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CASE REPORT

Facial Onset Sensory and Motor Neuronopathy with Neurotrophic Keratitis: A Case Report

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ABSTRACT:
Facial-onset sensory and motor neuronopathy (FOSMN) is a rare, progressive neurodegenerative disorder characterized by sensory loss and motor deficits, primarily affecting the face and upper extremities. The condition begins with sensory impairments in the trigeminal nerve distribution, extending to involve the scalp, neck, upper limbs, and trunk. Symptoms include facial weakness, bulbar disturbances (dysphonia, dysarthria, dysphagia, and sialorrhea), and lower motor neuron signs (weakness, atrophy, fasciculation, and cramps) in the limbs. A hallmark of FOSMN is the diminished or absent corneal reflex, indicating trigeminal nerve involvement and leading to potential complications like neurotrophic keratitis (NK), which can cause corneal ulceration and blindness. The etiology of FOSMN remains uncertain, with theories proposing autoimmune or neurodegenerative origins. Diagnosis is challenging due to the overlap with other ocular surface disorders, necessitating careful examination and differential diagnosis. Management focuses on symptomatic relief, including eye protection to prevent corneal complications. Awareness and early detection of ocular symptoms in FOSMN are crucial for preventing severe outcomes like NK and blindness.

Key points: Facial-onset sensory and motor neuronopathy, Corneal reflex, Neurotrophic keratitis

Introduction

Facial-onset sensory and motor neuronopathy (FOSMN) is a rare, progressive neurodegenerative disorder first reported in 2006[1], characterized by initial sensory deficits in the distribution of the trigeminal nerve in the face. This condition gradually extends to involve the scalp, neck, upper limbs, and eventually the trunk. Patients with FOSMN often experience facial weakness and bulbar symptoms, including dysphonia, dysarthria, dysphagia, and sialorrhea.[2] As the disease progresses, it manifests lower motor neuron signs, including weakness, muscle atrophy, fasciculations, and cramps in the affected areas.[3,4]

The pathogenesis of FOSMN is still under investigation, with theories suggesting autoimmune or neurodegenerative mechanisms.[3,5] Notably, the disorder involves the absence or reduction of the corneal reflex, hinting at central trigeminal pathway impairment.[6,7] This diminished reflex, crucial for eye protection, correlates with delayed or absent blink reflexes, a defining feature of FOSMN.[3,8,9]

Corneal reflex deficiency poses significant risks, such as neurotrophic keratitis (NK), a condition characterized by corneal ulceration and reduced sensation due to impaired corneal innervation. NK in FOSMN patients results from the degeneration of trigeminal nerve fibers, essential for corneal sensitivity and ocular surface maintenance. This nerve deterioration compromises the cornea's protective and sensory functions, potentially leading to severe ocular complications. The diagnostic journey for FOSMN includes differentiating its symptoms from other neurological disorders and identifying its unique clinical features, like the electrophysiologically confirmed delayed blink reflex. Management of FOSMN and its ocular manifestations, particularly NK, requires a multidisciplinary approach. It emphasizes the importance of early recognition and patient education about potential complications to prevent severe outcomes like corneal ulceration and blindness.[8,10]

Given the complexity and rarity of FOSMN, ongoing research is crucial to unravel the underlying mechanisms and develop effective treatments. The medical community's awareness and understanding of FOSMN's impact on the nervous system and ocular health are vital in improving patient care and outcomes in this challenging clinical landscape.

Case Presentation

A 67-year-old Caucasian man presented with complains of worsening difficulty with chewing and swallowing solid food for two months. He also had right sided facial numbness, with difficulty talking for the past 1½ years. Past medical history included coronary artery disease with CABG, hypertension, hyperlipidemia, longstanding hearing loss. He worked as a construction worker and did smoke 1 pack of cigarettes a day for many years, and he did not drink. Initial evaluation included normal CT head and CT angiogram which showed some stenosis of the vertebral arteries but no significant blockages and MRI brain and stem with and without contrast which showed no acute finding, chronic microangiopathy and small remote microhemorrhage within the right caudate nucleus. The work-up also included normal CSF findings including MS panel, normal CT of the chest, and bronchoscopy and laryngoscopy were normal. The Patient was treated with steroid without help. ENT evaluation included flexible laryngoscopy was unremarkable. Ophthalmological exam showed red eyes, blurred vision, and diagnosed with keratoconjunctivitis [Figure 1].

