Isaacs syndrome is a rare neuromuscular disorder characterized by chronic muscle stiffness, cramping, fasciculations, myokymia, and hyperhidrosis. Pathogenesis includes autoimmunity, paraneoplastic disorders, genetic predisposition, or toxin exposure. There is no known cure for Isaacs syndrome.

This case report describes a patient who had been given the diagnosis of Isaacs syndrome and received osteopathic manipulative treatment to manage fascial and cranial dysfunctions and reduce nervous system hyperexcitability. Long-term decrease of myokymia and reduction of severity and frequency of exacerbations resulted.

Isaacs syndrome was first described in 1961 by neurologist Hyam Isaacs, MD, after he observed 2 patients with persistent muscle activity, hyperhidrosis, and muscle stiffness. Peripheral nerve hyperexcitability (PNH) encompasses involuntary continuous muscle activity that can include muscle cramps, fasciculations, myokymia, and pseudomyotonia, often developing from pathologic changes to voltage-gated potassium channels (VGKCs). Fasciculations are spontaneous discharges of a single motor axon. Group fasciculations at slower rates are called myokymia, where undulating movements of muscles can be seen on the skin surface. Faster rates occur in patients with neuromyotonia. Pathogenesis includes autoimmunity, paraneoplastic disorders, genetic predisposition, or toxin exposure, all of which affect VGKCs. It is recommended that nonmalignant causes be managed symptomatically with carbamazepine, and with phenytoin and gabapentin as second-line treatment. Additional medications include valproic acid, acetazolamide, lamotrigine, clonazepam, and dronabinol. According to the National Institute of Neurological Disorders and Stroke, Isaacs syndrome is considered rare and has no cure. The current case describes a patient with a diagnosis of Isaacs syndrome caused by long-term exposure to toluene.

Report of Case

A 55-year-old-man with Isaacs syndrome presented to the University of Pikeville Kentucky College of Osteopathic Medicine student teaching clinic in August 2014 seeking additional relief of pain and muscle rigidity. He had been undergoing sporadic osteopathic structural examinations (OSEs) and osteopathic manipulative treatment...
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(OMT) sessions for the past 5 years, since 2009. The patient received a diagnosis of Isaacs syndrome in 2006, 8 years before the current presentation, but irregular OMT sessions and medication at the time of presentation did not relieve his symptoms. He reported that the symptoms began 1 year before diagnosis and included myokymia and total muscle contractions that caused dislocations and muscle tearing. The patient had worked in automotive restoration for more than 20 years before the diagnosis and wore only shorts and a face mask while painting cars. His medical record indicated that the disease was caused by chronic transdermal absorption of toluene, confirmed by muscle biopsy and electromyography, which showed fasciculations and cramping predominantly in proximal muscles. The patient was bedridden at the time of diagnosis. Carbamazepine was prescribed after diagnosis, which restored his mobility, and his medication was later switched to lamotrigine. At the time of presentation to the osteopathic medical school teaching clinic, disease management included 100 mg of lamotrigine and 10 mg of baclofen twice per day. During severe exacerbations the dose was increased. Hearing loss and muscle atrophy had been observed since the onset of the disease. During that time, he had constant myokymia, neuromyotonia, and peripheral neuropathy. He recollected a baseline pain score of 5 out of 10 using the Numeric Rating Scale. His symptoms increased to incapacitating levels, during which the patient had experienced myocardial infarction due to coronary artery spasm, respiratory failure, muscle tearing, bone fractures, joint dislocations, and severe bruising as a result of muscle cramps and contractures. These exacerbations were worsened by increased activity and cold weather.

Analysis of the patient’s response to OMT ranged from August 2014 to September 2015. The patient was scheduled to receive OMT weekly; however, treatment occurrence varied depending on the clinic’s schedule and the severity or frequency of exacerbations, which limited his ability to travel. Osteopathic structural examinations and OMT sessions were performed by student teaching fellows and faculty from the Department of Osteopathic Principles and Practices. All providers followed the same OSE process of assessing the cranium and thoracic, lumbar, and pelvic rigidity.

