BRITISH JOURNAL OF HOSPITAL MEDICINE

CASE REPORT

Delayed Diagnosis of Dysphagia: Consider "FOSMN"

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Abstract

An 80-year-old lady had a history of progressive swallowing difficulty over several years with significant weight loss, but prior investigations in several medical departments proved negative. Neurological assessment noted her complaint of impaired feeling for food in her mouth and examination showed impaired corneal reflexes and facial sensory function. Blink reflex electrodiagnostic testing was consistent with a diagnosis of facial onset sensory and motor neuronopathy (FOSMN). This article raises awareness of the diagnosis, investigation and treatment of FOSMN.

Key words: dysphagia; FOSMN; blink reflex testing

Submitted: 7 August 2024 Revised: 24 September 2024 Accepted: 26 September 2024

Introduction

First described in 2006, facial onset sensory and motor neuronopathy (FOSMN) is characterised by facial sensory symptoms (numbness) which may spread to affect the neck, trunk and upper limbs, along with bulbar symptoms such as dysarthria and dysphagia, muscle weakness, cramps and fasciculation, slowly progressive over a period of years (Vucic et al, 2006). The clinical features have prompted comparisons between FOSMN and motor neurone disease (MND), even though sensory features are not found in MND and the onset and progression of FOSMN is generally slower than in MND (Vucic, 2014). Neuropathological data on FOSMN are limited but have suggested that this is a form of proteinopathy involving the transactive response DNA binding protein 43 (TDP-43), as found in MND and some forms of frontotemporal dementia with or without MND (Sonoda et al, 2013; Ziso et al, 2015). FOSMN is now conceptualised, at least in some cases, as a localised form of MND, with supporting evidence from occasional cases showing mutations in genes implicated in MND (Dalla Bella et al, 2014; Vázquez-Costa et al, 2019; Zhang et al, 2019).

Virtually all previous reports of FOSMN in the literature acknowledge delay in diagnosis (Hu et al, 2023). The objectives in presenting the following case are to raise awareness of a diagnosis which may currently be underascertained and to show that antemortem diagnosis of FOSMN relies on recognising the clinical phenotype, supplemented with specific electrodiagnostic investigations. Rather than attempt to provide an exhaustive differential diagnosis of all possible causes of "dysphagia", we show that, without additional qualification, the breadth of this term may conceal useful clinical pointers.

How to cite this article:
Fratalia L, Larner AJ. Delayed Diagnosis of Dysphagia: Consider "FOSMN". Br J Hosp Med. 2025. https://doi.org/10.12968/hmed.2024.0499

Case Report

Patient Baseline Data

An 80-year-old lady was re-referred to the neurology clinic with a history of difficulty swallowing dating back six or seven years. Specifically, she complained of choking with solids and occasionally with liquids, dribbling of saliva from the mouth and occasional nasal regurgitation, with a numb sensation inside the mouth, over the lips and possibly the tongue. Symptoms had become progressively worse over the years and she had a documented weight loss of around 20 kg over this time period. She was otherwise in good health. She had atrial fibrillation and symptomatic aortic stenosis for which she had undergone a transcatheter aortic valve implantation procedure without complication.

Previous consultations and their outcomes for the assessment of the swallowing symptoms had included: gastroenterology (endoscopy to duodenum normal; possible oesophageal dysmotility on barium swallow); otorhinolaryngology (nasendoscopy normal); maxillo-facial surgery to investigate a tendency to bruxism and to bite her tongue (no abnormality found); and neurology (no neurological signs found; magnetic resonance [MR] brain imaging normal for age). By exclusion, a working diagnosis of "oesophageal dysmotility" had been made.

Clinical Assessment

At neurological re-referral consultation, the patient's principal complaint was of numbness (impairment of sensation) of the mouth such that she could not feel food in her mouth when chewing, and hence did not know the appropriate moment to swallow. On neurological examination, her voice had a nasal quality, she was noted to be drooling, but there was no facial weakness. Testing facial sensory function, the corneal reflex was absent bilaterally and there was reduced sensation to pinprick on left side of the nose extending laterally to the maxillary area. Tongue movements were normal and no tongue fasciculation was seen. The rest of the neurological examination was normal, in particular the limb reflexes were not exaggerated.

Investigations

There were no clinical indications of either motor neurone disease or myasthenia gravis, the key neurological differential diagnostic considerations in patients with swallowing problems, in the patient history or examination, but nevertheless investigations for these common neurological causes of dysphagia were pursued, specifically appropriate blood tests were checked (creatine kinase normal; acetylcholine receptor antibodies negative). MR imaging of both brain and cervical spinal cord showed only age-appropriate changes.

Because of the prominence of the orofacial sensory symptoms along with the swallowing difficulties, a diagnosis of FOSMN was considered. Accordingly, standard neurophysiological investigation was performed, in which needle electromyography (EMG) was reported to show mild-to-moderate chronic neurogenic change

in selected cranial innervated muscles but no fibrillations or fasciculation to suggest acute denervation in facial and bulbar muscles.

In light of the presumptive diagnosis of FOSMN, more detailed neurophysiological investigation was also undertaken. Trigeminal somatosensory evoked potentials (SSEPs) for the inferior alveolar and auriculotemporal nerves were within normal limits bilaterally, hence these studies provided no diagnostic evidence of trigeminal nerve sensory dysfunction above and below the mouth.

