

[CASE REPORT]

Chronic Brachial Plexus Neuritis That Developed into Typical Neuralgic Amyotrophy and Positively Responded to Immunotherapy

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Abstract:

Based on the hypothesis that autoimmunity plays a role in the pathogenesis of neuralgic amyotrophy (NA), immunotherapy is sometimes administered. Early intervention is recommended for a good prognosis. We herein report the case of a 55-year-old man who presented with neuralgia, weakness, and muscle atrophy in his right shoulder girdle and upper arm, which progressed for ten months following a marine sports accident. The patient was diagnosed with NA. His neurological deficits gradually improved after several courses of immunotherapy, suggesting that in addition to being effective for treating early-stage disease, immunotherapy may be effective for treating chronic cases.

Key words: neuralgic amyotrophy, intravenous immunoglobulin, chronic brachial plexus neuritis

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Introduction

Neuralgic amyotrophy (NA) is a syndrome characterized by the sudden onset of pain in one or both shoulders and the rapid onset of weakness in the muscles of the shoulder girdle and upper arm (1). Patients with NA generally have a good prognosis, with previous studies reporting that 80-90% of patients recovered within 2-3 years after the onset (2). However, some recent reports have described a less favorable prognosis. van Alfen et al., for instance, reported that only 4.1% of NA patients showed a total recovery from paresis (3). Such reports strongly demonstrate the need to establish an effective treatment for this syndrome.

Based on studies reporting an association between the immune response and NA, the efficacy of immunotherapy was investigated. An observational study reported that corticosteroid use resulted in the development of pain and weakness in the early phase of this syndrome (4). While some case reports have examined the efficacy of intravenous immunoglobulin (IVIG) therapy, none of these studies were of high quality (5-9). The optimal therapy for NA is still unclear; however, treatment in the early phase of this syn-

drome is generally thought to be more effective (6). Only three cases of late-stage NA have been treated with IVIG (6, 7). It is difficult to be certain of the diagnosis of one of the cases, as the results of electrophysiological and radiographic studies were normal (6). In the remaining two cases, the period from the onset to treatment was up to six months. Two of the three cases improved after a single course of methylprednisolone pulse therapy (MPPT) and IVIG (7). We herein report a case of chronic progressive plexopathy that was thought to be a subtype of NA, and which was responsive to immunotherapy that was administered at ten months after the onset of symptoms.

Case Report

A 55-year-old man was admitted to our hospital complaining of malaise, muscle atrophy, weakness, and right upper extremity pain. Ten months before his admission, he fell into shallow water while engaged in marine sports and struck his right shoulder and neck on the sea bed. He then felt a tingling in his right arm and was unable to move for approximately 20 seconds after the accident. Later, his symptoms resolved completely. Three months later, he again

Table. Review of MMTs, Distribution of Atrophy, NEMG Findings, and MRI Findings of Right Upper Extremity.

Muscle (rt.) date	MMT		Atrophy	nEMG at rest		nEMG (MUP/recruitment)		MRI (STIR) X+1/7
	X/4	X+1/7		X/4	X+1/7	X/4	X+1/7	
TPZ	5	5	-	Silent	Silent	Polyphasic, Long/Normal	Normal/Normal	Iso
C5 paraspinal	NA	NA	NA		Silent		Normal/Normal	NA
SA	5	5	-					Iso
PM	4-	4	+					Iso
ISP	4-	4-	+		FP		Polyphasic, Long/Normal	Hyper
SSP	4-	4-	-					Iso
Del	3-	5-	+		FP		Polyphasic, High, Long/ Reduced	Iso
BB	3-	4-	+	FP	Silent	Polyphasic, High, Long/ Normal	Polyphasic/Reduced	Hyper
TB	5	5	-		Silent		Normal/Normal	Iso
Supinator	4-	4-	+					Iso
ECR	5	5	+	Silent		Polyphasic, High, Long/ Reduced		Iso
ED	5	5	-	Silent		Normal/Normal		Iso
FDI	5	5	-	Silent		Normal/Normal		Iso

