Original Article

Diagnostic Accuracy of Clinical Characteristics to Diagnose Neuralgic Amyotrophy

Khanittanuphong P, MD[1], Boonmeeprakob A, BNS[1]

[1] Division of Rehabilitation, Department of Orthopedics and Rehabilitation Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Objective: To evaluate the diagnostic accuracy of clinical symptoms in neuralgic amyotrophy (NA).

Materials and Methods: The present study was a retrospective 10-year review of patients suspected of NA and referred to an electrodiagnostic clinic for confirmation. Symptoms including first presenting symptom, duration, natural history of disease, pain area, and characteristics were collected, and sensitivity, specificity, positive and negative likelihood ratios were analyzed using the electrodiagnostic findings (EDX) as the gold standard.

Results: Ninety-six patients were included, and 52 patients were confirmed to have NA by the EDX. The first presentation of pain showed a sensitivity of 84.6% and the lowest negative likelihood ratio of 0.38. Hand pain, finger pain, pins and needles pain, and electrical shock-like pain had the highest specificity of 95.5%, but low positive likelihood ratios (PLRs) of 0.85, 1.27, 0.42, and 1.27, respectively. However, pain followed by abrupt weakness revealed a specificity of 88.6% with the highest PLR of 3.55.

Conclusion: The highest sensitivity and a good specificity to diagnose NA were the first presentation of pain and clinical course of pain followed by abrupt weakness, respectively.

Keywords: Diagnostic accuracy, Clinical characteristics, Neuralgic amyotrophy

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Neuralgic amyotrophy (NA) is a neurological disorder that results possibly from multifocal inflammation at the brachial plexus[1]. NA was initially recorded by Dreschfeld in 1887 in two cases of non-traumatic brachial plexopathy[1,2]. A comprehensible description of this clinical syndrome was researched by Parsonage and Turner in 1948[3]. They found 136 cases that presented with an abrupt onset of shoulder pain followed by weakness and some numbness of the shoulder girdle.

This syndrome is usually classified as an uncommon disease. Epidemiology studies reported that the incidence ranged from 1.64 to 3 per 100,000 persons per year[4-6]. NA is divided into two types, hereditary and idiopathic forms. Hereditary NA is an autosomal dominant disorder in which the brachial plexus is periodically attacked[7-9]. Idiopathic NA presumably results from an autoimmune mechanism, but the pathophysiology of this type is unknown[10-12].

Frequent clinical symptoms are presented by instant shoulder pain, especially at night, for a few days to weeks followed by weakness and numbness around the shoulder blade or upper limb regions[1,13,14]. The upper or middle trunk or both are usually involved including the long thoracic nerve[3,13-15]. Autonomic symptoms or vasomotor dysfunction, trophic skin changes, edema at onset, temperature dysregulation, and increased sweating were significantly found in lesions related to posterior cord and the lower part or all parts of the brachial plexus[13].

The current standard for a diagnosis is based on electrodiagnostic studies (EDX)[1,13,16,17]. As soon as a diagnosis can be confirmed, proper treatment can be initiated resulting in a good clinical outcome.

Correspondence to:

Khanittanuphong P.

Division of Rehabilitation, Department of Orthopedics and Rehabilitation Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Phone: +66-74-451601

Email: khanittanuphong.p@gmail.com

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Table 1. Demographic data of all referred patients and groups based on electrodiagnostic findings

Demographic data	Total patients (n=96) n (%)	EDX conclusion of NA; n (%)	
		Yes (n=52)	No (n=44)
Age (year); mean±SD	51.3±16.8	51.8±16.0	50.8±17.8
Sex: male	57 (59.4)	35 (67.3)	22 (50.0)
Underlying disease			
Hypertension	16 (16.7)	5 (9.6)	11 (25.0)
Dyslipidemia	5 (5.2)	3 (5.8)	2 (4.5)
Affected side			
Right	46 (47.9)	23 (44.2)	23 (52.3)
Left	42 (43.8)	25 (48.1)	17 (38.6)
Bilateral	8 (8.3)	4 (7.7)	4 (9.1)

EDX=electrodiagnostic study; NA=neuralgic amyotrophy; SD=standard deviation; n=number

Van Alfen et al discovered that the time of onset until the start of paresis recovery was shorter in the NA patients treated with corticosteroids than the untreated group[13]. However, the gold standard for investigation is not available in all healthcare settings. Useful information that aids a physician to recognize NA is a clinical history and physical examination. As far as the authors know, no previously published study has reported the diagnostic accuracy of clinical presentations in NA. Therefore, the objective of the present research was to evaluate the diagnostic accuracy of clinical symptoms in NA patients when an EDX is used as the reference standard.

