Introduction

Chronic autoimmune neuropathies are a heterogeneous group of disorders of the peripheral nervous system. Representative entities include chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), anti-myelin-associated glycoprotein (MAG) neuropathy, and the recently recognized autoimmune nodopathy (AN) [1, 2]. Although these conditions share overlapping clinical features, advances in antibody testing and diagnostic criteria have increasingly distinguished them as separate disease groups with distinct pathophysiological mechanisms and therapeutic responses.

Cranial nerve involvement is a well-known feature in Guillain–Barré syndrome (GBS), an acute autoimmune neuropathy, affecting up to 50% of patients [3–6]. By contrast, its prevalence, patterns, and clinical significance in chronic autoimmune neuropathies remain incompletely defined. Earlier reports suggested that cranial neuropathies may occur in a subset of CIDP patients, typically affecting the facial or extra-ocular motor (EOM) nerves [7–10]. However, most of these investigations were conducted using earlier diagnostic criteria and before the recognition of AN, which may limit the interpretation of their findings. Cranial nerve manifestations have also been described in anecdotal AN cohorts, but their frequency, patterns, and diagnostic relevance remain to be fully elucidated [11, 12].

These uncertainties underscore the need to examine cranial nerve involvement across the spectrum of chronic autoimmune neuropathies in a large, contemporary cohort. In this study, we investigated an international, multicenter cohort to (i) determine the prevalence and clinical patterns of cranial nerve involvement across different disease entities, and (ii) compare the clinical characteristics of CIDP patients with cranial nerve involvement with those without.

2 | Methods

2.1 | Study Participants and Approval

This study recruited consecutive patients with chronic autoimmune neuropathies between January 2015 and April 2025 from 4 Korean and 1 UK centers. Patients were eligible if (i) they had been diagnosed with either CIDP, MMN, anti-MAG neuropathy, or AN, and if (ii) they had documented symptoms of cranial nerve involvement supported by corresponding signs and/or tests. Clinical diagnoses were made based on the relevant disease-specific guidelines, and the diagnosis of AN was established in subjects who tested positive by cell-based assay or enzyme-linked immunosorbent assay [1, 13]. Ganglioside IgG/IgM and MAG IgM antibodies were systematically tested using enzyme-linked immunosorbent assay (ELISA) in all subjects. AN antibodies were tested using cell-based assays and ELISA. At the three centers in Seoul, testing was performed in all patients. At University Hospitals Birmingham, all patients with a clinical diagnosis of suspected CIDP or AN underwent AN antibody testing. At Dong-A University Hospital, testing was performed in patients who exhibited guideline-defined clinical features suggestive of AN, as suggested by current guidelines [1]. To investigate the clinical characteristics of CIDP patients with cranial nerve involvement, consecutive CIDP patients evaluated at Seoul National University Hospital during the same period were also collected as a control group.

The study protocol was approved at the local institutional review boards (Korea: 2504–118-1632, UK: CARMS-20702). Informed consent was waived due to the retrospective nature of this study.

2.2 | Data Collection

Neuromuscular specialists at each center (YGM, HK, HHJ, BAY, YAR) retrospectively collected data on patient demographics, onset patterns, and clinical course, phenotypes, disability, detailed clinical patterns of cranial nerve involvement, and immunotherapies administered [14]. Symptoms and signs of olfactory nerve impairment were not assessed systematically and were therefore excluded from the analysis. The accessory nerve was also excluded because isolated evaluation is difficult, as the trapezius and sternocleidomastoid muscles receive overlapping innervation from the upper cervical nerves. If available, neurophysiological tests related to cranial nerves, such as blink reflex, visual and auditory evoked potentials, facial nerve conduction studies, as well as brain, spinal cord, and cranial nerve magnetic resonance imaging, were also collected. In cases with central nervous system (CNS) lesions, the presence of oligoclonal bands (OCBs) and serum autoantibodies against aquaporin-4 (AQP4) and myelin oligodendrocyte (MOG) were also evaluated.

