Case report

Oculopharyngeal muscular dystrophy (OPMD) and dementia in a 75-year-old female

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SUMMARY

Oculopharyngeal muscular dystrophy (OPMD) is a relatively rare, adult-onset disorder characterised by proximal limb weakness, progressive eyelid drooping and swallowing difficulties. Preliminary research suggests there could be a link between OPMD and dementia; however, the current literature is relatively limited and inconsistent. This case study describes a 75-year-old female with OPMD, presenting to an older adults community mental health team with memory problems and word finding difficulties. A neuropsychological assessment was carried out. The results of her assessment were difficult to interpret; she demonstrated impairments in most cognitive domains tested and her presentation did not appear to reflect any typical dementia profile. It was thought she was most likely presenting with a dementia; however, the exact aetiology remains unclear. The dementia could be a result of OPMD, vascular changes or both. This report emphasises the need for further research into the possible causal link between OPMD and dementia/cognitive decline.

BACKGROUND

Oculopharyngeal muscular dystrophy (OPMD) is a genetic disorder (often inherited), caused by a mutation in the Poly (A) binding protein nuclear 1 gene. It is characterised by a slow progressive muscle disease affecting the muscles of the upper eyelids and throat, which affects swallowing. People also have difficulties with weakness of the tongue and muscles closer to the centre of the body. OPMD typically starts in the fifth or sixth decade of life¹ and reports of prevalence can vary between 1:1000 and 1: 100 000.²

Individuals diagnosed with OPMD are either homozygotes (an individual having two identical alleles of a particular gene) for the OPMD mutation or heterozygote (two different alleles of a particular gene).

Previous research suggests that on average, homozygote patients have earlier onset for the disease³ and a reduced life span.⁴

A review of the literature from 2008 to 2018, conducted by the authors, found seven papers on OPMD and cognitive decline/impairment/dementia. Extending the search date to 1983 generated another six papers; however, these appeared to focus solely on OPMD. There is preliminary evidence to suggest there may be a link between OPMD and cognitive decline and/or dementia. Studies by Blumen *et al* (2009) and Baldanzi *et al*⁵

investigated homozygote patients with OPMD and found evidence of cognitive decline across multiple cognitive domains.^{4 5} There is also evidence that suggests heterozygote patients with OPMD exhibit cognitive deficits. Van Der Sluijs *et al*⁶ reported two patients simultaneously diagnosed with fronto-temporal dementia and heterozygous OPMD. The researchers proposed that in some cases, cognitive decline may precede muscle weakness.

There is little research on OPMD and the conclusions drawn from the small research studies conducted are fairly limited and somewhat inconsistent. This case study presents an unusual presentation of a patient diagnosed with both OPMD and dementia, supporting previous literature which suggests there is a link. However, this patients' profile does not correspond with a typical dementia profile and does not match any of the case studies previously published. A better understanding is required to infer whether there is a direct link between OPMD and dementia, and if there are comparable cognitive deficits typically seen within this population. The findings highlight that it would be useful for clinicians working with patients with OPMD to enquire around any changes in the patients' thinking abilities as a routine part of assessments/reviews.

CASE PRESENTATION**Presenting problems**

The patient is a 75-year-old female with OPMD, living in Scotland with her husband. She was referred for a neuropsychological assessment and reported word finding difficulties. Both she and her husband noticed a slow and gradual decline over the past year. Her balance and mobility had also declined over the past several years. The OPMD affected her swallowing and eye sight.

Her husband noted that she was doing less around the house and he had begun to 'take over' the meal preparations, which had always been a joint task. He reported she had faecal and urine incontinence within the last 6 months and described her as being more 'irritable'. No other changes in cognitive abilities, affect or functioning were reported. She did not drive.

Background information

The patient grew up in a non-aversive environment. She described herself as being in the 'middle' of the class academically at school and trained to become a book keeper. She worked in accounts until she

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Figure 1 Whole brain SPECT scan showing some reduction in perfusion within the temporal lobes.

married and had a family. She was diagnosed with OPMD when she was 50 years old. She did not undergo genetic testing so it is unclear whether she has heterozygous or homozygous OPMD. She reported drinking wine occasionally and has never smoked. Her medical history includes osteopenia, OPMD, diaphragmatic hernia, pure hypercholesterolaemia and hypertension. Prescribed medication included the following: lercanidipine hydrochloride, calcichew, latanoprost, simvastatin and telmisartan. She reported no family history of OPMD or memory problems (however, her father died at young age). She reported no past difficulties with her mental health.