Materials and Methods

The present study design was a retrospective medical chart review. The medical records were reviewed by the first researcher at Songklanagarind Hospital of all patients between 2008 and 2018 suspected of NA and referred to the electrodiagnostic clinic. The exclusion criteria were patients with a history of trauma to the neck or shoulder region, tumor or metastatic cancer to the brachial plexus, radiation to the brachial plexus area, and other neurological diseases such as motor neuron disease, cervical radiculopathy or myelopathy, nerve entrapment, and myopathy. A patient with diabetes was also excluded.

Demographic data collected from the patients were age, sex, and underlying disease. The documented medical history from a referring physician included first presenting symptom(s), duration, natural history of disease, pain area, and characteristics. Then, the findings of the EDX were recorded as the gold standard. All studies were professionally performed and concluded by five certified physiatrists. The protocol consisted of i) sensory nerve conduction studies such as radial, median, ulnar, and lateral antebrachial cutaneous nerves, ii) motor nerve conduction studies such as median and ulnar nerves, and iii) a comprehensive needle electromyography (EMG) as directed by the physical examination including the cervical paraspinal muscles. The present study was approved by the Ethics Committee of the Faculty of Medicine at Prince of Songkla University.

Statistical analysis

Descriptive data for continuous variables were presented as mean and standard deviation (SD) and categorical variables were presented as numbers and percentages. The diagnostic accuracies in terms of sensitivity, specificity, positive and negative likelihood ratios including 95% confidence interval from the findings of the clinical characteristics were calculated and compared with the electrodiagnostic findings. All data were analyzed using R software, version 3.5.1 (R Core Team, Vienna, Austria).

Results

The data were collected from 96 patients suspected of NA diagnoses. Fifty-two patients were confirmed to have NA by an EDX. The prevalence of disease according to the present study was 54%. Table 1 shows the demographic data of all patients and the two patient groups with and without NA. There were no significant differences between the two groups.

The first presenting symptom of pain had the highest sensitivity of 84.6% and a negative likelihood ratio of 0.38 (Table 2). There were four clinical findings that showed the highest specificity of 95.5%, hand pain, finger pain, pins and needles pain, and electrical shock-like pain. However, they revealed a low value of positive likelihood ratio. Pain followed by abrupt weakness revealed a high specificity of 88.6% and the highest positive likelihood ratio of 3.55. The comparison of sensitivity and specificity among the clinical characteristics are shown in Figure 1.

Discussion

The present study reported the presenting symptom was predominately pain that had the highest sensitivity to diagnose NA, while the clinical course of pain followed by abrupt upper limb weakness had a high specificity. Eighty-five percent of the patients

Table 2. Diagnostic accuracy of clinical characteristics in patients with and without neuralgic amyotrophy

