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CASE REPORT

Parkinsonism may aggravate dysphagia in myotonic dystrophy type 1: two case reports

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Introduction. Weakness of trunk muscles, fatigue and reduced mobility are features of myotonic dystrophy type 1 (DM1) and may also characterize patients with extrapyramidal disorders.
Dysphagia is common in DM1 and parkinsonism and can be predominant compared to other symptom, often requiring surgical tratment.
Methods. We describe two cases of patients with DM1 and parkinsonism who arrived at our Center for worsening dysphagia and who showed very similar and peculiar clinical features.
Case reports. The first patient presented initially at the outpatient clinic reporting a 7 year history of progressive difficulties in swallowing and movement slowness. Neurologic examination showed a general bradykinesia, plastic rigidity of upper limbs, diffuse hypotrophy and deep tendon reflexes weakness. MRI scan of brain and spine was unremarkable, but neurophysiological evaluation revealed diffuse myotonic discharges on distal limb muscles. Genetic testing confirmed DM1 diagnosis (CTG range E1).
The second patient, presented with an initial diagnosis of parkinsonism due to a 10 years history of gait impairment, generalized weakness and dysphagia. Due to low back pain a neurophysiological study was performed after 5 years from diagnosis of parkinsonism detecting diffuse myotonic discharges and genetic testing confirmed diagnosis of DM1 (CTG range E2).
Percutaneous endoscopic gastrostomy (PEG) was severe and burdensome for both patients.
To date, only one case of molecularly confirmed DM1 along with parkinsonism has been described.
We have described two cases of DM1 and parkinsonism in which swallowing function has been affected by a synergic effect triggered by both muscle condition and extrapyramidal disease.

Key words: dysphagia, myotonic dystrophy type 1, parkinsonism, swallowing disorders, endoscopic gastrointestinal surgical procedures

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Introduction

Myotonic dystrophy type 1 (DM1) is a genetic disease caused by the expansion of a CTG triplet repeat in the 3' non-coding region of *DMPK*, the gene encoding the DM protein kinase. DM1 is considered a multisystemic disorder involving multiple organs and the central nervous system [1]. In skeletal muscles, DM1 may involve an RNA-dominant disease mechanism in which transcripts from the mutant DMPK allele accumulate in the nucleus and compromise the regulation of alternative splicing. To date only 2 cases of DM1 along with parkinsonism have been reported [2,3].
Here, we describe two DM1 patients who developed unusually severe dysphagia in whom there was a concomitant diagnosis of DM1 and parkinsonism. Parkinsonian and muscular features differed in both cases with regards to the time of onset and the presentation of symptoms.
Dysphagia instead rapidly worsened, misleading the diagnosis of DM1 in the first case and requiring a percutaneous endoscopic gastrostomy (PEG) in both cases.

Case 1

A 62-year-old man was referred to the neurology department for slowly worsening dysphagia and dysphonia along with gait impairment that had begun approximately 7 years prior to his first neurological examination.

Neurological evaluation revealed bilateral right-predominant hypertonus of upper limbs, postural –small amplitude – bilateral right-predominant tremor of hands and camptocormic posture. Moderate diffuse muscle hypotrophy and reduced deep tendon reflexes were also recognized. Total MDS-UPDRS part III score was 32.

The initial diagnostic suspicion was of a motor-neuron-disease/parkinsonism overlap syndrome possibly due to a heredodegenerative disease.

Patient was hospitalized and he underwent a brain/whole-spine MRI scan (subcortical white-matter-changes, no brainstem atrophy) (Fig. 1A) and a neurophysiological evaluation which revealed the presence of a myopathic pattern with myotonic discharges. This finding raised the suspicious of DM1 finally confirmed by genetic testing: *DMPK* gene mutation showed an abnormal CTG repeat length within E1 range (between 51 and 150).