INVESTIGATIONS

She scored 56/100 on an Addenbrooke’s Cognitive Examination-III scoring: attention 13/18, memory 8/26, fluency 2/14, language 20/26 and visuospatial 13/16. A single-photon emission computed tomography (SPECT) brain scan (figure 1) showed ‘... some reduction in perfusion within the temporal lobes; however, the significance of these findings was viewed to be uncertain’. An MRI brain scan (figures 2) demonstrated a ‘...minor degree

Table 1 Neuropsychological assessment results	
Test	Percentile rank/range
Test of premorbid functioning	40%–55%
Wechsler Abbreviated Scale of Intelligence:	
Verbal Comprehension Index	1%
Perceptual Reasoning Index	0.5 %
Full Scale IQ-4	0.5 %
Repeatable Battery for the Assessment of Neuropsychological Status-B:	
Immediate memory:	0.1 %
Delayed memory:	12 %
Language:	7%
Attention:	2%
Visuospatial/constructional:	0.1 %
Hayling Sentence Completion Test: overall score	Impaired
Zoo Map subtest from Behavioural Assessment of Dysexecutive Syndrome	Impaired

of generalised parenchymal atrophy without any lobar/regional preponderance noted. Multiple focal areas of T2-weighted hyperintensity within the supratentorial parenchyma slightly confluent around the ventricular margins, sparing the brainstem and cerebellum are non-specific but are likely to be related to microvascular causes’. The results from the neuropsychological assessment are summarised in table 1. Although her vision is affected by OPMD, she stated she was able to see the test materials without difficulty. She was seen for a total of six sessions.

Results of neuropsychological assessment

The patient’s premorbid intellect was estimated to fall within the average range, which is in keeping with her employment and educational history. On a test of current intellectual functioning, she performed in the impaired range, demonstrating a significant decline. She performed within the average range in areas of confrontational naming (within Repeatable Battery for the Assessment of Neuropsychological Status-B (RBANS-B))

Figure 2 Actual MRI brain scan demonstrating T2-weighted hyperintensities within cerebral hemispheres, in keeping with ischaemic changes.

and her ability to recognise previously heard auditory information. Her digit span (from RBANS-B) was relatively preserved as she performed in the low average range. She was orientated to temporal information asked at each session; however, on one occasion, she was incorrect on year.

She performed in the impaired range in her immediate auditory memory ability; however, this improved to the cusp of the borderline/low average range for delayed recall. Despite performing within the average range for confrontational naming abilities (from RBANS-B), her overall language ability was in the borderline impaired range. There was no evidence of word finding difficulties in the sessions. She demonstrated significant difficulties in semantic fluency, visuospatial/constructional abilities, planning and organising, and inhibition. Her ability to pay attention on a more complex task was also impaired.

Within Part 1 of the Hayling and observationally throughout the other tests, her processing speed was slowed.

DIFFERENTIAL DIAGNOSIS

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition classification criteria was used to consider whether the patient's presentation and results were indicative of a type of dementia or not. It was difficult to interpret the results of her neuropsychological performance due to her diagnosis of OPMD and her poor performance across most of the domains. The results demonstrated difficulties with visuospatial/constructional abilities, memory, fluency tasks, complex attention and executive functioning tasks. Consistent with previous research on OPMD, she presented with deficits in visuospatial processing, memory and executive functioning.

Given her relative strengths in delayed recall, recognition of auditory information and confrontational naming, it was deemed unlikely that she was presenting with Alzheimer's disease. This patient had some evidence of vascular risk factors (hypertension) and her scans suggested some microvascular changes. These factors and her difficulties in executive and visuospatial functioning could indicate evidence of a vascular dementia. A frontotemporal dementia diagnosis was excluded due to the domains affected and that there had not been a report of change in her behaviour.

In conclusion, it was thought that she was most likely presenting with a dementia; however, the exact aetiology was unclear. The dementia could be a result of OPMD, vascular changes or both. It was thought that her increased irritability could have been a result of her cognitive changes.

TREATMENT

The patient was advised to use a diary to keep track of appointments, significant dates and important information. The family was also informed that she may need more time to process information. She was advised that she may require extra support when problem-solving/making decisions for example, provide time to consider her options fully and be informed of the advantages and disadvantages of her options. She was also advised to look after her vascular health.

OUTCOME AND FOLLOW-UP

The patient accepted the offer of post-diagnostic support (PDS) and has been placed on the waiting list for a Dementia Link Worker. PDS involves helping the individual and their family to understand the condition and manage the symptoms, while developing a personal plan that utilises their own natural supports, develops and maintains peer support and community connections, and plans for future care and decision-making.

DISCUSSION

This patient has OPMD and now appears to have developed a dementia. Her neuropsychological profile did not fit with any particular dementia profile, nor does it exactly fit with findings from previous research. This may be due to the fluctuating picture of vascular aetiology or due to her OPMD.

The literature suggests patients with OPMD can present with a broad psychopathological spectrum including cognitive decline and dementia. Baldanzi *et al* (2018) profiled brain functioning in conditions involving muscular dystrophies including OPMD. They found cognitive decline in amnesic, visuo-constructive and executive domains.⁵ Blumen *et al*⁴ investigated 10 homozygote patients with OPMD and found all patients demonstrated reduced life expectancy and depression. The majority of patients also received input from psychology/psychiatry for cognitive decline and/or psychotic manifestations.