Clinical characteristics	EDX conclusion of NA; n (%)		Sn (%) (95% CI)	Sp (%) (95% CI)	+LR (95% CI)	–LR (95% CI)
	Yes (n=52)	No (n=44)				
First presenting symptom						
Pain	44 (84.6)	26 (59.1)	84.6 (71.9 to 93.1)	40.9 (26.3 to 56.8)	1.43 (1.09 to 1.88)	0.38 (0.18 to 0.78)
Paresis	26 (50.0)	26 (59.1)	50.0 (35.8 to 64.2)	40.9 (26.3 to 56.8)	0.85 (0.59 to 1.22)	1.22 (0.78 to 1.91)
Sensory change	7 (13.5)	8 (18.2)	13.5 (5.6 to 25.8)	81.8 (67.3 to 91.8)	0.74 (0.29 to 1.88)	1.06 (0.89 to 1.26)
Atrophy	0 (0.0)	4 (9.1)	0.0 (0.0 to 6.9)	90.9 (78.3 to 97.5)	0.00	1.10 (1.00 to 1.21)
Duration of symptom						
≤4 weeks	30 (57.7)	13 (29.5)	57.7 (43.2 to 71.3)	70.5 (4.85 to 83.2)	1.95 (1.17 to 3.26)	0.60 (0.41 to 0.87)
>4 weeks	22 (42.3)	31 (70.5)	42.3 (28.7 to 56.8)	29.6 (16.8 to 45.2)	0.60 (0.41 to 0.87)	1.95 (1.17 to 3.26)
Course of disease						
Pain then abrupt weakness	21 (40.4)	5 (11.4)	40.4 (27.0 to 54.9)	88.6 (75.4 to 96.2)	3.55 (1.46 to 8.64)	0.67 (0.53 to 0.86)
Pain then gradual weakness	10 (19.2)	6 (13.6)	3.9 (0.5 to 13.2)	86.4 (72.7 to 94.8)	0.28 (0.06 to 1.33)	1.11 (0.98 to 1.27)
Pain and weakness	12 (23.1)	11 (25.0)	23.1 (12.5 to 36.8)	75.0 (59.7 to 86.9)	0.92 (0.45 to 1.88)	1.03 (0.82 to 1.29)
Only pain	4 (7.7)	7 (15.9)	7.7 (2.1 to 18.5)	84.1 (69.9 to 93.4)	0.48 (0.15 to 1.54)	1.10 (0.94 to 1.28)
Abrupt weakness	3 (5.8)	9 (20.5)	5.8 (1.2 to 16.0)	79.6 (64.7 to 90.2)	0.28 (0.08 to 0.98)	1.18 (1.01 to 1.40)
Progressive weakness	2 (3.8)	6 (13.6)	3.9 (0.5 to 13.2)	86.4 (72.7 to 94.8)	0.28 (0.06 to 1.33)	1.11 (0.98 to 1.27)
Pain area						
Shoulder	32 (61.5)	17 (38.6)	61.5 (47.0 to 74.7)	61.4 (45.5 to 75.6)	1.59 (1.04 to 2.45)	0.63 (0.41 to 0.95)
Arm	12 (23)	11 (25.0)	23.1 (12.5 to 36.8)	75.0 (60.0 to 86.8)	0.92 (0.45 to 1.88)	1.03 (0.82 to 1.29)
Neck	9 (17.3)	13 (29.5)	17.3 (8.2 to 30.3)	70.5 (54.8 to 83.2)	0.59 (0.28 to 1.24)	1.17 (0.93 to 1.47)
Scapular	9 (17.3)	5 (11.4)	17.3 (8.2 to 30.3)	88.6 (75.4 to 96.2)	1.52 (0.55 to 4.21)	0.93 (0.79 to 1.10)
Hand	2 (3.8)	2 (4.5)	3.9 (0.5 to 13.2)	95.5 (84.5 to 99.4)	0.85 (0.12 to 5.76)	1.01 (0.93 to 1.10)
Finger	3 (5.8)	2 (4.5)	5.8 (1.2 to 16.0)	95.5 (84.5 to 99.4)	1.27 (0.22 to 7.26)	0.99 (0.90 to 1.08)
None	5 (9.6)	13 (29.5)	9.6 (3.2 to 21.0)	70.5 (54.8 to 83.2)	0.33 (0.13 to 0.84)	1.28 (1.04 to 1.58)
Pain characteristics						
Dull pain	40 (76.9)	25 (56.8)	76.9 (63.2 to 87.5)	43.2 (28.4 to 59.0)	1.35 (0.01 to 1.82)	0.53 (0.29 to 0.97)
Radicular pain	7 (13.5)	12 (27.3)	13.5 (5.6 to 25.8)	72.7 (57.2 to 85.0)	0.49 (0.21 to 1.14)	1.19 (0.96 to 1.47)
Electrical shock-like pain	3 (5.8)	2 (4.5)	5.8 (1.2 to 16.0)	95.5 (84.5 to 99.4)	1.27 (0.22 to 7.26)	0.99 (0.90 to 1.08)
Pins and needles	1 (1.9)	2 (4.5)	2.0 (0.1 to 10.3)	95.5 (84.5 to 99.4)	0.42 (0.04 to 4.51)	1.03 (0.95 to 1.11)

