Factors Influencing the Diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy

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ABSTRACT

BACKGROUND: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a neurological disorder that leads to demyelination of peripheral nerves presenting with an array of symptoms. Symptoms of CIDP include but are not limited to loss of sensation, loss of reflexes, tingling and pain, and weakness. European Federation Neurological Society (EFNS) has developed guidelines for the diagnosis of this disorder. The objective of this study is to look at the relationship between the EFNS diagnostic criteria and whether patients that have the diagnosis of CIDP met this criteria. Data collection was completed on the patients diagnosed with CIDP and then the patients that were diagnosed but did not meet the criteria were analyzed to see what common outliers exist that led to the diagnosis.

RESULTS: A total of 20 patients (13 males and 7 females) were included in the study. Eighty-three percent of patients that were correctly diagnosed using the EFNS/PNS guidelines displayed hyporeflexia at the time of their diagnosis. A large majority of the patients (83%) correctly diagnosed using the EFNS/PNS guidelines displayed distal weakness at the time of their diagnosis. At the time of their diagnosis, EMG showed that majority of those who did not meet the EFNS/PNS criteria had no nerves that displayed increased latency. Fifty-eight percent of those who did meet the criteria outlined by the EFNS/PNS guidelines had two or more nerves that presented with increased latency. Testing the velocity of patients displayed that all of the patients that did not meet the EFNS/PNS criteria did not present with nerves that had diminished velocity.

CONCLUSION: CIDP misdiagnosis continues to be an issue leading to mismanagement of these patients. This study showed a preference of the clinical component for diagnosis of CIDP even if electrophysiological criteria was not met.

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is the most common chronic immune-mediated disorder of the peripheral nervous system.[1] CIDP incidence rate is 0.33 per 100,000 people/year, whereas the prevalence rate is 2.81 per 100,000 people.[2] CIDP is an immune mediated disorder where many autoantibodies (NF155, NF186, CNTN1, etc) have been identified yet the mechanism and etiopathology of this disease is still not fully understood.[1] CIDP is classified into typical and atypical subtypes. The key to differentiate between the two is that typical CIDP presents as symmetric and distal weakness and sensory dysfunction of all extremities, whereas atypical may have varying presentations.[3] Accurate diagnosis of CIDP remains a challenge due to the range of clinical symptoms and presentations that the disorder can have.[5] Thus, there have been several diagnostic criteria developed including American Academy of Neurology (AAN), Inflammatory Neuropathy Cause And Treatment (INCAT), and European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS).[4] These criteria focus on clinical, electrophysiological, and supportive criteria when diagnosing the condition. The clinical criteria aspect assesses for distal weakness and sensory dysfunction of extremities. The various criteria present primarily differ in the electrophysiological criteria proposed. The most utilized diagnostic criteria is the EFNS/PNS diagnostic criteria. The EFNS/PNS electrophysiological criteria requires only 1 of its 7 criteria to be met, conveying the impression of being less conservative than other guidelines. The correct diagnosis of a CIDP is vital for administration of appropriate treatment. The objective of this study is to look at the relationship between the EFNS diagnostic criteria and whether patients that have the diagnosis of CIDP clinically meet this criterion.

Methods

This study is a retrospective chart review of patients that underwent care from a university-based hospital for their diagnosis of CIDP. A total of 20 patients diagnosed with CIDP were included in the study. Variables including but not limited to age, gender, race, history of diabetes, alcohol use, deep tendon reflexes, presence of proximal or distal weakness, sensory deficits, and EMG data were collected.

Data collected was analyzed to identify whether they meet the European Federation of Neurological Societies (EFNS)/Peripheral Nerve Society (PNS) criteria for diagnosis of CIDP. The patients were then categorized in one of the two groups – those who met the EFNS criteria (definite, probable, or possible) and those patients that did

not meet the criteria but were still diagnosed as patients with CIDP. Patient demographics and pain scores in form of descriptive statistical variables were analyzed, and mean, standard deviation, ranges, and percentages were calculated. All statistical analyses were done using SPSS v22 software (IBM, Armonk, NY).

Results

Demographics

A total of 20 patients (13 males and 7 females) were included in the study. The average age of the participants was 59 years old for the true positives and 61.63 for the false positives. For this study, the ethnicity for the patient population consisted mostly of Caucasians in the patients that met criteria (100%) and patients that did not meet criteria (75%). The analysis and breakdown of the patient demographic is displayed in Table 1.

Table 1. Demographics of the patients who were diagnosed with CIDP including the patients who correctly met the guidelines of the EFNS/PNS criteria and those who did not meet the criteria.

	True Positives	False Positives
Average Age	59.00 +/- 14.92	61.63 +/- 10.39
Gender (M/F)	(10/2)	(3/5)
Race (White/AA/Hisp)	(12/0)	(6/1/1)
Diabetes	4	2

Clinical Factors

Clinical variables of the patients are presented in Table 2 and Table 3. Almost all the patients that were correctly diagnosed using the EFNS/PNS guidelines displayed hyporeflexia at the time of their diagnosis. When assessing reflexes, 10 of 12 participants that met criteria (83%) had hyporeflexia present whereas 4 of 8 participants that did not meet criteria (50%) had hyporeflexia. A large majority of the patients correctly diagnosed using the EFNS/PNS guidelines displayed distal weakness at the time of their diagnosis. Motor and sensory abnormalities were present in all patients including 10 patients that met criteria with distal weakness (83%), 6 patients that met criteria with proximal weakness (50%), and 12 patients that met criteria with sensory deficits (100%).

Table 2. Results from the patient reflex assessment at the time of the patient's diagnosis. Almost all the patients that were correctly diagnosed using the EFNS/PNS guidelines displayed hyporeflexia at the time of their diagnosis.