Korean centers employed the Inflammatory Neuropathy Cause and Treatment (INCAT) scores, while disability in the Birmingham (UK) cohort was assessed using the Overall Neuropathy Limitation Scale (ONLS), which is closely related to the INCAT scale [15, 16]. The ONLS provides a more gradual assessment of lower limb function, with subscores ranging from 0 to 7. To harmonize disability measurements across cohorts, the lower limb ONLS subscores of the Birmingham subjects were converted as follows: $0 \rightarrow 0$, $1–2 \rightarrow 1$, $3 \rightarrow 2$, $4 \rightarrow 3$, $5 \rightarrow 4$, and $6–7 \rightarrow 5$. Upper limb ONLS subscores were regarded as equivalent to the corresponding INCAT subscores.

2.3 | Statistical Analysis

Data were presented as mean (standard deviation [SD]) for continuous variables and as frequency (%) for categorical variables. Differences between groups were assessed using *t*-tests, Mann–Whitney *U* tests, Chi-square tests, or Fisher's exact tests as appropriate. Pairwise comparison results were adjusted using the Benjamini–Hochberg method. All analyses and graphical presentations were performed using R version 4.4.2.

3 | Results

3.1 | Prevalence of Cranial Nerve Involvement Across Neuropathy Subtypes

We reviewed the medical records of 582 patients with chronic autoimmune neuropathies (CIDP, $n = 431$; MMN, $n = 64$; anti-MAG neuropathy, $n = 54$; AN, $n = 33$) from 5 centers (Seoul National University Hospital, $n = 182$; University Hospitals Birmingham, $n = 224$; Severance Hospital, $n = 94$; Asan Medical

Center, $n=62$; Dong-A University Hospital, $n=31$). Among the 33 patients with AN, 22 had NF155, 5 had CNTN1, 4 had CASPR1, and 1 patient each had NF186 and pan-NF antibodies. Cranial nerve involvement was identified in 38 CIDP and 8 AN patients. Prevalence of cranial nerve involvement was highest in AN (24.2%), followed by CIDP (8.8%), whereas there was no cranial nerve involvement in patients with anti-MAG neuropathy or MMN (Figure 1A).

3.2 | Patterns of Cranial Nerve Involvement in CIDP and AN

Clinical characteristics of cranial nerves involving CIDP and AN patients are summarized in Table S1. Overall, the two groups were comparable in terms of onset age ($p>0.9$), sex ($p=0.12$), disease duration ($p=0.4$), initial symptom ($p=0.7$), presence of motor weakness (proximal: $p>0.9$, distal: $p=0.13$), and INCAT scores at baseline ($p>0.9$) and at last follow-up ($p=0.4$). However, AN patients were significantly more likely to exhibit ataxia (100% vs. 49%, $p=0.007$) and tremor (75% vs. 19%, $p=0.006$) compared to those with CIDP. Ganglioside antibodies were detected in foru patients with CIDP (3 multifocal and 1 distal subtype), whereas none of the AN patients were positive ($p>0.9$).

Phenotypic or serologic subtypes in cranial-involving CIDP and AN patients are illustrated in Figure 1B. Among the 38 subjects with cranial-involving CIDP, typical CIDP was the most common subtype (17/38, 44.7%), closely followed by multifocal CIDP (14/38, 36.8%). The remaining 7 patients had distal CIDP. Among 8 patients with cranial-involving AN, 5 (62%) were positive for NF155 antibodies, while 1 patient each was positive for pan-NF, NF186, and CNTN1 antibodies. The frequency of cranial nerve involvement according to target antigens of AN was 22.7% (5/22) in NF155, 20% (1/5) in CNTN1, 0% (0/4) in CASPR1, and 100% (2/2) in NF186/pan-NF, with no statistically significant differences overall ($p=0.09$).

The frequency and laterality of involvement for each cranial nerve in CIDP and AN are summarized in Table 1, with case-level details illustrated in Figure 2. The most commonly affected nerve in both CIDP (17/38, 45%; bilateral in 5) and AN (4/8, 50%, bilateral in all) was the facial nerve. Bilateral facial neuropathy was significantly more common in AN than in CIDP ($p=0.036$). No clinical evidence of vestibulocochlear nerve involvement was observed in any subject. Overall, CIDP was more frequently associated with trigeminal nerve involvement (12/38, 32%, bilateral in 4 vs. 0/8), oculomotor neuropathy (12/38, 32%, bilateral in 3 vs. 1/8, 13%, bilateral in 0), and hypoglossal neuropathy (4/38, 11%, bilateral in 0 vs. 0/8) compared with AN. In contrast, AN patients more frequently exhibited optic neuropathy (3/8, 38%, bilateral in 3 vs. 4/38, 11%, bilateral in 1). Bilateral optic neuropathy was significantly more common than in CIDP ($p=0.013$).

