

Case Report

A CASE REPORT OF ACQUIRED NEUROMYOTONIA IN A 16 YEAR OLD GIRL

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ABSTRACT

Introduction: Acquired neuromyotonia (Isaacs' syndrome) is a rare disorder characterized by hyperexcitability of peripheral motor nerves. The characteristic features consist of myokymia, pseudomyotonia and contracture of hands and feet. The diagnosis of Isaacs' syndrome is based on the clinical features and classic electromyographic findings. Serum antibodies against Voltage-Gated Potassium Channels (VGKCs) are detected in some cases. **Case Presentation:** We present a case of 16 year old girl complaining of continuous muscle cramps of right calf muscles since last 2 years. Clinically there was myokymia of right sided calf muscles with myotonia. There was no spine pathology. Electromyography revealed specific spontaneous activity in the form of continuous repetitive MUAP discharges with period of silence in between in right gastrocnemius muscle with waxing and waning pattern. The investigations for conditions associated with Isaacs' syndrome were done excluding most of the causes. Voltage-Gated Potassium Channels (VGKCs) antibodies were not performed. Treatment with intravenous immunoglobulin (IVIg) along with long term course of oral carbamazepine helps in substantial improvement of the symptoms. **Conclusion:** There are various treatment options available for management of neuromyotonia and each one has unpredictable outcome. Some cases respond to short term oral anticonvulsants while some of the refractory cases may require intravenous immunoglobulin along with long term anticonvulsants for better outcome.

Keywords: Neuromyotonia, IVIG

INTRODUCTION

Neuromyotonia is a form of peripheral nerve hyperexcitability with spontaneous and continuous muscle fibre activity (Maddison, 2006). It has variously been called undulating myokymia, Isaac's syndrome and cramp-fasciculation syndrome (Hart *et al.*, 2002). It might be hereditary or acquired and there have been a variety of reported causes and associations. It was first described in 1961 in two men with persistent, generalised muscle stiffness, in addition to spontaneous, rapid discharges of motor-unit potentials on electromyography (Isaacs, 1961). Disease onset is usually between the ages of 15 and 60 years but has also been reported in childhood. Acquired neuromyotonia has been found to be associated with various autoimmune disorder, thymus cancer, lung cancer or lymphoma (Paterson *et al.*, 2014). Approximately 40% of affected individuals have antibodies to voltage-gated potassium channels (VGKC's) (Vernino and Lennon, 2002; Paterson *et al.*, 2014). The disorder is characterized by progressive stiffness, cramping, and weakness. Muscle activity is constant, and patients describe the feeling of continuous writhing or rippling of muscles under the skin. In some patients there may be hyperhidrosis, tachycardia and weight loss. Diagnosis is based on clinical findings and electromyography picture. Treatment with anticonvulsants medications has reported to improve neuropathic pain and fasciculations. In refractory cases plasmapheresis and intravenous immunoglobulin (IVIg) along with anticonvulsants helps to improve symptoms.

CASES

We present a case of 16 year old girl complaining of muscle cramps of right calf muscles since last 2 years without prior history of any trauma. Muscular cramps increased progressively and used to remain throughout the day and night which hampered her daily routine activity. There was no history of similar complaints involving other parts of body. On examination, there were continuous muscle fasciculation of

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right calf muscles without local rise of temperature or any tenderness. There wasn't any spine deformity and neurological examination of all four limbs was normal. Her x-ray of right leg [figure 1] and x-ray Lumbosacral spine [figure 2] shows no significant abnormality. Due to the increasing symptoms, she underwent a MRI right leg [figure 3] which shows medial tibial stress syndrome and therefore, managed conservatively for one year in the form of rest, oral analgesics, ice application and usage of splints. Later on electromyographic study of right leg [figure 4] suggests specific spontaneous activity in the form of continuous repetitive MUAP discharges with period of silence in between in right gastrocnemius muscle with waxing and waning pattern. Initially patient was started on tablet Carbamazepine 200mg twice a day and tablet Prednisolone 40mg in tapering dose for 3 weeks but her symptoms doesn't improve. Later on patient was given intravenous immunoglobulin (IVIG) (2gm/kg body weight) along with tablet carbamazepine 200mg twice a day for 8 months which substantially improves her symptoms. Voltage-Gated Potassium Channels (VGKCs) antibodies were not performed.



