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Case report

Acute Motor Conduction Block Neuropathy After Initiation of Omalizumab: Case Report and Literature Review for Possible Causality

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ABSTRACT

Background: Omalizumab is an established therapy for allergic conditions, yet its neurological effects remain underexplored compared to other biological agents.
Case description: A 45-year-old male with asthma developed acute quadriparesis one week after receiving the first dose of omalizumab. Electrophysiological studies have shown partial motor conduction block in multiple nerves, with reduced CMAP amplitudes and absent F-waves in others. CSF showed cyto-albuminous dissociation. The diagnosis was a variant of Guillain-Barré syndrome. Despite intravenous immunoglobulin (IVIG) therapy, the patient experienced persistent neuropathic symptoms.
Discussion: The patient presented with acute quadriparesis devoid of sensory or cranial nerve involvement, suggestive of a variant of Guillain-Barré syndrome (GBS) known as acute motor conduction block neuropathy (AMCBN). Electrophysiological studies have indicated conduction block without demyelination, implicating axonal degeneration. Despite negative findings for common etiologies, the temporal association between omalizumab administration and symptom onset suggests a potential link, supported by criteria for drug-induced illness. Conflicting evidence exists regarding omalizumab's neurological effects, with proposed mechanisms including autoimmune reactions and mast cell dysfunction. Comparisons to TNF-α antagonists highlight similar neuropathy patterns, indicating a need for further research to clarify omalizumab's neurotoxicity.
Conclusion: In conclusion, while omalizumab holds promise for allergic conditions, including chronic urticaria, its potential impact on peripheral nerves necessitates vigilance among clinicians. Further studies are imperative to ascertain the risk-benefit profile and elucidate underlying mechanisms and risk factors of neurological complications associated with omalizumab therapy.

1. Introduction

Omalizumab has emerged as a pivotal therapy for allergic conditions such as asthma, by preventing immunoglobulin E (IgE) interaction with mast cell receptors, thus reducing mediator release. Despite its generally safe profile, documented adverse effects include anaphylaxis, injection site reactions, neurological symptoms such as headache and sleep disturbances, and musculoskeletal issues [1]. Research on omalizumab's neurological effects is scarce, unlike other biological agents linked to various neurological side effects affecting both central and peripheral nervous systems.

We explore a rare variant of Guillain-Barré Syndrome (GBS), Acute Motor Conduction Block Neuropathy (AMCBN), and its potential association with omalizumab through literature review.

1.1. Case description

A 45-year-old male, previously diagnosed with asthma, with no history of other allergies, presented to our facility on the second day after experiencing the acute onset of quadriparesis. The weakness began in his right upper limb and then progressed to involve the right lower limb before affecting the left side of his body. The patient reported receiving his first dose of Omalizumab for asthma management two weeks before the onset of symptoms. Coinciding with the drug administration, he experienced a fever lasting 24 h, which resolved spontaneously. There were no accompanying symptoms of diarrhea, upper respiratory tract infection, or other systemic manifestations.

Upon admission, neurological examination revealed grade 4 weakness on the Medical Research Council (MRC) scale in all four limbs, with

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hyperreflexia, equivocal Babinski reflexes, preserved abdominal reflexes, and intact light touch and pinprick sensations. Mild impairment of vibration sensation was noted in the lower limbs, while cranial nerves, autonomic functions, respiratory muscles, and cerebellar examination were all normal. Magnetic resonance imaging (MRI) of the brain and cervical spine with contrast showed no abnormalities.

Over the subsequent two days, the patient's muscle power gradually declined, rendering him bedridden with grade 2 power and involvement of trunk muscles with the loss of all reflexes. However, there were still no signs of cranial, bulbar, respiratory, or neck muscle weakness, nor were there any sensory symptoms. On the fifth day of admission, lumbar puncture (LP) revealed cyto-albuminous dissociation with a protein level of 60 and 7 WBCs, mainly lymphocytic. Stool culture and serologic tests were negative for *Campylobacter jejuni* infection. Additionally, titers for IgG anti-GD1a and IgG anti-GM1 antibodies were not elevated.

Initial electrophysiological studies revealed partial motor conduction block in the wrist-elbow segments of both median and ulnar nerves, as well as in the knee-ankle segment of both tibial and peroneal nerves. Motor conduction velocities and distal motor latencies were normal bilaterally. Reduced distal compound muscle action potential (CMAP) amplitudes were noted in the peroneal nerve bilaterally, with absent F-waves in the median and ulnar nerves bilaterally (Table 1) (Fig. 1A, C). Sensory nerve conduction studies of the median and ulnar nerves and sural nerves were within normal limits. EMG revealed a variable reduced recruitment pattern with high-frequency discharging motor units in the upper limbs (biceps brachii and abductor pollicis brevis) and lower limbs (tibialis anterior and vastus lateralis), without spontaneous activity detected.