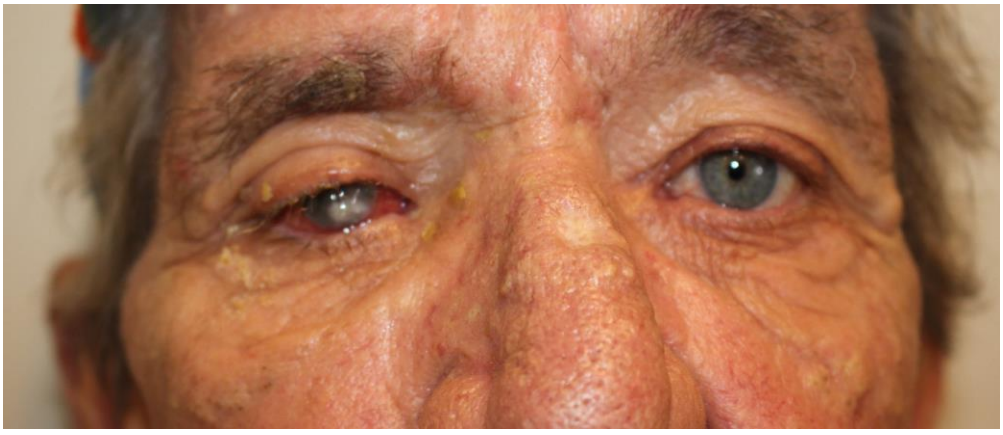

Figure 1: corneal opacity and blindness in the right eye

The patient became blind in the right eye secondary to corneal deterioration. On initial evaluation in the clinic, he endorsed drooling and hoarseness. On exam his speech was slurred with tongue atrophy and weakness, he had no clear fasciculation. He had bilateral facial weakness. The jaw muscles were atrophic. He had decreased sensation in the right side of the face with normal strength in the upper and lower extremities, and normal limb reflexes, except for ankle reflexes. Gait, coordination, plantar reflex and sensation in the limbs were both normal. He had corneal opacity and blindness in the right eye [Figure 1]. Chemistry profile was normal. Serum CK was normal [Table 1].

Table 1. Lab reports

Tests	Results
CK: Immunofixation serum	48: No monoclonal protein
ANNA1 (HU) AB ANNA2 (RI) AB ANNA3 AB PCA1 (YO) AB PCA2 AB PCA TR (DNER) AB AGNA (SOX1) Amphiphysin AB CRMP5 (CV2) AB GAD65 AB MA2/TA AB Myelin AB Aquaporin 4 (AQP4) AB, IFA, CBA NMDAR1 AB AMPAR1 AB AMPAR2 AB GABABR AB LGI1 AB CASPR2 AB DPPX AB	Negative
Acetylcholine receptor ganglionic alpha	Negative
VGCC P/Q type AB VGCC N type AB VGKC AB	Negative
LRP4 Autoantibody	Negative
MUSK AB	Negative
Myasthenia Gravis panel 2 w/REFL MUSK AB Acetylcholine Receptor Blocking AB Acetylcholine Receptor Binding AB Acetylcholine Receptor Modulating AB	Negative
SMN1 gene SMN2 gene	Negative
SBMA gene	Normal

EMG showed no clear evidence of neuropathy, but abnormal blink reflex with low amplitude R1 and R2 delayed responses. The facial motor latency was normal, but the amplitude was very low at 0.5 mV on the left and 0.3 mV on the right. Needle electromyography reveals chronic motor unit changes in the facial muscles but no fasciculation [Table 2-3 with normal values[11,12]]. This was normal in the leg.

Table 2. Blink reflex, Trigeminal – Orb Oculi (Bilateral) with Normal values in milliseconds

Stim. Side	Ipsilateral R1 (Normal value)	Ipsilateral R2 (Normal value)	Contralateral R2 (Normal value)	Difference R2
Left	10.9 (<13)	35.4 (<41)	39.1 (<44)	3.7 (<8)
Right	13.4 (<13)	37.1 (<41)	41.6 (<44)	4.5 (<8)
L-R	2.5 (<1.2)	1.7 (<5)	2.5 (<7)	

Table 3. Facial – Nasalis (Bilateral)

#	Sites	Muscle	Latency ms	Amplitude mV
A1	L Postauricular	Nasalis	3.3 (<4)	0.5 (>1.8)
A2	R Postauricular	Nasalis	3.3 (<4)	0.3 (>1.8)