From August to December 2014, the patient underwent 10 OMT sessions. An OSE was performed before and after each treatment session to assess structural and functional improvement. Findings of the OSEs consisted primarily of cervical spine dysfunctions, thoracic and lumbar paraspinal hypertonicity, rib dysfunctions, fascial restrictions of the upper extremity, gait rigidity, pelvic restrictions, and any sequelae related to recent exacerbations. Management included balanced ligamentous tension, direct or indirect myofascial release, functional, facilitated positional release, and articulatory techniques. Techniques that did not use the patient’s active muscle contraction and avoided the potential for excessive or rapid stretch were selected. For the first 8 visits, the patient stated that the myofascial release techniques were the most beneficial, as they provided relief of rigidity and pain and decreased hypertonicity in the regions addressed. The relief lasted a few hours. The cranium was not initially a focus of his care owing to consistent findings of soft tissue injury and somatic dysfunction caused by exacerbations, but after finding somatic dysfunctions during the ninth session, osteopathic cranial manipulative medicine (OCMM) was performed. The patient’s myokymia resolved for 2 days after the treatment.

From January to September 2015, the patient received 17 OMT sessions with accompanying OSEs. Because the patient had a positive response to OCMM, the cranium was examined and treated first. The majority of findings related to the cranium were sidebending rotations and torsions, but other strain patterns were also observed. Management began with addressing the strain pattern followed by individual sutural restrictions. Techniques used included balanced membranous tension and dural venous sinus release. The fasciculations on the right side of the patient’s neck and right eye lacrimation...
Our initial hypothesis was that myofascial release was the most effective way to manage the current patient’s symptoms, until OCMM was used, which resulted in greater positive effects. Both techniques provided results that were systemic, not only resolving dysfunction in the specific body region addressed, but also dysfunctions in other body regions.

Through systemic connections, fascia has the potential to influence multiple body systems. Fascia is connective tissue consisting of multiple anatomic layers that unite and support the entire body. Highly innervated and vascularized, fascia is involved in metabolic activity and immune surveillance. Studies have shown fascia to be a mechanosensitive signaling system with many potential systemic influences. Symptoms related to dysfunction of the deep fascia include disturbance in proprioception, myofascial pain, and muscle cramps. Muscle spindles are connected to the epimysium of deep fascia. Tension in the deep fascia can lengthen the muscle spindles connected to it and activate them by passive stretch. Over-activated muscle spindles cause muscle fibers to contract, which can produce muscle cramps and cause muscular imbalances and an increase in acetylcholine. One study demonstrated that an independent myofascial force influences the transmission of muscle force. This relationship demonstrates that the adaptability of the fascia can allow muscle spindles to respond appropriately to gamma stimulus, and, when tension occurs in the fascia, it can induce muscle cramps. In the present case, managing the fascia dysfunction benefited our patient by reducing the cramps caused by fascial tension and by reinstating the muscle spindle reflex for protection of muscle fibers in future exacerbations.

Fascia, muscle, and connective tissue surrounding nerves have primary afferent nociceptor innervations, which, when activated, involve facilitation of the spinal dorsal horn. The large fiber system within the primary afferent neurons serves as regulator to the small fiber system in the dorsal horn and prevents...
Conclusion

Management of the patient’s cranial dysfunction in conjunction with myofascial release was necessary to more effectively address facilitation of the nervous system, although OCMM resolved multiple dysfunctions on its own as a single treatment. Although OMT is not a cure for Isaacs syndrome, it can reduce symptoms, lengthen the time between exacerbations, improve mobility, and enhance the overall quality of life for patients with Isaacs syndrome and, potentially, patients with other PNH disorders.

References


Table.

Peripheral Nerve Hyperexcitability Disorders

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<td>Muscle cramps, fasciculations, myokymia, pseudomyotonia, and hyperhidrosis</td>
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<td>Morvan syndrome</td>
<td>Similar physical presentation to Isaacs syndrome, in addition to encephalopathy, headaches, drowsiness, and hallucinations</td>
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<td>Amyotrophic lateral sclerosis</td>
<td>Weakness, atrophy, and fasciculations</td>
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