The patient was diagnosed with a variant of Guillain-Barré syndrome (GBS) and received intravenous immunoglobulin (IVIG) at a dosage of 0.4 g/kg/day for five days. During this time, he also experienced severe lumbar back pain with radicular pain in both lower limbs. Despite some improvement in lower limb strength and the ability to extend his knees with difficulty following the IVIG treatment, the pain persisted. Subsequently, the patient received pregabalin and intravenous methylprednisolone (IVMP), which provided partial relief. Aggressive rehabilitation in the form of exercise intervention included upper and lower limb exercises, abdominal exercises, balance exercises, and fine motor skill exercises. These efforts led to ambulation with minimal assistance within one year.

Upon follow up one year later, the patient exhibited distal weakness in both upper and lower limbs, with bilateral wasting in ulnar and posterior tibial innervated muscles. Electrophysiological examination showed resolution of the conduction block, with decreased compound muscle action potential (CMAP) mainly in ulnar and posterior nerves bilaterally (Table 2) ((Fig. 1B, D).EMG findings revealed signs of denervation in the abductor digiti minimi and soleus muscles. The patient discontinued omalizumab following the neurological illness and is now stable on montelukast sodium and tiotropium bromide.

Table 1
Motor nerve conduction studies at presentation.

Motor Nerve Conduction Study					
Nerve	Latency	Amplitude	Conduction Velocity	F latancy	F-M Latency
	ms	mV	m/s	ms	ms
Median Motor Right					
Wrist - APB	2.97	2.9			
Elbow-Wrist	7.85	0.76	57.4		
Peroneal Motor Left					
Ankle - EDB	4.31	2.9		58.1	53.6
Bl. Knee-Ankle	12.4	2.3	42.0		
Ab. Knee-Bl. Knee	15.0	1.50	42.3		
Peroneal Motor Right					
Ankle - EDB	4.04	4.1		57.1	53.0
Bl. Knee-Ankle	12.1	0.50	43.4		
Ab. Knee-Bl. Knee	14.0	0.48	52.6		
Peroneal TA Motor Left					
Bl.knee - Tib. ant	3.96	0.51			
Ab.knee-Bl. knee	6.24	0.18	43.9		
Peroneal TA Motor Right					
Bl.knee - Tib. ant	4.25	0.48			
Ab.knee-Bl. knee	6.70	0.43	44.9		
Tibial Motor Left					
Med. mal - Abd hal	5.08	1.93			
Bl. knee-Med. mal	14.7	1.22	44.7		
Tibial Motor Right					
Med. mal - Abd hal	5.82	4.0		62.7	58.3
Bl. knee-Med. mal	16.3	2.1	40.1		
Ulnar Motor Right					
Wrist - ADM	2.33	2.1			
Bl. elbow-Wrist	6.73	0.38	56.8		

APB = Abbductor Pollicis brevis, EDB = Extensor Digitorum Brevis, AB. = above, BL. = Below, Tib. Ant = Tibialis anterior, Med. Mal = Medial malleolus, Abd hal = Abductor halluces, ADM = Adductor digitiminimi.

2. Discussion

The patient presented with acute pure motor quadriplegia over one week, devoid of sensory or cranial nerve involvement. Electrophysiological studies revealed motor neuropathy with conduction block in all examined nerves, while distal latency and conduction velocity remained normal, excluding a demyelinating Guillain-Barré syndrome (GBS) variant. At this juncture, establishing an exact pathological and etiological diagnosis for the patient posed a challenge.

Nerve conduction studies (NCS) in our patient revealed conduction block, indicative of segmental demyelination. However, conduction block can also result from sodium channel blockade at the nodes of Ranvier, as seen in Acute Motor Axonal Neuropathy (AMAN). In AMAN, complement deposition at these nodes causes paranodal myelin distortion and occasional myelin loop breakdown, disrupting impulse conduction and leading to paralysis followed by either rapid recovery or axonal Wallerian degeneration [2]. This aligns with Capasso and Unicini's (2003) concept that Acute Motor Conduction Block Neuropathy (AMCBN) is an "arrested" form of AMAN, sharing similar immunopathology but with a less intense immune reaction [3]. Our case thus classifies as AMCBN progressing into axonal degeneration.

Regarding the etiology, there were no signs of alternative causes such as diarrhea or respiratory tract infection. Laboratory tests ruled out common causes like *Campylobacter jejuni*, connective tissue disorders, viral infections, thyroid abnormalities, and vitamin deficiencies. However, the timing of symptom onset following the initial administration of omalizumab suggests a potential causative relationship between the medication and the neurological condition.