To further investigate extrapyramidal symptoms, patient underwent a Ioflupane(123 I)-FP-CIT

SPECT imaging (Fig. 1B) which documented a bilateral hypocaptation of putamen and caudate. An oral L-DOPA therapy was titrated up to 600 mg/die, with improvement of motor symptoms (particularly of upper limbs plastic rigidity, less prominent on bradykinesia).

Respiratory function was also evaluated considering the bulbar involvement. A sleep study using polysomnography did not show oxygen desaturation. The spirometric values were also within the normal limits.

Swallowing was assessed during the hospitalization by a speech therapist who detected dysphagia, primarily with liquids; in particular fiberoptic endoscopic evaluation of swallowing (FEES) revealed (after administration of few drops of methylene blue in a glass of water) pre-swallowing fall, stagnation at the right piriform sinus level and incomplete cleaning after swallowing. Dysphagia progressively worsened during hospitalization affecting both liquids and solids. The Gugging Swallawing Screen scale was used to evaluate dysphagia, obtaining a score of 9. Parkinsonism, although considered as the main cause of dysphagia, did not alone explain such a rapid deterioration.

As a result of the worsening of dysphagia, aspiration pneumonia occurred but resolved after antibiotic therapy.

The evolution of dysphagia in the present patient, rapidly worsened requiring a percutaneous endoscopic gastrostomy (PEG).

Case 2

A 75-year-old woman came to our center due to a long history of dysphagia lasting over a decade. Her medical history included breast surgery followed by chemotherapy. A few years post-surgery, she complained weakness in her legs, low back pain and mild bradykinesia. Subsequently, a mild extrapyramidal symptomatology appeared with hypomimic facies, bradykinesia and plastic hypertonus in her right limbs. Inconstant rest tremor of right hand was also observed. Total MDS-UPDRS part III score was equal to 18.

A diagnosis of parkinsonism was made after a Ioflupane(123 I)-FP-CIT SPECT imaging which confirmed the involvement of the dopa-