When stratified by CIDP subtype, bilateral trigeminal nerve involvement was more common in typical CIDP than in variants (4/17, 24% vs. 0/21, 0%, $p=0.032$). Bilateral involvement of other cranial nerves also tended to be more frequent in typical CIDP, but these differences did not reach statistical significance. Multifocal CIDP showed a marginally higher frequency of EOM palsy compared with typical CIDP (10/14, 71% vs. 6/17, 35%, $p=0.073$), with oculomotor nerve palsy being the most frequent manifestation.

Brain and/or spinal cord lesions on MRI were identified in five CIDP (2 typical, 2 multifocal, and 1 distal) and one AN patient with NF155 IgG. In the CIDP group, three had combined brain and spinal cord involvement, and one had brain and spinal cord lesions only. The NF155 AN patient had brain lesions. Among these five patients, three (2 CIDP and 1 AN) also exhibited optic nerve involvement. One patient with typical CIDP experienced recurrent brain attacks with multiple sclerosis-like features and was treated with disease-modifying treatment. Among the seven patients with CNS lesions (including optic neuropathy), none had detectable CSF OCBs (0/5 tested), serum AQP4 (0/4 tested), or MOG (0/7 tested) antibodies.

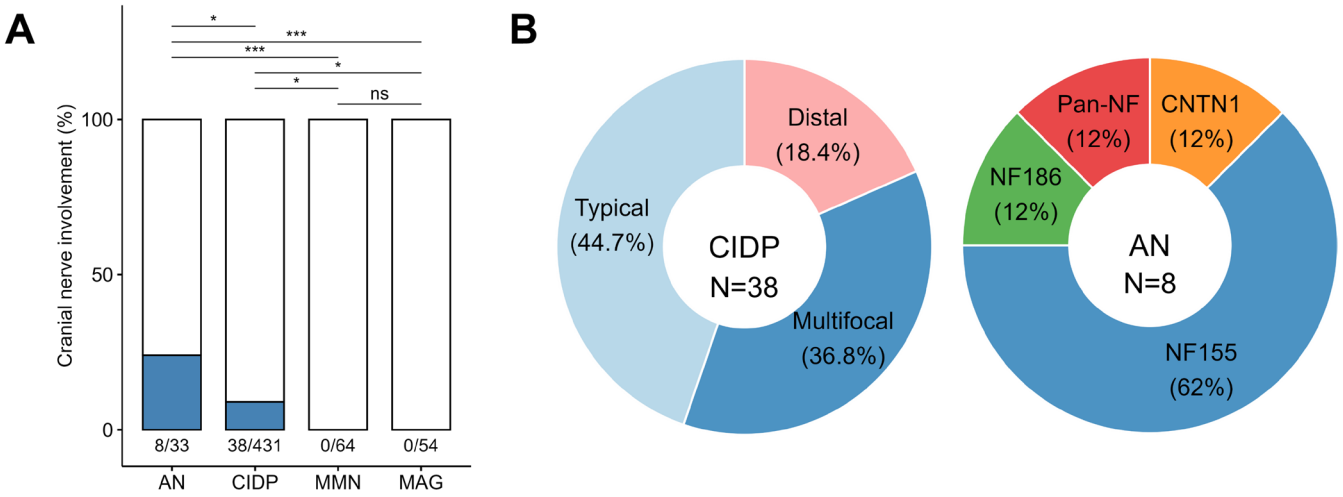

FIGURE 1 | Summary of cranial nerve involvement in chronic autoimmune neuropathies (A) Prevalence of cranial nerve involvement (*$p<0.05$, **$p<0.01$, ***$p<0.001$, ns = not significant). (B) Phenotypic and serologic subtypes of CIDP and AN patients involving cranial nerves. AN, autoimmune nodopathy; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; MAG, anti-myelin-associated glycoprotein neuropathy; MMN, multifocal motor neuropathy.