According to Miller et al.'s 2000 criteria [4], an illness is considered

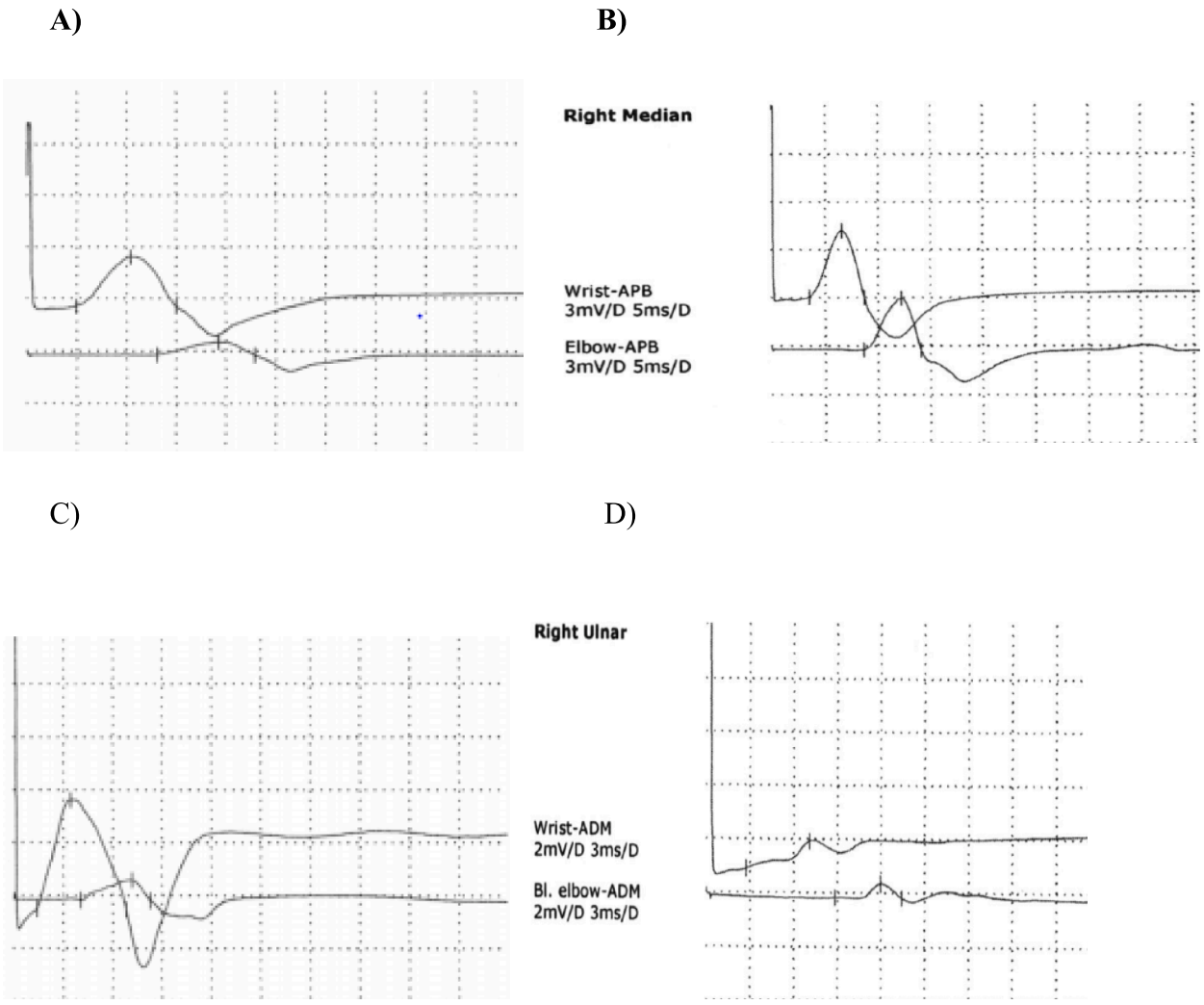

Fig. 1. Motor nerve conduction study of the right median nerve done 5th day of admission (A) show conduction block with normal distal latency and velocity, repeated one after 1y (B) show resolution of the conduction block with relative increase in amplitude. Motor nerve conduction study of the right ulnar nerve done 5th day of admission (C) show conduction block with normal distal latency and velocity, repeated one after 1y (D) show resolution of the conduction block with decrease in amplitude indicating axonal degeneration.

drug-induced if at least four of eight criteria are met. In our case, the motor neuropathy likely correlates with omalizumab, meeting three criteria: close temporal relationship, absence of alternative explanations, and biological plausibility of omalizumab triggering an immune reaction affecting the nerves. The dechallenge possibility remains uncertain; while the drug was discontinued and the patient improved, Guillain-Barré Syndrome (GBS) typically has a monophasic course. We will review literature to explore omalizumab's influence on the nervous system, highlighting biological plausibility and potential analogy.