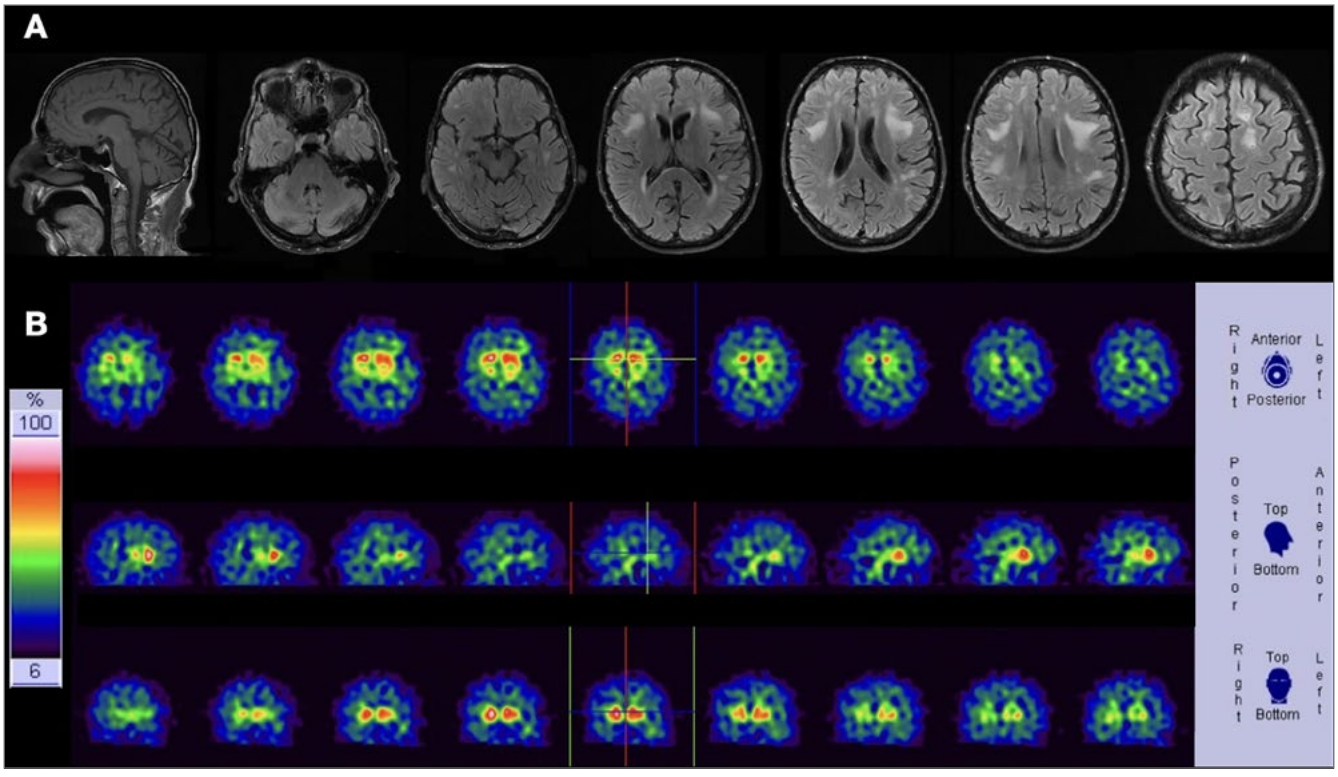

Figure 1. Structural and functional brain imaging of case 1. Brain sagittal and axial brain MRI sequences (A), and Ioflupane(^{123}I)-FP-CIT SPECT (B).

minergic system at the level of putamen bilaterally and left caudate nucleus. Levodopa therapy was slowly titrated up to 300mg/die with early onset of dyskinesia after 3 months. Levodopa was later replaced with dopamine agonist (ropinirole 6 mg/die) for about 3 years but without benefit.

Due to persistent lumbar pain, a neurophysiological study was performed after 5 years from diagnosis of parkinsonism detecting diffuse myotonic discharges on the distal muscles examined with a myopathic electromyographic pattern. A molecular investigation eventually confirmed a concomitant DM1 diagnosis with expansion estimated in the E2 class interval (> 150-1000 CTG) in the *DMPK* gene. The clinical picture has evolved over time, with initial dysphagia events causing pneumonia episodes and a subsequent worsening of the swallowing ability and severe cachexia.

Parkinsonism misled to consider extrapyramidal disorder as the main cause of dysphagia; after consulting with the neurologist colleagues who were following the patient, the transfer to our center was agreed for a complete assessment of dysphagia. FEES revealed presence of salivary secretions in the hypopharynx and in the glossoepiglottic sulcus, with penetration into the laryngeal aditus of secretions; administration of few drops of methylene blue in a glass of water showed a pre-swallowing fall and stagnation in the hypopharynx. Gugging Swallawing Screen score was equal to 7. The progressive worsening of the dysphagia, although already started a few years ago but rapidly progressing in the months preceding our hospitalization, led to a percutaneous endoscopic gastrectomy (PEG) placement.

Respiratory function was assessed prior to surgery. Although spirometry was difficult to perform due to poor compliance and technical difficulties related to the nasogastric tube, night oximetry was found to be normal without of oxygen desaturation during the night.

Given the good respiratory function, neither adaptation to cough assist nor to non-invasive nocturnal ventilation was necessary.

Discussion

We have observed two patients with both DM1 and atypical parkinsonism who showed a very peculiar and similar phenotypic pattern. Both patients showed worsening dysphagia which resulted in hospitalization, diagnostic investigations, and ultimately percutaneous endoscopic gastrectomy. Although dysphagia is one of the symptoms related to DM1, it rarely progresses rapidly enough to require surgery treatment.

Swallowing disorders (oropharyngeal dysphagia) are a common and clinically significant symptom

in people with Parkinson disease (PD) and parkinsonism with a prevalence of more than 80% during lifetime [4] although dysphagia is typically more severe and occurs earlier in atypical parkinsonism compared to PD [5].