TABLE 1 | Frequency and laterality of cranial nerve, brain, and spinal cord involvement according to CIDP and AN subtypes.

	CIDP				AN			
Group	**Total**	**Typical**	**Multifocal**	**Distal**	**Total**	**NF155**	**NF186 / Pan-NF**	**CNTN1**
Subjects, N	38	17	14	7	8	5	2	1
Cranial nerve involvement, *n* (%) Bilateral, *n*/Unilateral, *n*								
II	4 (11%) 1/3*	2 (12%) 1/1	0 (0%)	2 (29%) 0/2	3 (38%) 3/0	2 (40%) 2/0	1 (50%) 1/0	0 (0%)
III	12 (32%) 3/9	4 (24%) 2/2	6 (43%) 1/5	2 (29%) 0/2	1 (13%) 0/1	1 (20%) 0/1	0 (0%)	0 (0%)
IV	1 (3%) 1/0	1 (6%) 1/0	0 (0%)	0 (0%)	1 (13%) 0/1	0 (0%)	0 (0%)	1 (100%) 0/1
V	12 (32%) 4/8	8 (47%) 4/4#	3 (21%) 0/3	1 (14%) 0/1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
VI	7 (18%) 2/5	2 (12%) 1/1	4 (29%) 1/3	1 (14%) 0/1	1 (13%) 0/1	1 (20%) 0/1	0 (0%)	0 (0%)
VII	17 (45%) 5/12*	9 (53%) 4/5	6 (43%) 1/5	2 (29%) 0/2	4 (50%) 4/0	2 (40%) 2/0	1 (50%) 1/0	1 (100%) 1/0
VIII	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IX–XI	6 (16%)	4 (24%)	1 (7%)	1 (14%)	2 (25%)	1 (20%)	1 (50%)	0 (0%)
XII	4 (11%) 0/4	2 (12%) 0/2	2 (14%) 0/2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Brain or Spinal cord involvement, *n* (%)								
Brain	4 (11%)	2 (12%)	1 (7%)	1 (14%)	1 (13%)	1 (20%)	0	0
Spinal cord	4 (11%)	2 (12%)	1 (7%)	1 (14%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Note: ($p < 0.05$: *, CIDP vs. AN; #, Typical CIDP vs CIDP variants).

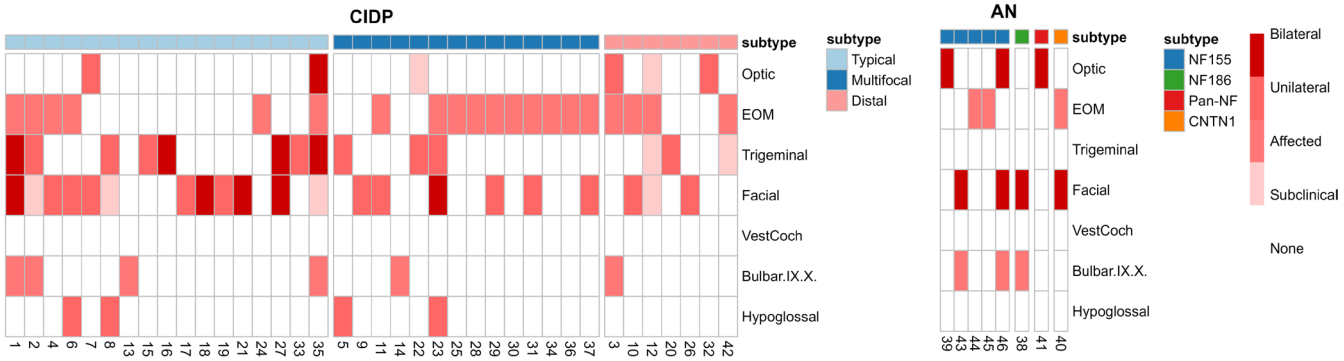

FIGURE 2 | Case-by-case summary of cranial nerve involvement in CIDP and AN patients. AN, autoimmune nodopathy; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; EOM, extra-ocular motor; VestCoch, vestibulo-cochlear nerve.

