

A Young Male with ISAACS' Syndrome - A Case Report

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Abstract: *Peripheral nerve hyperexcitability syndromes are a group of disorders characterized by muscle stiffness, cramps, and muscle twitches with involuntary abnormal electrical activity on needle EMG. These rare diagnoses include cramp-fasciculation syndrome, Isaacs syndrome, and Morvan syndrome. We report a case of a 31-year-old young male, presented with history of multiple episodes of cramps of both lower limbs, burning sensation of both thighs, twitching over both calves, increased sweating. Auto immune encephalitis panel showed CASPR 2 and LGI 1 (VGKC associated antibodies) and improved with pulse steroid therapy, gabapentin, carbamazepine treatment.*

Keywords: Peripheral nerve hyperexcitability, muscle cramps, muscle twitching, CASPR2 antibodies, LGI1 antibodies

1. Introduction

Isaacs' syndrome is a peripheral nerve hyperexcitability (PNH) syndrome that is characterized by continuous muscle twitching, myokymia, muscle hypertrophy, and dysautonomia, and sometimes associated with neuropathic pain and paresthesias. Electro diagnostic tests had unique spontaneous motor activities including fasciculation, myokymic discharges, and neuro myotonic discharge. Presently, an acquired Isaacs' syndrome is recognized as a paraneoplastic autoimmune condition that correlates with voltage-gated potassium channels (VGKC) complex antibodies and underlying tumors, especially thymoma disease in a same person in young age

2. Case Presentation

A 31-year-old young male, newly diagnosed hypertensive presented with history of multiple episodes of cramps of both lower limbs which lasts for 10 minutes, burning sensation of both thighs, twitching over both calves, increased sweating since 1 month

3. Discussion

- Patient had myokymia in both calves, global hyporeflexia, decreased pain and temperature both lower limbs and left upper limb, impaired vibration sense over both great toes, intact joint position sense, 4+ grade of proximal power in both lower limbs and left upper limb
- Routine blood Investigations, Thyroid function test, Cerebrospinal fluid analysis, Nerve conduction study of all 4 limbs, HRCT chest was normal
- Electromyography (EMG) studies showed spontaneous motor unit discharges including fasciculation, neuromyotonic discharge, and myokymic discharge (triplet and doublet) at rest
- Serum Auto immune encephalitis test showed positive VGKC complex antibodies, including leucine-rich glioma-inactivated 1 (LGI1) and contactin-associated protein-like 2 (CASPR2) antibodies
- Patient symptoms started to improve with Pulse steroid therapy, Gabapentin, Carbamazepine treatment



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DEPARTMENT OF NEUROPATHOLOGY

Autoimmune Laboratory

MRN	EXT1202514871	Department	Neuropathology (Auto Immune Lab)
Name	[REDACTED]	Specimen	Serum
Age / Sex	31 Y/MALE	Visit Type	OP
Sample No	AU0503250040	Collected On	05/03/2025 15:23
Lab Reference No	XAU-2037	Received On	05/03/2025 15:24
Consulting Doctor	DR HARIHARAN	Reported On	05/03/2025 15:27

Test Name	Result	Comments
ANA PROFILE		
nRNP-Sm	Negative.	
Sm	Negative.	
SS-A	Negative.	
Ro-52	Negative.	
SS-B	Negative.	
Scl-70	Negative.	
PM-Scl	Negative.	
Jo-1	Negative.	
CENP B	Negative.	
PCNA	Negative.	
dsDNA	Negative.	
Nucleosomes	Negative.	
Histones	Negative.	
Ribosomal P-protein	Negative.	
AMA M2	Negative.	
Autoimmune Encephalitis Mosaic - SERUM (NMDA and VGKC)		
Glutamate receptor, NMDA	Negative.	
Glutamate receptor, AMPA1	Negative.	
Glutamate receptor, AMPA2	Negative.	
CASPR (contactin - associated protein 2/VGKC associated)	Positive.	Dual positive seen rarely. Correlate clinically.
LGI-1 (Leucine rich glioma-inactivated protein 1/ VGKC associated)	Positive.	Dual positive seen rarely. Correlate clinically.
GABAB receptor (GABAB1,B2)	Negative.	

4. Conclusion

Clinical presentation of peripheral nerve hyper excitability syndrome with cramps, myokymia, dysautonomia without CNS involvement, which is proven by positive serum VGKC complex antibodies, including leucine-rich glioma-inactivated 1 (LGI1) and contactin-associated protein-like 2 (CASPR2) antibodies. Hence, we report a case of Isaacs' syndrome in young male.

References

- [1] Hart IK, Maddison P, Newsom-Davis J, Vincent A, Mills KR. Phenotypic variants of autoimmune peripheral nerve hyperexcitability syndromes. *Brain*. 2002;125(Pt 8):1887-1895.
- [2] Useful for classification of Isaacs syndrome, Morvan syndrome and related PNH disorders. Newsom-Davis J, Mills KR. Immunological associations of acquired neuromyotonia (Isaacs' syndrome). Report of five cases and literature review. *Brain*. 1993;116(Pt 2):453-469.
- [3] Sinha S, Newsom-Davis J, Mills K, et al. Autoimmune aetiology for acquired neuromyotonia (Isaacs' syndrome). *Lancet*. 1991;338(8769):75-78.
- [4] Ahmed A, Simmons Z. Isaacs syndrome: A review. *Muscle Nerve*. 2015;52(1):5-12. doi:10.1002/mus.24632.
- [5] Newsom-Davis J, Buckley C, Clover L, et al. Autoimmune disorders of neuronal potassium channels. *Ann N Y Acad Sci*. 2003; 998: 202-210. doi:10.1196/annals.1254.022.
- [6] Klein CJ, Lennon VA, Aston PA, et al. Chronic pain as a manifestation of peripheral nerve hyperexcitability syndromes associated with antibodies to voltage-gated potassium channels. *Arch Neurol*. 2010;67(12):1480-1484.
- [7] Irani SR, Alexander S, Waters P, et al. Antibody to CASPR2 and clinical phenotype in autoimmune encephalitis. *Neurology*. 2010;75(16):1495-1503.
- [8] Particularly relevant to the manuscript's CASPR2-positive findings. Psimaras D, Carpentier AF, Rossi C. Chronic neuromyotonia associated with CASPR2 antibodies: clinical and electrophysiological features. *Neuromuscul Disord*. 2012;22(5):429-434.

- [9] Shillito P, Molenaar PC, Vincent A, et al. Acquired neuromyotonia: evidence for autoantibodies directed against K⁺ channels of peripheral nerves. *Ann Neurol*. 1995;38(5):714-722.
- [10] Mizuno Y, Shimoe Y, Matsuda S, et al. Isaacs syndrome with CASPR2 antibody: a series of three cases. *Intern Med*. 2017; 56: 2367-2370.