FP: fibrillation potentials, TPZ: trapezius, SA: serratus anterior, PM: pectoralis major, ISP: infraspinatus, SSP: supraspinatus, Del: deltoid, BB: biceps brachii, TB: triceps brachii, Spin: supinator of forearm, ECR: extensor carpi radialis, ED: extensor digitorum, APL: abductor pollicis longus, FDI: first dorsal interosseous, ADM: abductor digiti minimi, Iso: isointense, Hyper: hyperintense

experienced a tingling sensation and severe pain in his right arm, which prevented him from raising it. A CT scan and MRI of his neck and shoulder performed at a local orthopedic clinic showed no abnormal findings. At four months after the accident he experienced weakness in his right upper extremity while swimming. Despite physical therapy, the weakness in his right arm worsened. At seven months after his accident, he continued to experience difficulty raising his right arm. At twelve months after the accident, he visited our clinic because his condition had not improved.

The patient's medical history included herpes zoster on his right neck and arm two years prior to his admission and a severe burn on his right chest and arm 53 years prior to his admission. At the time of his admission he suffered from alcoholic fatty liver but was not taking any medication. His family history was unremarkable. On admission his vital signs were normal. The burn scar on his right chest and arm were visible. The results of other physical examinations were normal. A neurological examination showed weakness and muscular atrophy in the deltoids (Del; 3/5), biceps brachii (BB; 3/5), supraspinatus (SSP; 4/5), infraspinatus (ISP; 4/5), and pectoralis major (PM; 4/5). The patient also showed weakness with supinator of the right forearm (4/5) (Table). The BB tendon and brachioradialis (BR) reflexes were diminished. No pathological reflexes were found. Fasciculation of the BB muscle was observed. Although he complained of a tingling sensation in his forearm and rapid, shooting pain across his neck and arm when placing his right hand on the floor to raise himself, no sensory deficit was found.

Investigation

A laboratory analysis detected anti-GD1a-IgG antibodies

(a type of antiganglioside antibody). The results of other tests, including tests of the thyroid function, and tests to detect antinuclear antibodies, and antineutrophil cytoplasmic antibodies, were normal. A cerebrospinal fluid study revealed that the pressure (160 mmH₂O), cell count (1/μL), and protein level (24 mg/dL) were normal.

A nerve conduction study (NCS) revealed a decreased compound muscle action potential (CMAP) amplitude in the right deltoid following stimulation of the axillary nerve at Erb's point in comparison to the left deltoid (2.7 mV in the right side vs. 11.3 mV in the left side). Sensory nerve action potential (SNAP) tests of the bilateral lateral antebrachial cutaneous nerves (LACNs) showed normal results. The other nerve conduction study findings (including the median, ulnar, and radial nerves) were normal. The somatosensory evoked potentials (SEPs) of the right median nerve and tibial nerve was also normal. Concentric needle electromyography (nEMG) revealed active denervation in the BB and chronic neurogenic changes in the trapezius (TPZ), BB, and extensor carpi radialis (ECR) (Table). Follow-up nEMG, performed at two years after the onset, revealed active denervation in the Del and ISP and chronic neurogenic changes in the Del, ISP, and BB. The C5 paraspinal muscle was normal.

Cervical and brachial plexus MRI showed C3/4-C6/7 mild spondylosis but no signal changes in the spinal cord or root. In addition, no narrowing of the intervertebral foramen or crosswise difference was seen. Brachial plexus MRI showed no signal changes; however, gadolinium enhancement was not performed. Skeletal muscle MRI revealed atrophy of the muscles of the upper extremities. Areas of high signal intensity on T2WI and short tau inversion recovery (STIR) imaging were observed in the BB, ISP, subscapularis (SSc), supi-