Discussion

Facial-onset sensory and motor axonal neuronopathy (FOSMN) is a rare lower motor neuron disease which initially reports in 2006 characterized by progressive weakness and sensory loss in the face and upper extremities, caused by degeneration of the facial and upper motor neurons in the brainstem and spinal cord.[1,13] This chronic progressive neurodegenerative syndrome initiates with sensory impairment which starts from the face in trigeminal distribution and slowly progresses to involve the scalp, neck, upper limbs, and trunk. The paresthesia of the face is usually unilateral with an asymmetric pattern in trigeminal distribution that can progress to bilateral and cape-like sensory disturbance.[14,15,16]

It also can be accompanied by bulbar symptoms (dysphonia, dysarthria, dysphagia, and sialorrhea) that dysphagia can be severe to the point that it causes chocking, weight loss, PEG tube insertion, recurrent aspiration pneumonia, and death.[2] In the course of the disease, it may develop lower motor neuron findings such as weakness, atrophy, fasciculation and cramps in facial muscle and limbs.[8,16,17]

Neurotrophic keratitis (NK) is a rare disorder characterized by corneal ulceration and decreased corneal sensation resulting from a lack of corneal innervation.[18] FOSMN can also cause Neurotrophic Keratitis due to the degeneration of the trigeminal nerve which is responsible for the sensation of the face and cornea.[19]

The cornea, a part of the eye, receives a dense supply of nerve fibers, with the majority being sensory nerves that originate from the ophthalmic branch of the trigeminal nerves. These nerves end in the corneal epithelium, while some extend supra-choroidally and form a plexus at the corneoscleral limbus. Approximately 40 thick nerve bundles penetrate the cornea, and they are equally distributed around the limbus. The corneal nerves play a critical role in transmitting sensory information of touch, temperature, and pain to the brain. They are also responsible for promoting lacrimal gland secretion by a trigeminal-parasympathetic reflex, which helps to maintain tear volume and composition. Disruption of these vital neural circuits can contribute to pathologic ocular conditions such as NK, characterized by diffuse or localized corneal anesthesia, and dry eye disease (DED) related symptoms of discomfort or irritation, or in more severe cases, neuropathic pain. Further investigation is needed to understand the intricacies of each type of innervation.[18,19,20,21]

Corneal reflex is absent or diminished in FOSMN can be reliably detected by delayed blink reflex which is pathognomonic for FOSMN in electrophysiologic tests.[3,8] Corneal reflex is a protective mechanism against corneal abrasion, ulceration, and opacities which can cause blindness. Loss of corneal reflex is evidence of decreased corneal sensitivity and can be accompanied with decreased tear secretion which both are vital components for maintaining the integrity of corneal surface.[22]

The degeneration of the trigeminal nerve in FOSMN leads to a lack of neurotrophic support for the cornea, resulting in corneal ulceration and decreased sensation. This association is not common but should be considered in patients with FOSMN who have symptoms of ocular surface disorders.[23]

The diagnosis of NK in patients with FOSMN can be challenging, as the symptoms of corneal ulceration and decreased sensation can be similar to those of other ocular surface disorders. It is important to perform a thorough examination of the cornea and to rule out other causes of corneal ulceration and decreased sensation.

Treatment for FOSMN-associated NK is similar to that for other forms of NK. Lubrication, antibiotics, and bandage contact lenses are used to prevent corneal ulceration and to promote healing. In addition, patients should be referred to an ophthalmologist for regular monitoring of the condition and for management of any complications that may arise.[21]

After reviewing this case, we recommend that even with earliest signs of FOSMN, physicians educate patients regarding this important complication to prevent neurotrophic keratopathy and blindness.[5,10]

Conclusion:

Facial-onset sensory and motor axonal neuronopathy is a rare and complex condition, initially identified in 2006[1], characterized by progressive sensory and motor impairments starting in the facial region and potentially advancing to other body parts. Its pathophysiology, marked by the degeneration of neurons in the brainstem and spinal cord, underscores the importance of early and accurate diagnosis. The condition's association with neurotrophic keratitis due to trigeminal nerve degeneration highlights the critical need for comprehensive management strategies to mitigate the risk of severe ocular complications. The diminished corneal reflex, a hallmark of FOSMN, necessitates vigilant monitoring for ocular surface disorders, emphasizing the importance of interdisciplinary collaboration in patient care. Effective treatment and patient education on the potential risks, especially concerning ocular health, are imperative for improving outcomes and quality of life for those affected by this debilitating disease.

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