Studies on omalizumab's neurological effects have been mixed. Goknur et al. (2018) studied 30 chronic spontaneous urticaria (CSU) patients treated with omalizumab and noted potential changes in nerve parameters like amplitude, latency, and velocity before and three months after treatment. However, these changes were deemed insufficient to diagnose neuropathy. The study suggested omalizumab might exacerbate neuropathy severity when used with other peripheral nerve-affecting drugs, but noted limitations such as small sample size and short study duration [5].

Proposed mechanisms for omalizumab's neurological effects include triggering autoimmune processes, increased infection susceptibility, and mast cell function distortion. This distortion may either increase activation, elevating neuropeptide production and sensory nerve excitability, or inhibit neuromediator expression, impacting peripheral nerve involvement [6].

In contrast, Altunisik and Dogan (2021) studied 47 CSU patients treated with omalizumab and found no signs of neuropathy before or three months after treatment, with no significant changes in nerve conduction velocity, amplitude, or latency [7].

As for other biological agents specially TNF-α antagonists, such as infliximab, are linked to adverse effects like drug-induced lupus and demyelinating syndromes, with an incidence of 233 cases per million patients. Studies (Tektonidou et al. 2006; Jarand et al.; Lozeron et al. 2009; Carrilho et al. 2010) reported peripheral neuropathy in rheumatic patients, presenting as Guillain-Barre syndrome, multifocal motor neuropathy, axonal sensory polyneuropathy, and optic neuritis. Symptoms typically appeared weeks to months after treatment initiation and often resolved upon discontinuation, indicating a potential causal relationship. Other disorders include Miller-Fisher syndrome and chronic inflammatory demyelinating polyradiculoneuropathy [8– 13]. Pathogenesis likely involves myelin damage from T-cell-dependent immune activation and antibody production, ischemic damage from vasculitis, and disrupted axon support signals. Prolonged use can exacerbate autoimmune responses by affecting antigen-presenting cells, amplifying T-cell signaling, and reducing apoptosis of auto-reactive T cells [14,15].

Given the differing mechanisms of action, it remains unclear if

Table 2
Motor nerve conduction studies after 1 y.

Motor Nerve Conduction Study					
Nerve	Latency	Amplitude	Conduction Velocity	F latancy	F-M Latency
	ms	mV	m/s	ms	ms
Median Motor Right					
Wrist - APB	3.49	4.2		30.9	27.6
Elbow-Wrist	8.65	3.2	50.4		
Peroneal Motor Left					
Ankle - EDB	5.04	3.8		51.9	47.3
BI. Knee-Ankle	11.9	3.6	46.6		
Ab. Knee-BI. Knee	14.0	3.6	47.6		
Peroneal Motor Right					
Ankle - EDB	4.97	2.3		57.1	53.1
BI. Knee-Ankle	12.5	2.5	45.2		
Ab. Knee-BI. Knee	14.6	7.5	47.6		
Tibial Motor Left					
Med. mal - Abd hal	4.78	0.59		57.8	54.6
BI. knee-Med. mal	14.3	0.49	43.1		
Tibial Motor Right					
Med. mal - Abd hal	5.66	0.21		60.4	53.5
BI. knee-Med. mal	17.2	0.17	44.4		
Ulnar Motor Right					
Wrist - ADM		1.04			
Bl. elbow-Wrist	8.84	0.52	42.6		

APB = Abbductor Pollicis brevis, EDB = Extensor Digitorum Brevis, AB. = above, BL. = Below, Tib. Ant = Tibialis anterior, Med. Mal = Medial malleolus, Abd hal = Abductor halluces, ADM = Adductor digitiminimi.

omalizumab can induce neuropathy patterns akin to TNF-alpha antagonists. Further research with larger cohorts and extended follow-up is warranted to elucidate this matter.

3. Conclusion

In conclusion, while omalizumab holds promise for allergic conditions, including chronic urticaria, its potential impact on peripheral nerves necessitates vigilance among clinicians. Further studies are imperative to ascertain the risk-benefit profile and elucidate underlying mechanisms and risk factors of neurological complications associated with omalizumab therapy.

Ethics approval and consent to participate

The study was performed in accordance with the Declaration of Helsinki. Written Informed consent to participate was obtained from the patient.

Consent for publication

Written consent to publish was obtained from study participants.

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Authors' contributions

- H. E.: Literature search, data acquisition and analysis, manuscript preparation and editing.
- A. A: Manuscript reviewing and editing
- All authors have read and approved the manuscript

CRediT authorship contribution statement

Hosna S. Elshony: Writing – review & editing, Writing – original draft, Visualization, Methodology, Data curation, Conceptualization. **Abdulaziz Al-Ghamdi:** Writing – review & editing, Visualization, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interests that may influence the manuscript.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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