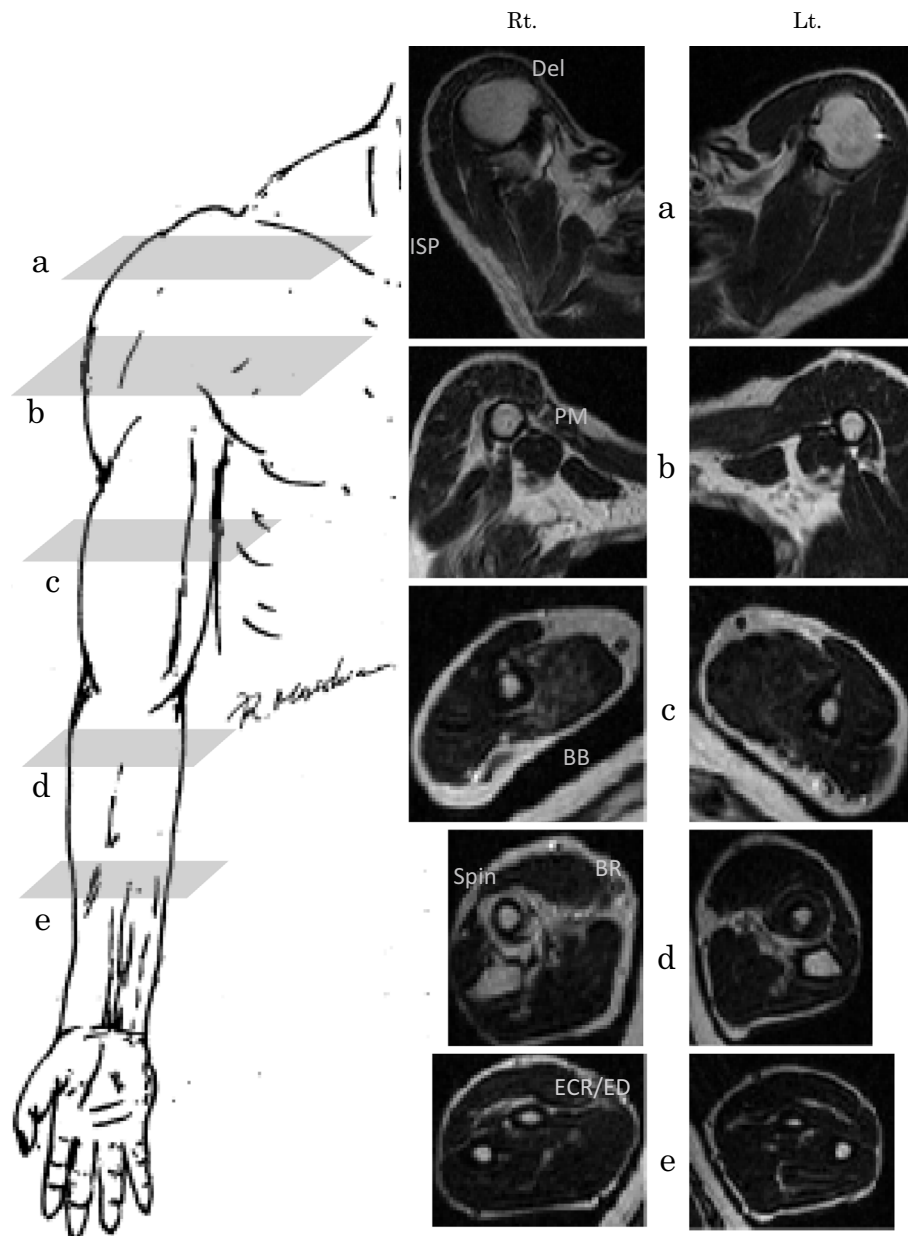


Figure 1. MRI of the bilateral upper extremities and axial T2WI of the bilateral upper extremities. Areas of high signal intensity on T2WI and STIR imaging were observed in the BB, ISP, subscapularis (SSc), supinator, BR, and ECR on the right side. Del: deltoid, ISP: infraspinatus, PM: pectoralis major, BB: biceps brachii, BR: brachioradialis, Spin: supinator, ECR: extensor carpi radialis, ED: extensor digitorum

nator, BR, and ECR on the right side (Fig. 1).

Treatment

The clinical findings strongly suggested NA under an active denervation process. The presence of serum anti-ganglioside antibodies suggested the involvement of an autoimmune process. Based on these findings, methylprednisolone pulse therapy and IVIG were administered, despite ten months having already elapsed from the onset of the symptoms. The patient underwent four courses of this therapy, which continued until 16 months after his first visit to our hospital. After each course his manual muscle test (MMT) results, anti-GD1a-IgG antibody titer, and axillary CMAP

amplitude showed staggered improvement (*i.e.*, improvement immediately after the administration of the drug followed by a plateau until the next treatment) (Fig. 2). At two years after the onset he had improved to the point of being able to perform push-ups and was able to lift a glass to his mouth without spilling its contents.