Figure 1: X-ray Right Tibia-Fibula



Figure 2: X-ray Lumbosacral Spine

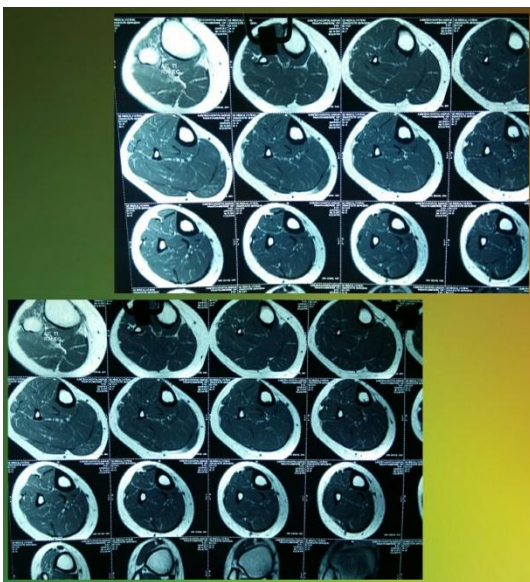


Figure 3: MRI Right Leg

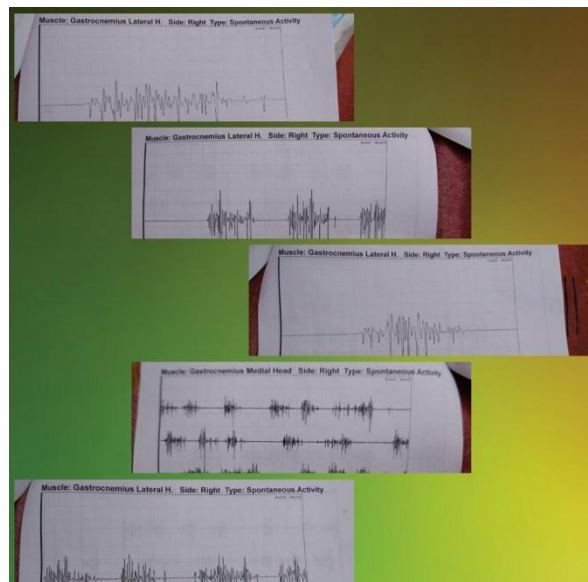


Figure 4: Electromyographic Study of Right Gastrocnemius Muscle

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DISCUSSION

Acquired neuromyotonia (Isaacs' syndrome) is a rare disorder where hyperexcitability of peripheral motor nerves leads to incapacitating muscle twitching, cramps, myokymia, pseudomyotonia (slow muscle relaxation after forceful contraction) and mild weakness (Isaacs, 1961). The muscle cramp may be prominent and accompanied by excessive sweating and weight loss (Lahrman *et al.*, 2001). This uncommon disorder was first described by Isaacs (1961) in his paper 'A syndrome of continuous muscle-fibre activity giving the triad of myokymia, muscular stiffness, and decreased deep tendon reflexes the paper's name.

Isaac's syndrome has been long recognized by several physicians (Ian, 2000), however its rarity and the variability of its clinical manifestation and ways of presentation is probable the most important reason why its frequently misdiagnosed or wrongly treated (Foyaca-Sibat *et al.*, 2001). An acquired neuromyotonia is frequently associated with autoimmune disorders, thymus cancer, lymphoma, or lung cancer.

The diagnosis of Isaacs' syndrome is based on clinical features and electromyographic findings. The cardinal features consist of myokymia, pseudomyotonia and stiffness of trunk and limbs (Isaacs, 1961; Paterson *et al.*, 2014). Most patients are sporadic. This is related to the autoimmune mechanism where the autoantibodies are usually detected against the Voltage-Gated Potassium Channels (VGKCs) (Shillito *et al.*, 1995). Clinical evidence suggesting a possible autoimmune etiology included the presence of oligoclonal bands in the spinal fluid of some patients and clinical improvement following plasma exchange (Nakatsuji *et al.*, 2000).

Treatment of Isaac's syndrome with antiepileptic drugs or immunotherapy often improves the clinical and electrophysiologic findings. Carbamazepine, phenytoin, lamotrigine and sodium valproate can be used alone or if necessary in combination with prednisolone or methotrexate (Foyaca-Sibat and Ibañez-Valdés, 2001; Schwarz and Grigat, 1989). Plasma exchange often produces useful clinical improvement lasting from 6 weeks up to 6-17 month accompanied by a reduction in EMG activity and a fall in VGKC antibody titres. Intravenous immunoglobulin (IVIG) is one the important and recent lines of management with good response (Nakatsuji *et al.*, 2000; Jaben and Witers, 2012; Hayat *et al.*, 2000; Shillito *et al.*, 1995). In patients with positive findings of VGKC antibodies it is recommended to commence the therapy with plasmapheresis with subsequent oral immunosuppressive therapy applying corticoids or azathioprine (Merchut, 2010). In patients without VGKC antibodies plasmapheresis is not efficient, and it is recommended to start with a full dose of Intravenous immunoglobulin (IVIG) (2g/kg body weight), and then continue with a maintenance dose of corticoids (Rinaldi *et al.*, 2009). Carbamazepine at a dose of 400 to 600mg per day leads to disappearance of fasciculations and neuropathic pain (Foyaca-Sibat and Ibañez-Valdés, 2001; Schwarz and Grigat, 1989).