Areas of cognitive decline included attention, executive functioning, memory, language and visuo-perceptual and constructional abilities. They suggested OPMD progresses faster in homozygote patients and not only involves the muscles but also the central nervous system. The rate of progression and pattern of cognitive disorder appeared to be similar in all patients and the researchers suggested similarities between this and subcortical dementia.

Furthermore, a case study⁷ reported a 65-year-old man with OPMD who demonstrated a decline in memory and executive functioning with mild deficits in visuospatial processing. An MRI scan showed moderate atrophy in frontal lobes and bilateral hippocampi and a positron emission tomography (PET) scan showed changes most consistent with Alzheimer's disease. The authors suggest the link between OPMD and dementia could mean this kind of genetic disorder may share a common mechanism leading to neurodegeneration.

Dubbioso *et al*⁸ performed a neuropsychological and neuropsychiatric evaluation on 11 heterozygote patients with OPMD. They found individuals with OPMD were less efficient on several neuropsychological tests, particularly those measuring executive functioning, compared with matched controls. However, it should be noted that only the oldest patient showed diffuse cognitive impairment, and there were no significant differences between matched controls for long-term memory and general cognitive abilities. Moreover, a large observational study from Brisson *et al*⁹ which retrospectively described impairments in 338 patients with OPMD, found no evidence of cognitive decline or dementia.

The sequence in which patients present with muscular and cognitive symptoms appears to differ in the patients reported so far.^{3 6–8 10} Dubbioso *et al*⁸ noted a negative correlation between the severity of OPMD mutations and some neuropsychological scores. It could be the case that patients with more severe genotypes are more likely to experience declines in cognition during the normal life span. It is also unclear whether patients with OPMD are more likely to present with cortical or subcortical dementia. Some studies suggested individuals demonstrate subcortical presentations^{4 8} while others present with cortical dementias most consistent with Alzheimer's disease⁷ and frontotemporal dementia.⁶

Future research is required to further investigate possible cognitive change in patients with OPMD, to better understand the relationship between OPMD and dementia or cognitive impairment. If there is a causal link, providing patients with this information will give them a better understanding of their condition and clinical management of the disease could improve.

Patient's perspective

I would say I was in my 50's before things started to go wrong. I had two operations on my eyes but they didn't help. My muscles weren't working and so they weren't holding my eyelids up. That's when I was diagnosed by the specialist. Then I started to notice I couldn't remember some words.

I didn't mind {the neuropsychological assessment} at all. Everything was explained, quite clearly, I knew there was something not right, I just didn't know exactly what it was. It was difficult hearing the diagnosis, but I accepted it quite quickly.

Learning points

- ▶ There is little research that explores the cognitive sequelae of oculopharyngeal muscular dystrophy (OPMD).
- ▶ There may be a direct link between OPMD and dementia and/or cognitive decline.
- ▶ Clinicians working with patients with OPMD should ask about changes in the patients' thinking abilities as a routine part of assessments/reviews.

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REFERENCES

- 1 Brais B, Rouleau GA, Bouchard JP, *et al.* Oculopharyngeal muscular dystrophy. *Semin Neurol* 1999;19:59–66.
- 2 Fan X, Rouleau GA. Progress in understanding the pathogenesis of oculopharyngeal muscular dystrophy. *Can J Neurol Sci* 2003;30:8–14.
- 3 Blumen SC, Brais B, Korczyn AD, *et al.* Homozygotes for oculopharyngeal muscular dystrophy have a severe form of the disease. *Ann Neurol* 1999;46:115–8.
- 4 Blumen SC, Bouchard JP, Brais B, *et al.* Cognitive impairment and reduced life span of oculopharyngeal muscular dystrophy homozygotes. *Neurology* 2009;73:596–601.
- 5 Baldanzi S, Ricci G, Simoncini C, *et al.* Profiling Brain Functioning in Muscular Dystrophies (MD): Upgrading Knowledge from on-Going Research. *Acta Myologica* 2018;37:55–6.
- 6 van der Sluijs BM, te Riele MGE, Hammink JKN, *et al.* Oculopharyngeal muscular dystrophy with frontotemporal dementia. *Eur Geriatr Med* 2017;8:81–3.
- 7 Frederick MC, Woltjer R, Silbert LC, *et al.* Dementia syndrome in oculopharyngeal muscular dystrophy: A trinucleotide expansion disorder commonly presenting with muscle weakness. *Alzheimer's & Dementia* 2014;10:P682–P683.
- 8 Dubbioso R, Moretta P, Manganelli F, *et al.* Executive functions are impaired in heterozygote patients with oculopharyngeal muscular dystrophy. *J Neurol* 2012;259:833–7.
- 9 Brisson J-D, Gagnon C, Brais B, *et al.* The natural history of impairments and disabilities in Oculopharyngeal Muscular Dystrophy: a large retrospective study. *Neurology* 2018;90(15 Supplement):S31.001.
- 10 Mizoi Y, Yamamoto T, Minami N, *et al.* Oculopharyngeal muscular dystrophy associated with dementia. *Intern Med* 2011;50:2409–12.

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