Discussion

We reported the case of a 55-year-old man who presented with neuralgia, weakness, and muscle atrophy in his right shoulder girdle and upper arm, which progressed for ten months following a marine sports accident. The distribution

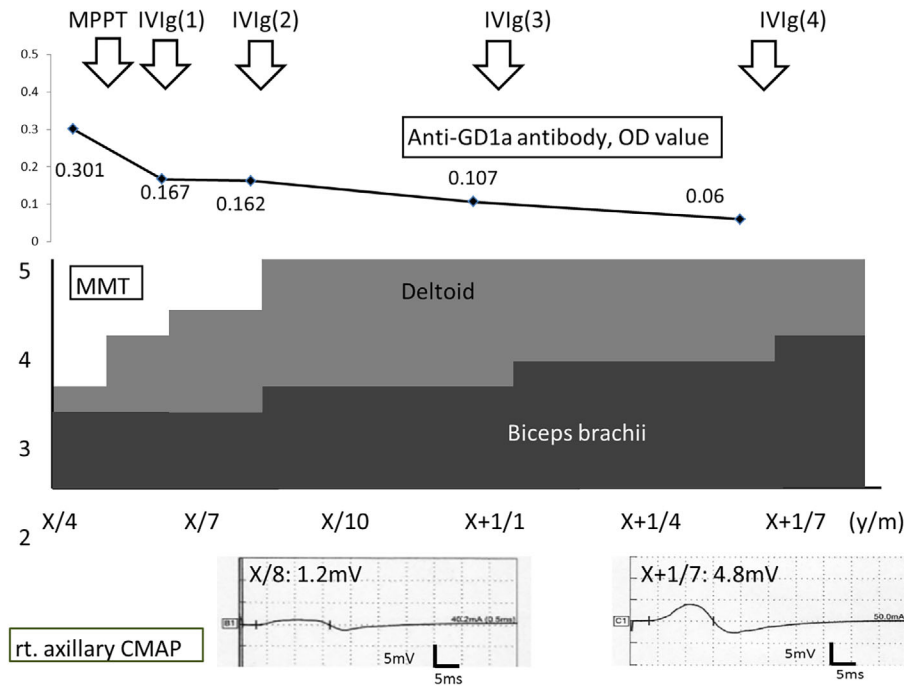


Figure 2. The clinical course. The recovery of MMT (right-side deltoid and biceps brachii) and compound motor nerve action potential in the right deltoid following the stimulation of the axillary nerve at Erb's point. OD value: optical density value (normal range ≤ 0.1), MPPT: methylprednisolone pulse therapy, IVIg: intravenous immunoglobulin

of weakness, amyotrophy, the high STIR intensity on muscle MRI, and denervation potentials suggested multifocal and incomplete right brachial plexus impairment. Nonetheless, immunotherapy was clearly effective in spite of the chronic progressive course.

Kuhlenbaumer et al. made the first diagnostic guidelines for NA (10). Other researchers have advocated different diagnostic criteria. van Alfen et al. emphasized five core features of NA in their 2015 report: 1) acute (or subacute) onset; 2) initial pain with a numerical rating scale (NRS) value of ≥ 7 ; 3) multifocal distribution, mainly in the upper brachial plexus and winged scapula; 4) a monophasic course, with a slow recovery; 5) the exclusion of preceding trauma, malignancy, diabetes mellitus, and radiation exposure (11). Our case fulfilled criteria 1-4 and was diagnosed as NA.