Blink reflex testing involves stimulating the supraorbital nerve (afferent arm of reflex arc via ophthalmic division of trigeminal nerve) and measuring the timing and amplitude of response in the orbicularis oculi muscle (efferent arm of reflex arc via facial nerve) which comprises two components: a direct ipsilateral response, R1, and an indirect bilateral response, R2. In our patient this study showed absent R1 response, and delayed ipsi- and contra-lateral R2 responses (latency ca. 50–60 ms; normal is around 35 ms), findings compatible with pathology affecting either the afferent, efferent or brainstem pathways underlying the blink reflex; these findings were consistent with a diagnosis of FOSMN.

Treatment Methods

The patient has been followed up for three years during which time her condition has remained relatively stable with no further weight loss, and hence from her perspective the symptoms are manageable. In the absence of any published consensus management strategy or guidelines on FOSMN, far less any intervention of proven (double-blind randomised controlled trial) efficacy, no specific treatment has been given. Provision of a diagnosis in place of the previous uncertainty has reassured the patient and avoided any further unnecessary investigation. Ongoing follow up will permit any new clinical developments to be assessed and addressed.

Discussion

A number of learning points emerge from consideration of this case. Consistent with practically all reports of FOSMN in a systematic review of the literature (Hu et al, 2023), and with previous local experience (Ziso et al, 2015), there was significant delay between symptom onset and diagnosis, in this case at least six years. In a recent systematic review, the median disease duration at time of diagnosis was 60 months, with a range reported to extend up to 46 years (Hu et al, 2023). Hence a high index of clinical suspicion for this condition is key to diagnosis, and justification for further awareness-raising case reports such as this one. We suggest that the diagnosis of FOSMN merits consideration in any person, especially if an older person, with persistent and undiagnosed swallowing difficulty accompanied by any history of facial sensory impairment and documented weight loss.

Part of the explanation for delayed diagnosis may relate to the very broad differential diagnosis of “dysphagia”, encompassing both gastroenterological and neurological causes. Definition of the exact nature of the swallowing difficulty in FOSMN might assist with diagnosis. This has been little investigated, but a videofluoroscopic swallowing study of five patients indicated poor oral retention leading to bolus flowing into the pharynx before swallowing in four, and poor lin-

gual transfer in the fifth patient (Watanabe et al, 2018). Oral-phase dysphagia was almost twice as common as pharyngeal-phase dysphagia in a nationwide survey of FOSMN cases in Japan (Ko et al, 2024). These difficulties presumably relate to the oral sensory loss, and hence impairment of reflex arcs underpinning adequate chewing, bolus manipulation, and deglutition. There is a need to characterise "swallowing difficulty" beyond the merely cognate label of "dysphagia". The definition of "oral-phase" dysphagia, related to oral sensory loss, should raise suspicion of FOSMN in the appropriate clinical context.

Once the diagnosis of FOSMN is considered on clinical grounds, the importance of appropriate electrodiagnostic testing is paramount. Standard needle EMG may be helpful, since chronic neurogenic change in bulbar muscles suggestive of denervation is reported in around 50% of cases (De Oliveira et al, 2022). However, blink reflex testing is more likely to be of value, especially in those patients with normal standard needle EMG. In both a recent systematic review (Hu et al, 2023) and a nationwide survey from Japan (Ko et al, 2024), blink reflex abnormalities were present in more than 90% of patients tested (no study providing data on test sensitivity and specificity for FOSMN has been found). Other specialised electrodiagnostic testing has been recommended, such as upper limb SSEP central conduction times, which may be increased, and tests of upper motor neurone function (motor evoked potentials; intra-cortical inhibition on threshold-tracking transcranial magnetic stimulation; beta-band intermuscular coherence) which may be abnormal (De Oliveira et al, 2022). However, such tests may not be widely available. The value of trigeminal SSEPs remains to be clarified; in our case, these were normal despite the clinical history.

As FOSMN is a relatively unusual condition, no randomised controlled clinical trials of treatment on which to base management decisions have been published hitherto, nor are there any consensus management guidelines. Treatment is necessarily therefore empirical, but with face validity, such as ensuring adequate nutrition, for example with percutaneous endoscopic gastrostomy (PEG) feeding. Although no specific treatment is currently available for FOSMN, response to immunological therapies, particularly intravenous immunoglobulin (IvIg), has been reported on occasion, in about one third of cases in a nationwide study in Japan. Subjective improvements in facial numbness were reported along with return of the corneal reflex and improvements in blink reflex testing but these effects were temporary, lasting only a few months. No consistent improvement in dysphagia was noted. Of note in this survey, immunotherapy appeared most effective if given in the early stages of disease (Ko et al, 2024), a further argument for increased awareness and early diagnosis of FOSMN. Should agents generic for the treatment of proteinopathies, or specific for TDP-43 proteinopathy, become available in the future, one would anticipate that to have any meaningful effect their use would have to be early in the disease course.

Conclusion

The diagnosis of FOSMN merits consideration in any person, especially older persons, with persistent and undiagnosed swallowing difficulty accompanied by any history of facial sensory impairment and documented weight loss.

Learning Points

- Diagnosis of FOSMN may be delayed for months or years if the condition is not considered.
- The swallowing difficulty in FOSMN may be an oral-phase dysphagia.
- Electrodiagnostic testing of blink reflexes may be key to diagnosis of FOSMN.
- FOSMN may be a localized form of MND.
- There is no specific treatment but supportive care with nutritional support should be given.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

LF and AJL designed the research. AJL drafted and revised the manuscript. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as amended in 2013. The patient signed an informed consent form.

Acknowledgement

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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