Reflexes	True Positives	False Positives
Hyporeflexia	10	4
Normal reflexes	2	2
Hyperreflexia	0	1
Unknown	0	1

Table 3. Clinical symptoms that the patients displayed at the time of their diagnosis with CIDP. A large majority of the patients correctly diagnosed using the EFNS/PNS guidelines displayed distal weakness at the time of their diagnosis. All of the true positives also displayed sensory deficits.

Clinical Symptoms	True Positives	False Positives
Distal weakness (No weakness/ weakness)	(2/10)	(4/4)
Proximal weakness (No weakness/weakness)	(6/6)	(6/2)
Sensory deficits (No deficits/ deficits)	(0/12)	(2/6)

Electromyography

Electromyography was conducted on each patient. Subjects were stratified into groups with 0, 1, or 2+ nerves with abnormal latency or velocity. These groups are presented in Table 4 and Table 5. Results of the latency that was observed in patients at the time of their diagnosis showed that those who did not meet the EFNS/PNS criterion mostly had no nerves that displayed increased latency. The majority of those who did meet the criteria outlined by the EFNS/PNS guidelines had two or more nerves that presented with increased latency. In this study, 63.6% of patients that met criteria had increased latency of 2 more nerves, whereas 25% of these patients had diminished velocity. None of the patients, that did not meet criteria, in this study had 2 or more nerves with abnormal latency or velocity.

Table 4. Results of the latency that was observed in patients at the time of their diagnosis showed that those who did not meet the EFNS/PNS criterion mostly had no nerves that displayed increased latency. The majority of those who did meet the criteria outlined by the EFNS/PNS guidelines had two or more nerves that presented with increased latency.

		Number of Patients
True Positive	2 or more nerves with increased Latency	7
	1 nerve with increased Latency	3
	No nerves with increased Latency	2
False Positive	2 or more nerves with increased Latency	0
	1 nerve with increased Latency	1
	No nerves with increased Latency	7

Table 5. Velocity displayed in the patients at the time of their diagnosis with CIDP. Testing the velocity of patients demonstrated that all of the patients who did not meet the EFNS/PNS criteria did not present with nerves that had diminished velocity.

		Number of Patients
True Positive	2 or more nerves with diminished Velocity	3
	1 nerve with diminished Velocity	5
	No nerves with diminished Velocity	4
False Positive	2 or more nerves with diminished Velocity	0
	1 nerve with diminished Velocity	0
	No nerves with diminished Velocity	8

Discussion

CIDP has a spectrum of phenotypic presentations where different autoimmune mechanisms have been discovered that lead to similar clinical features. CIDP continues to be diagnosed clinically, and without a gold standard, it continues to make proper evaluation and diagnosis difficult.

The EFNS/PNS criteria that was investigated in this study has been found to most sensitive compared to AAN criteria.[3] "Possible" electrophysiological CIDP as outlined by EFNS/PNS criteria still has a poor specificity of 69.2%.[3]

This study looked at 20 patients diagnosed with CIDP and found that 40% of those patients failed to meet the EFNS/PNS criteria. These findings are supported by other studies such as the one conducted by Allen and company.[6] Allen and company completed a retrospective study of 59 patients diagnosed with CIDP. The study found that 47% of those patients failed to meet the minimal CIDP diagnostic criteria by EFNS/PNS criteria.[6]

The data above looks at the EMGs conducted in the patients diagnosed with CIDP. When comparing patients that met criteria to those that did not, it appears that the EMG data is not resulting in improper diagnosis of the disorder. On the other hand, clinical symptoms such as reflexes and sensory deficits have shown to be increased in both groups. These results show the presentation of these clinical symptoms may be leading to the misdiagnosis of CIDP when the patient is not meeting all of the clinical and electrophysiologic criteria as outlined by the EFNS/PNS guidelines. Patients who showed no diminished velocity also did not meet the criteria outlined by the EFNS/PNS guidelines. These patients additionally had little to no nerves that displayed increased latency. These factors assessed have revealed potential components that led to the misdiagnosis of CIDP.

Conclusion

The guidelines outlined in the EFNS/PNS criteria were developed to provide set criteria to be used for correct diagnosis of CIDP. Since there are several guidelines used to diagnose CIDP throughout the world the specificity of the diagnosis is not consistent. The EFNS/PNS guidelines requires the patient to meet certain electrodiagnostic criteria as well as clinical criteria leading to a more concise diagnosis of the neurological symptoms. CIDP misdiagnosis continues to be an issue leading to mismanagement of these patients. This study identified potential components that led to the misdiagnosis of CIDP. Further evaluation and investigation into the misdiagnosis of CIDP is required due to the limitation of sample size. Another limitation of this study is that this was a prospective chart review where only the data documented was available.

Declarations

Ethical Approval and Consent to Participate

This study is a retrospective chart review of patients that underwent care from a university-based hospital for their diagnosis of CIDP. The study was approved by MU Human Subjects Research Protections Program and Institutional Review Board of MU School of Medicine and the need to collect informed consent was waived by the institutional review board named above. The study was performed in accordance with the MU Human Subjects Research Protections Program Institutional Review Board of MU School of Medicine Guidelines and procedures. The need to collect informed consent was waived by the institutional review board named above. Data was de-identified upon extraction and stored on a hospital encrypted server, that leads to minimal risk to research subjects. There was no direct patient contact for this study.

Consent for publication: Not applicable

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Authors' contributions: AA conducted the study and wrote the manuscript.

TM aided with data analysis, editing, and reviewing the manuscript.

KS researched other literature related to our topic and aided in editing.

RG is the PI for this study and supervised all data collection and analysis and reviewed manuscript.

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