3.3 | Clinical Characteristics of CIDP Patients With Cranial Involvement

Thirty-eight CIDP patients involving cranial nerves ("Cranial+ CIDP") were compared with 93 patients without cranial nerve involvement ("Cranial− CIDP"). Compared to the Cranial− CIDP cohort, patients with cranial+ CIDP developed disease at a younger age (37.4 (17.5) vs. 50 (14.2) years, $p < 0.001$), were more frequently of the variant subtype (55% vs. 31%, $p < 0.001$), had an acute or subacute onset (82% vs. 15.3%, $p < 0.001$), and more often had preceding infections or vaccinations (24% vs. 2%, $p < 0.001$). A relapsing–remitting course was more common in cranial+ CIDP subjects than those with cranial− CIDP (55% vs. 12%, $p < 0.001$) rather than progressive

disease. CSF protein levels were marginally higher in cranial+ CIDP, but this difference did not reach significance ($p = 0.052$). Baseline INCAT scores were marginally worse in cranial+ CIDP ($p = 0.057$), primarily due to greater upper limb disability ($p = 0.003$), despite comparable lower limb involvement ($p = 0.2$). At follow-up, INCAT scores were better in cranial+ CIDP subjects ($p = 0.003$), and the degree of INCAT improvement was also greater in this group ($p < 0.001$). There was no significant difference in the type of first-line treatment between groups. They received a greater number of different immunotherapies overall ($p < 0.001$); while rituximab use did not differ between groups, oral immunosuppressants were more frequently administered in cranial+ CIDP (68% vs. 40%, $p = 0.004$) (Table 2).

4 | Discussion

In this multicenter cohort of 582 patients with 4 chronic autoimmune neuropathies, cranial nerve involvement was identified in 8.8% (38/431) of CIDP patients and 24.2% (8/33) of AN patients, whereas no such cases were observed in MMN (0/64) or anti-MAG neuropathy (0/54). Facial palsy was the most frequent cranial nerve manifestation overall. AN patients more often exhibited bilateral optic neuropathy and facial diplegia, while CIDP patients more frequently showed trigeminal and oculomotor nerve involvement. Compared to CIDP without cranial involvement, patients with cranial+ CIDP were younger, more often had variant subtypes, presented acutely or subacutely, and followed a relapsing–remitting course with preceding immune triggers. Despite greater disability at baseline, cranial+ CIDP patients demonstrated greater improvement and outcomes, and were treated with a higher number of immunotherapies.

In our cohort, cranial nerve involvement was observed in nearly one-quarter of AN patients, a frequency significantly higher than that of other forms of chronic autoimmune neuropathies. This aligns with previous European cohorts, where cranial neuropathies were documented in approximately 30% of patients with NF155 ($n = 41$) or CNTN1 AN ($n = 31$) [11, 12], most commonly presenting as facial palsy. Similarly, the International CIDP Outcome Study (ICOS) reported a higher prevalence of cranial nerve involvement in AN (34%) compared to seronegative CIDP (11%), with facial palsy being present in all AN cases [17]. This observation was further corroborated by a large prospective study of 1500 patients [18]. Taken together, our data and prior evidence establish cranial nerve involvement as a characteristic feature of AN, distinguishing it from other forms of autoimmune neuropathies. From a mechanistic perspective, cranial nerve or brain involvement in AN may be related to intrathecal antibody synthesis [19]. Although our study was limited by the small number of AN subjects and could not draw definitive conclusions, emerging evidence indicates that the frequency and pattern of cranial nerve involvement in AN may vary according to the autoantibody type [17, 18, 20–22]. This hypothesis warrants further investigation in larger, well-characterized cohorts. Heterogeneity in the expression of AN antigens within the neuromuscular system may partly explain these differences. For example, CNTN1, unlike other AN antigens, has been reported to be expressed in annulospiral fibers of muscle spindles and may therefore contribute to proprioceptive dysfunction [23].

Cranial nerve involvement was identified in 8.8% (38/431) of our CIDP patients. This frequency is broadly comparable to previous studies (~11%) [17], although some studies described higher rates of >20% [7–9, 18, 20]. This discrepancy may be partly attributable to differences in diagnostic processes and study methodologies; earlier studies were done before AN was recognized and may therefore have included such cases under the CIDP category. In addition, although routine cranial nerve examinations were performed in all patients, mild cranial nerve involvement may have been difficult to confirm, as specialized assessment, including video head impulse tests were not performed systematically.