An electrophysiological examination and MRI imaging confirmed that - in the present case - the affected muscles were located in the upper-to-middle trunk along the right brachial plexus and its main branch, excluding the paraspinal muscle (3, 12-14). The clinical course was also compatible with that of NA, with the exception of chronic progression. Based on these findings we surmised that this case represented a subtype of NA. Although we were unable to exclude the possibility of vasculitis, as no biopsy was performed, systemic vasculitis was not likely as our case presented no symptoms of vasculitis. Diabetes is another possible cause of vasculitis plexopathy (15); however, there was no evidence of diabetes in the present case. Furthermore, the possibility of atypical chronic inflammatory demyelinating polyneuropathy (CIDP) - especially focal CIDP - could not

be ruled out. An electrophysiological examination revealed no evidence of demyelination; however, it should be noted that the study was incomplete due to the difficulty of assessing demyelination in the axillary and musculocutaneous nerves, especially in terms of the F wave elicited by distal (axillary) stimulation (16-18). Paraneoplastic neuropathy should also be considered in the differential diagnosis of brachial plexopathy (19); however, there was no evidence of malignancy in the present case.

Some reports have discussed the possible role of the autoimmune process and antiganglioside antibodies (3). Suarez et al. described the infiltration of mononuclear inflammatory cells in biopsy specimens obtained from patients with brachial plexus neuropathy (20). Vriesendorp et al. reported the presence of anti-peripheral nerve myelin antibodies in the serum of patients with 'acute brachial plexus neuritis' in 1993 (21). Three previous studies reported an 8-36% seroprevalence of antiganglioside antibodies in patients with NA (3, 22, 23). Stich et al. demonstrated a relatively high prevalence of IgM class antiganglioside antibodies in NA patients (23); however, their data using monkey tissue suggested nonspecific reactions. In short, the role of antiganglioside antibodies in NA is unclear, despite the evidence of an immune response. We further emphasize the heterogeneity of so-called 'NA'. The antiganglioside antibody is only detectable in a few patients with NA, suggesting that this feature is specific to a subgroup of NA cases.

Although there have been no prospective studies on IVIG therapy for NA, some case reports published after 2006 have reported its efficacy (5-9). Nonetheless the types of patient

who will respond to this therapy remain unclear. Furthermore, the type of treatment that is most appropriate for chronic progressive cases such as ours is even less clear; most previous studies have emphasized rapid intervention in the early stages of NA (4, 6-9). The efficacy of immunotherapy, including IVIG, has only been examined in three cases that were diagnosed at six months or more after the onset of symptoms (6, 7). Two of these cases responded to a single course of MPPT and IVIG; one did not. One of the responders was positive for anti-GM1 antibodies, which may be a nonspecific antiganglioside antibody; the other patient was not tested (7). Nonetheless, patients may respond to immunotherapy, even in the late phase of the disease; however, the clinical features of such cases must be carefully assessed to determine whether they can be located on the NA spectrum. Whether the recovery seen in our case was the effect of IVIG or an aspect of the natural disease course is a crucial but unanswered question. The staggered improvement that was seen after treatment and the monophasic recovery strongly suggested that the immunotherapy was effective.

With the exception of the painful phase in the early stage of the clinical course, the clinical picture of this case was similar to that of multifocal motor neuropathy (MMN). The efficacy of immunotherapy in this case was similar to cases of MMN, in which IVIG therapy is effective, even in the chronic phase of the disease (24) and irrespective of whether it is accompanied by a conduction block (25). With the exception of the electrophysiological criteria, this case fulfilled every point of the diagnostic criteria of European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) MMN (26). The diagnostic challenge in this case was to prove the presence of demyelination with an electrophysiological investigation because all of the affected nerve and muscles were too proximal to be properly studied. Anti-GM1-IgM antibodies are detected in 25-30% of MMN cases (27); however, our patient was negative for this antibody. Interestingly, one of the four cases in Suarez's report demonstrated onion-bulb formation in a biopsy specimen, which was accompanied by an enlarged C5 root on CT; the other cases in the report did not show these findings (20). Some so-called NA cases show demyelination, similarly to MMN. Thus, we think that there is an overlap between these two disease entities.

In summary, our case suggested the possibility that IVIG is effective for cases presenting as chronic NA, especially those involving patients who are positive for antiganglioside antibodies. No previous reports have discussed this condition, and the further accumulation of data, especially on chronic cases, is needed to clarify the pathological mechanism underlying this condition.

The authors state that they have no Conflict of Interest (COI).

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