EDX=electrodiagnostic study; NA=neuralgic amyotrophy; n=number; Sn=sensitivity; Sp=specificity; +LR=positive likelihood ratio; –LR=negative likelihood ratio; CI=confidence interval

in the study setting presented with pain. Similarly, former studies demonstrated that the initial symptom was pain in 65% to 95%, and the most common pain region was the shoulder[13,15,18]. However, pain had a specificity of only 40.9%.

A high specificity along with the highest positive likelihood ratio to diagnose NA was pain followed by abrupt weakness. This clinical presentation was the classic presenting symptom of NA, which was documented in several previous studies[2,6,11,13,15,19]. The present study findings also corresponded with this well-known clinical picture. The diagnostic guidelines for hereditary NA included a case who had severe pain that preceded the onset of weakness as well[20]. This typical symptom also had the highest positive likelihood ratio of 3.55. Although this value indicated a small impact on the probability of having NA, it was considered to be included in the differential diagnosis when a patient had shoulder pain with subsequent weakness in a clinical setting.

However, the authors found that 60% of patients had an atypical presentation such as pain followed by gradual weakness, pain and weakness simultaneously, and only weakness without pain symptom. These findings were consistent with the study by Clarke et al that reported that only four out of ten EMG-confirmed NA patients had a sudden onset attack[21]. Van Alfen et al also reported that one-third of patients who presented with an atypical clinical picture were referred to their center[13]. This possibly resulted