The overall pattern of cranial nerve involvement in our CIDP patients largely mirrors previous studies, with facial palsy as the most frequent manifestation, followed by EOM palsy. Notably, cranial+ CIDP in our cohort was disproportionately represented by the multifocal variant, with about 7-fold higher prevalence compared to cranial− CIDP. Within this subgroup, EOM palsy was particularly common. This parallels Japanese studies that reported subtype-specific differences in cranial nerve involvement [10, 24]. Shibuya and colleagues further noted that cranial neuropathies in typical CIDP were always bilateral, whereas multifocal patients tended to be unilateral, highlighting the potential mechanistic differences across CIDP subtypes [24]. In our data, bilateral involvement was also more common in typical versus multifocal CIDP, but unilateral presentations were also frequent, indicating that the laterality of cranial nerve involvement might be more heterogeneous and warrants further study in larger cohorts.

In contrast to AN or CIDP, cranial nerve involvement was exceedingly rare in anti-MAG neuropathy and MMN. None of the 54 anti-MAG neuropathy or 64 MMN patients in our cohort exhibited cranial nerve involvement. This aligns with prior studies, including a large series of 202 anti-MAG neuropathy patients, which confirmed a broad spectrum of clinical presentations but no cranial nerve involvement [9, 25]. This observation was consistent with recent nationwide studies from Korea (68 patients) and Japan (133 patients) [26, 27]. Similarly, in MMN, cranial nerve involvement has been described only in isolated case reports, and its absence remains a supportive diagnostic criterion in EFNS/PNS 2010 guidelines [28, 29]. Taken together, these observations indicate that cranial neuropathies should be considered highly atypical in anti-MAG neuropathy and MMN, and their presence should prompt careful diagnostic reassessment.

Compared to CIDP patients without cranial nerve involvement, those with cranial+ CIDP displayed a distinctive clinical profile. They were younger at onset, more often presented with variant subtypes, and had marginally higher CSF protein levels. Cranial+ CIDP patients also more frequently presented acutely or subacutely, often following preceding triggers, and showed a relapsing–remitting course rather than the progressive trajectory typical of cranial− CIDP. Although they showed greater disability at baseline (upper limb), they achieved greater improvement in disability after treatment, suggesting that cranial+ CIDP may represent a more immune-reactive phenotype with enhanced responsiveness to immunotherapy [30, 31]. Their clinical pattern partly overlaps with that of GBS; both are associated with preceding immune triggers, acute onset, and frequent

TABLE 2 | Clinical features of CIDP patients with versus without cranial nerve involvement.

	Cranial+ CIDP ($n=38$)	Cranial− CIDP ($n=93$)	p
Female (%)	18 (47%)	32 (34%)	0.2
Age at onset (year)	37.4 (17.5)	50 (14.2)	<0.001***
Disease duration (M)	131 (104)	145 (91)	0.5
Diabetes	5 (13%)	22 (24%)	0.2
Phenotype			<0.001***
Typical	17 (45%)	64 (69%)	
Multifocal	14 (37%)	5 (5.4%)	
Distal	7 (18%)	11 (12%)	
Sensory	0 (0%)	12 (13%)	
Motor	0 (0%)	1 (1.1%)	
Mode of onset			<0.001***
Acute	20 (53%)	10 (11%)	
Subacute	11 (29%)	4 (4.3%)	
Chronic	7 (18%)	79 (85%)	
Precedent event			<0.001***
None	29 (76%)	91 (98%)	
Diarrhea	1 (2.6%)	0 (0%)	
URI	4 (11%)	1 (1.1%)	
Vaccination	4 (11%)	1 (1.1%)	
Course			<0.001***
Progressive	16 (42%)	81 (87%)	
Relapsing–remitting	21 (55%)	11 (12%)	
Monophasic	1 (2.6%)	1 (1.1%)	
CSF[a]			
WBC (cells/μL)	1.7 (2.3)	3.6 (9.6)	0.15
Protein (mg/dL)	113.9 (103.1)	76.8 (49.3)	*0.052*
INCAT at baseline[b]	4.4 (2.8)	3.4 (1.8)	0.057
Arm/Leg	2.3 (1.2)/2.2 (1.7)	1.6 (1.1)/1.8 (1.1)	0.003**/0.2
INCAT at follow-up[c]	1.2 (2.2)	2.6 (2.2)	0.003**
Arm/Leg	0.6 (1.0)/0.6 (1.2)	1.2 (1.2)/1.4 (1.2)	0.008**/0.003**
INCAT improvement[d]	3.2 (3.1)	0.8 (2.3)	<0.001***
First-line treatment			0.058
CS	21 (55%)	52 (56%)	
IVIG	17 (45%)	29 (31%)	
CS and IVIG	0 (0%)	1 (1.1%)	
None	0 (0%)	12 (13%)	
Treatment lines (n)	2.6 (1.2)	1.4 (0.7)	<0.001***
Immunosuppressant	26 (68%)	37 (40%)	0.004**
Rituximab	6 (16%)	17 (18%)	0.8