Since neither of the two patients was found with myotonic phenomenon and considering the very modest limb muscle weakness, it is unlikely that the dysphagia was related to a pure muscle involvement; we can speculate that this bulbar symptom could be aggravated by a superimposed extrapyramidal component in our two patients with DM1.

Another shared aspect of the two reported cases is the respiratory pattern. Facing a bulbar involvement characterized by severe dysphagia, the overall respiratory function remained unaffected. Peak cough especially proved to be effective underlining this peculiarity.

Overnight oximetry data did not reveal any desaturation event that would require ventilatory support. This finding is quite atypical given the high frequency of sleep-related breathing disorders in patients with DM1 [6]. Unaffected respiratory function along with an unusual worsening dysphagia in patients affected by parkinsonism could mislead physician considering only an extrapyramidal pathogenic mechanism.

Currently, it is difficult to hypothesize which common mechanism could explain the peculiarity of this bulbar pattern, which causes a serious impairment of swallowing function despite normal respiratory function.

Previously conducted neuropathological studies have demonstrated the presence of RNA foci in patients with DM1 also at the level of the basal nuclei[7] thus suggesting a common pathogenetic mechanism with parkinsonism.

To date, only one case of molecularly confirmed DM1 along with parkinsonism has been described [2]; parkinsonism appeared atypical, with a slow course and without a significant correlated dysphagia; however no information on respiratory function is available.

In conclusion, we have described two cases of DM1 in which swallowing function has been probably affected by a synergic effect triggered by both muscle condition and extrapyramidal disease.

In both cases the focus was primarily on parkinsonism. This could mislead into not considering a muscular disease thus leading to a delay in the diagnosis of DM1.

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Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

SS: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis and interpretation of data. AB: study concept; analysis and interpretation of data. RB: analysis and interpretation of data. RZ: analysis and interpretation of data.

Ethical consideration

Since only anonymous data have been used and the data storage meets current data protection regulations, ethical committee approval was not required for this case report.

The patients provided their written informed consent to participate in this study.

References

1 Meola G, Cardani R. Myotonic dystrophies: an update on clinical aspects, genetic, pathology, and molecular pathomechanisms. Biochim Biophys Acta 2015;1852:594-606. https://doi.org/10.1016/j.bbadis.2014.05.019

2 Choi JH, Lee JY, Kim HJ, et al. A Patient with myotonic dystrophy type 1 presenting as parkinsonism. J Mov Disord 2018;11:145-148. https://doi.org/10.14802/jmd.18028

3 Okuma Y, Tanaka S, Nomura Y, et al. A 63-year-old woman with muscle weakness, myotonia, and parkinsonism. No To Shinkei 1996;48:287-297. Japanese. PMID: 8868342.

4 Cosentino G, Tassorelli C, Prunetti P, et al. Reproducibility and reaction time of swallowing as markers of dysphagia in parkinsonian syndromes. Clin Neurophysiol 2020;131:2200-2208. https://doi.org/10.1016/j.clinph.2020.06.018

5 Alfonsi E, Versino M, Merlo IM, et al. Electrophysiologic patterns of oral-pharyngeal swallowing in parkinsonian syndromes. Neurology 2007;68:583-589. https://doi.org/10.1212/01.wnl.0000254478.46278.67

6 Hawkins AM, Hawkins CL, Abdul Razak K, et al. Respiratory dysfunction in myotonic dystrophy type 1: A systematic review. Neuromuscul Disord 2019;29:198-212. https://doi.org/10.1016/j.nmd.2018.12.002

7 Jiang H, Mankodi A, Swanson MS, et al. Myotonic dystrophy type 1 is associated with nuclear foci of mutant RNA, sequestration of muscleblind proteins and deregulated alternative splicing in neurons. Hum Mol Genet 2004;13:3079-3088. https://doi.org/10.1093/hmg/ddh327