Conclusion

Though acquired neuromyotonia is rare entity of disease, it should not be misdiagnosed. Intravenous immunoglobulins (IVIG) along with long term carbamazepine is preferred treatment for unresponsive cases of acquired neuromyotonia.

Competing Interests

The authors declare that they have no competing interests.

REFERENCES

- Foyaca-Sibat H and Ibañez-Valdés L (2001).** Issacs' Syndrome Successfully Treated with Phenytoin at Low Doses. *The Internet Journal of Neurology* 1(2).
- Foyaca-Sibat H, Ibanez-Valdes LdeF and Awotedu A (2001).** Acute Renal Failure due to Herbal Medicine Intoxication in Acquired Neuromyotonia. Available: <http://www.uninet.edu/cin2001/paper/ibanez/foyaca.html>.
- Hart IK, Maddison P, Newsom-Davis J, Vincent A and Mills KR (2002).** Phenotypic variants of autoimmune peripheral nerve hyperexcitability. *Brain* 125 1887-1895. 10.1093/brain/awf178.

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Hayat GR, Kulkantrakorn K, Campbell WW and Giuliani MJ (2000). Neuromyotonia: Autoimmune pathogenesis and response to immune modulating therapy. *Journal of the Neurological Sciences* **181** 38-43.

Ian KH (2000). Acquired Neuromyotonia: A new Autoantibody-Mediated Neuronal Potassium Channelopathy. *The American Journal of the Medical Sciences* **319** 209-216.

Isaacs H (1961). A syndrome of continuous muscle-fiber activity. *Journal of Neurology, Neurosurgery & Psychiatry* **24** 319-25.

Jaben EA and Witers JL (2012). Plasma exchange as a therapeutic option in patients with neurologic symptoms due to antibodies to voltage-gated potassium channels: A report of five cases and review of the literature. *Journal of Clinical Apheresis* **27**(5) 267-73.

Lahrman H, Albrecht G, Drlicek M, Oberndorfer S, Urbanits S, Wanschitz J et al., (2001). Acquired neuromyotonia and peripheral neuropathy in a patient with Hodgkin's disease. *Muscle & Nerve* **24** 834-8.

Maddison P (2006). Neuromyotonia. *Clinical Neurophysiology* **117** 2118-2127. 10.1016/j.clinph.2006.03.008.

Merchut MP (2010). Management of voltage-gated potassium channel antibody disorders. *Neurologic Clinics* **28** 941-59.

Nakatsujii Y, Kaido M, Sugai F et al., (2000). Isaacs syndrome successfully treated by immunoadsorption plasmapheresis. *Acta Neurologica Scandinavica* **102** 271-273.

Paterson RW, Zandi MS, Armstrong R, Vincent A and Schott JM (2014). Clinical relevance of positive voltage-gated potassium channel (VGKC)-complex antibodies: experience from a tertiary referral centre. *Journal of Neurology, Neurosurgery & Psychiatry* **85**(6) 625-30 doi: 10.1136/innp-2013-305218.

Rinaldi C, Russo CV, Filla A, De Michele G and Marano E (2009). Course and outcome of voltage-gated potassium channel antibody negative Morvan's syndrome. *Neurological Sciences* **30** 237-9.

Schwarz DJ and Grigat G (1989). Phenytoin and carbamazepine: potential-and frequency-dependent block of Na currents in mammalian myelinated nerve fibers. *Epilepsia* **30** 286-294.

Shillito P, Molenaar PC, Vincent A, Leys K, Zheng W, van den Berg RJ, Plomp JJ, van Kempen GT, Chauplannaz G, Wintzen AR et al., (1995). Acquired neuromyotonia: evidence for autoantibodies directed against K⁺ channels of peripheral nerves. *Annals of Neurology* **38**(5) 714-22. PubMed PMID: 7486862.

Vernino S and Lennon VA (2002). Ion channel and striational antibodies define a continuum of autoimmune neuromuscular hyperexcitability. *Muscle & Nerve* **26** 702-07.