Note: Missing values in [a]34 (2: Cranial CIDP, 32: Cranial− CIDP), [b]2 (Cranial− CIDP), [c]6 (1: Cranial− CIDP, 5: Cranial+ CIDP), [d]8 subjects (3: Cranial− CIDP, 5: Cranial+ CIDP) (*, $p<0.05$; **, $p<0.01$; ***, $p<0.001$).
Abbreviations: CS, corticosteroid; IVIG, intravenous immunoglobulin; M, month; URI, upper respiratory infection; WBC, white blood cell.

cranial nerve involvement. Unlike GBS, however, cranial+ CIDP evolves into a chronic course rather than a monophasic illness. In this context, our cranial+ CIDP cohort may represent an intermediate phenotype, bridging features of CIDP and GBS in terms of temporal and spatial distribution of the autoimmune responses.

Our study has several limitations. First, the retrospective, multicenter design inevitably introduced heterogeneity in the methods and depth of cranial nerve evaluation, as testing such as blink reflex, cranial nerve MRI, evoked potentials, or facial nerve conduction studies were not uniformly performed across centers. Second, the relatively small sample size limited statistical power to detect subtype-specific and autoantibody-specific differences in cranial+ CIDP and cranial+ AN, respectively. Third, the control cohort of CIDP patients without cranial nerve involvement was derived from a single center, which may have introduced selection bias. Fourth, owing to variability in testing protocols across centers, correlations between cranial nerve electrophysiology or imaging findings and clinical features were not analyzed in the present study. Finally, AN testing was not performed in all patients; however, testing was conducted in all patients with suspected CIDP or AN at 4 of the 5 participating centers, and at the remaining center, it was performed in all cases with suspected AN, in accordance with the latest guidelines [1].

Despite these limitations, our study also has important strengths. We applied the most recent diagnostic criteria and disease-specific autoantibody testing, thereby minimizing the risk of diagnostic misclassification. Moreover, by recruiting a large, international, multicenter cohort, we were able to characterize the largest series to date of chronic autoimmune neuropathies with cranial nerve involvement, providing novel insights into their prevalence, patterns, and associated clinical features.

In conclusion, our study demonstrates that cranial nerve involvement and its specific patterns can serve as valuable diagnostic clues in the evaluation of chronic autoimmune neuropathies, particularly for recognizing AN and CIDP subtypes. Moreover, we show that CIDP patients with cranial nerve involvement exhibit a distinct clinical profile, suggesting that this group may represent a mechanistically unique subset within the CIDP spectrum and merits further investigation.

Author Contributions

Y.G.M.: design of the study, data curation, formal analysis, interpretation of data, original draft preparation, and review and editing of manuscript. H.K.: data curation, interpretation of data, original draft preparation, and review and editing of manuscript. H.J.H., B.-A.Y., J.K.K., W.J., S.-J.C., S.-M.K., K.H.K., Y.N.K., S.W.K., E.-J.L., Y.-M.L., K.K.N.: data curation, supervision, review and editing of manuscript. Y.A.R., H.Y.S., J.-J.S.: project administration, interpretation of data, supervision, original draft preparation, and review and editing of manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Demographic and clinical characteristics of CIDP and AN patients exhibiting cranial nerve involvement.