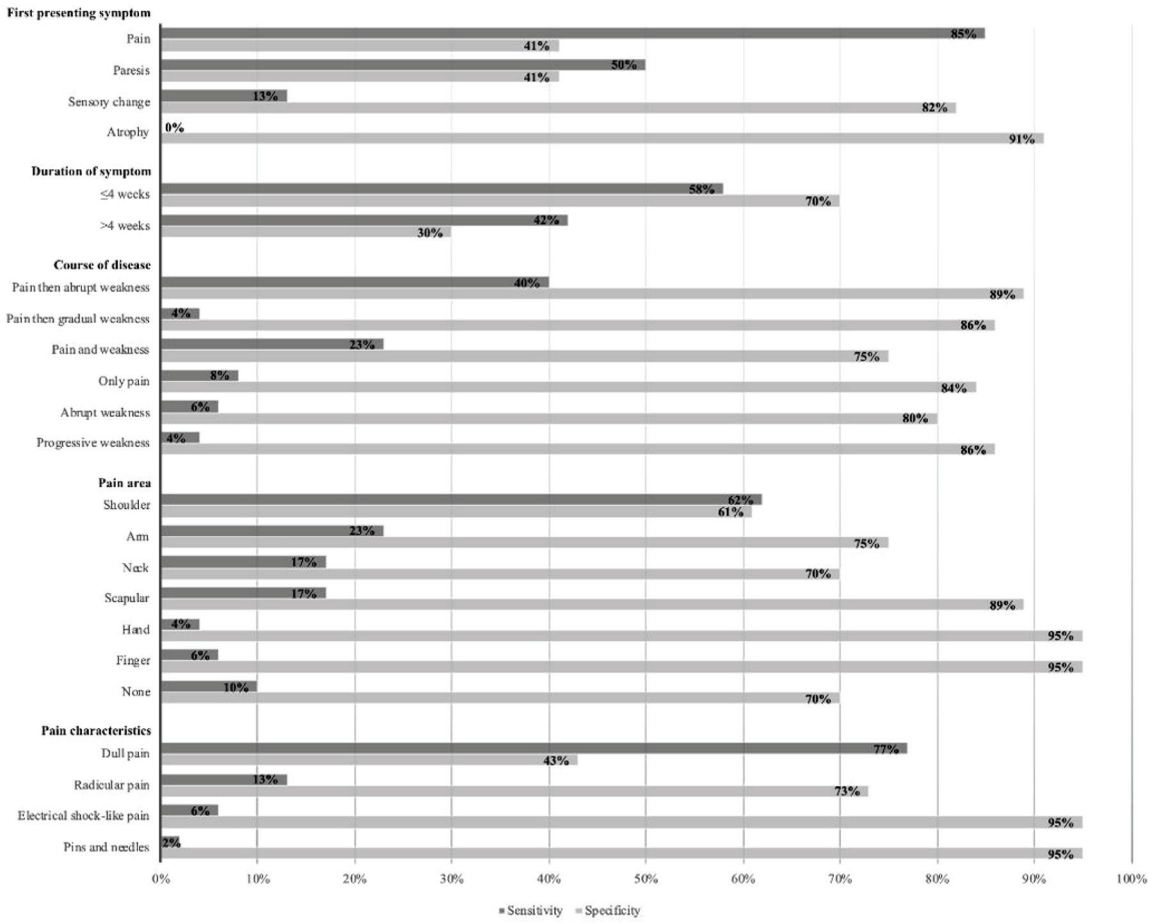

Figure 1. Bar graph indicating sensitivity and specificity of the clinical symptoms to diagnose neuralgic amyotrophy.

from a different immune mechanism of each patient. Considering the severity, some symptoms were very mild or recovered well, which were then difficult to recognize. A patient who presented with painless or unclear onset of NA always had shoulder or arm pain while performing daily activities[22]. It was presumably provoked by strenuous work of a compensatory muscle acting for a paralyzed muscle[23]. Therefore, a physician should remind this patient group to carefully review their symptoms.

The other clinical parameter that represented high specificity was a pain area in the hand or fingers and yet both positive and negative likelihood ratios were very low. According to a pain pattern from a previous study, only 6.1% in that pain area were confined to the lower brachial plexus, median arm, hand, or axilla[13]. Some research showed that there was no pain report in the hand or fingers[18,24]. Shoulder pain was more commonly found than pain in the hand region in NA[1]. However, the present study results evidenced that the sensitivity and specificity of pain in the shoulder were about 60%. It was a moderate screening tool to diagnose NA.

The pain characteristics of pins and needles and electrical shock-like pattern also revealed the highest specificity with low likelihood ratios. The majority of patients reported an initial continuous neuropathic pain followed by a severe shooting pain or a persistent musculoskeletal-type pain[13]. Both neuropathic and musculoskeletal pain had a tendency to worsen during the follow-up period. However, the present study findings revealed that 77% of patients presented with a dull pain, which represented the highest sensitivity among the types of pain. It was possibly associated with the compensatory muscles that generally produced persistent pain in subacute NA patients[23].

The limitations of the current study need to be considered. First, generalizability cannot be applied to all NA patients since the analysis included only

patients in the EMG-confirmed group who probably had moderate to severe NA by a clinical diagnosis. A group of NA patients with mild symptoms were possibly not referred to perform an EMG. Therefore, collecting all levels of severity of NA is required for an extensive clinical application. Second, the present study was a retrospective study that did not cover some necessary points such as autonomic symptoms and winged scapular. A prospective study covering all essential details is an alternative method.

Conclusion

The highest sensitivity and a good specificity in terms of clinical characteristics to diagnose NA were pain as the first presenting symptom and pain followed by abrupt weakness, respectively.

What is already known on this topic?

NA is a neurological disorder that is possibly caused by multifocal inflammation at the brachial plexus. Common symptoms present as instant shoulder pain followed by weakness of the upper limb region. However, no previous study reported on the diagnostic accuracy of these clinical characteristics.

What this study adds?

The first presenting symptom by pain had the highest sensitivity to diagnose NA, while the well-known course, which was expressed by shoulder pain and then abrupt arm weakness, revealed good specificity. The clinical application is that NA should be included in the differential diagnosis when a patient has shoulder pain. Moreover, NA was considered to be a likely diagnosis when weakness of upper limb suddenly occurred after initiation of the previous pain.

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Conflicts of interest

The authors declare no conflict of interest.

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