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Management of end stage sCJD from a palliative care perspective

Abstract

Sporadic Creutzfeldt-Jakob Disease (sCJD) is a rare, rapidly progressive neurological disorder, that is ultimately fatal. We have written a case report on a patient recently admitted to the hospice having been diagnosed 2 days earlier with sCJD. Unfortunately, she had an aggressive form and deteriorated very rapidly 10 days post admission. Our focus was on symptom control and supportive care, for both patient and family, with psychological and spiritual support a vital component of this. Of her multitude of symptoms, the most challenging were the fluctuating episodes of severe emotional distress, agitation and restlessness. Non-pharmacological approaches proved extremely helpful, but as the disease progressed, we found that in addition to this, a combination of midazolam, levomepromazine and morphine proved the most effective in her syringe driver. All of this care took place within the context of a holistic, multi-disciplinary team, vital for managing the rapidly changing symptoms of this complex disease and its effect on both patient and family. Given its rare nature, there is only limited research on the palliative care aspects of managing terminal sCJD. We therefore hope that by sharing our experience, this case report may prove helpful.

Keywords: Sporadic Creutzfeldt-Jakob disease, prion, neuro-degenerative disease, benzodiazepines, advanced care planning, anti-psychotics, multidisciplinary team

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Introduction

sCJD is a rapidly progressive, degenerative neurological condition which is ultimately fatal. The approach therefore is one of support and symptom management for this devastating and complex disease. In terms of guidance, we found there was no clear consensus on management of sporadic CJD at the terminal stages, most likely due to the rarity of the condition precluding the possibility of large studies. Thus, for our patient, we were reliant upon general guidance by expert centres such as the National Prion centre at University College London,[1] a handful of research reports and case studies. For this reason, we felt it would be beneficial to submit a case report based on our experience at the hospice of a multi-disciplinary approach to the palliative management of a patient with end stage sCJD.

Background – what is sCJD?

CJD is a rare, rapidly progressive neurodegenerative condition caused by abnormal prion proteins. Most cases of CJD are Sporadic accounting for 85%[2] of the total, with a mean age of onset of 65 years.[2] It has an incidence of approximately 1 per million per population per annum,[1] accounting for approximately 80-100 deaths per annum in the UK since 1990,[4] mostly due to associated infection or cardiorespiratory failure within 12 months of onset. The remaining forms of CJD are iatrogenic, genetic and variant.[3] sCJD occurs when normal prion protein spontaneously converts into an abnormal or "rogue" form which is abnormally folded and protease-resistant,[2] making it harder to break down. It can go on to cause further conversions, via a chain reaction, with subsequent aggregation into fibrils and plaques and thus small amounts are able to propagate throughout the central nervous system.[4] sCJD can present with rapid cognitive and functional decline, memory deficit, myoclonus, pyramidal/extrapyramidal signs and visual deficits.[3]

Case description

Ms M, a 61-year-old female was admitted to Isabel Hospice for symptom control and potential end of life care following a diagnosis of sCJD just two days earlier. She had been living with her husband and had recently retired from her role as PA at a pharmaceutical company. She had no significant relevant medical history. Her family history was unremarkable with both of her parents living into their 90s.

Ms M had originally presented to her general practitioner two months prior to the diagnosis with a one-to-two-week history of unsteadiness, vertigo, steering to the right side and "feeling odd". She also complained of non-specific visual disturbances with a sensation of bright light all the time and noted difficulty in depth perception. The initial physical and neurological examinations were unremarkable. In light of her somewhat unusual neurological symptoms, she was referred to the acute stroke team at her local hospital in the first instance in order to rule out a posterior stroke. The initial Computed tomography (CT) scan and Magnetic Resonance Imaging (MRI) of the head were unremarkable.

She was subsequently reviewed by a neurologist five weeks after her initial presentation to her GP and was found to have visuospatial disorientation, right sided attentional 'neglect' and also neurocognitive deterioration. She was diagnosed with sporadic sCJD 12 days later. She was transferred to the local hospice two days after the diagnosis for ongoing supportive care.

On admission to the hospice, she was noted to have right sided visual neglect, difficulty in focussing and aphasia. Furthermore, she displayed right sided hypertonicity and myoclonic movements. In terms of pharmacological therapy, she had recently been commenced on olanzapine 5mg by the National CJD Research and Surveillance Unit (NCJDRSU), based in Edinburgh. Her only other regular medications were sertraline 50mg and omeprazole 20mg.

Key management challenges in this case

Our initial impression was that Ms M unfortunately had a very rapidly progressive form of sCJD, and the evolving symptom of episodic severe agitation and emotional lability seemed most

prominent and distressing. During her first night at the hospice, she suffered from significant agitation and myoclonic jerks so she was commenced on subcutaneous continuous infusion of midazolam 10mg over 24 hours. By next morning she displayed fluctuating agitation/distress, confusion, myoclonic jerks and other abnormal movements, particularly on the left side. Initially in the morning she was able to communicate verbally with a few words on occasion, but later in the day was no longer able to do this. Given these difficulties, our initial management approach was:

1. Non-pharmacological measures: calm movements and voices, closing curtains to avoid bright light as this had previously appeared to trigger discomfort, fan (as warm to touch due to restlessness), bed re-orientated so that side of neglect on right was facing wall (enabling her to hold her husband's hand with her left side, these small gestures forming a crucial means of communication).
2. Pharmaceutical measures: This included lorazepam or SC midazolam if required in addition to the ongoing 10mg midazolam in the syringe driver. We had investigated the research as to optimal management of agitation with severe, end stage CJD. Evidence was limited and the main approach suggested from the few studies found were for benzodiazepines such as midazolam along with trials of anti-psychotics (already on regular olanzapine). Paracetamol was also given to help possible discomfort from any pain/or possible early infection (warm to touch). Suppositories were also given as we tried to address any potentially reversible cause of discomfort.

Despite the above, Ms M became increasingly emotionally labile and distressed, with frequent inconsolable crying episodes, restlessness and pacing, insomnia and was no longer able to effectively communicate verbally. Myoclonic jerks and abnormal movements were also becoming more prominent. PRN low dose SC midazolam was given with partial effect and later 12.5mg levomepromazine, again with partial effect.

We also noticed that even personal care could trigger an outburst of distress and agitation. Given the extreme communication difficulties, we felt this could potentially be due to pain or possibly hypersensitivity to normal stimuli. We started by trying a combination of 1.25mg SC morphine and 2.5mg midazolam and assessed her response on the first 24hours of her admission to the hospice. These proved effective and she was commenced on continuous subcutaneous infusion. We found levomepromazine to also be helpful for episodes of agitation, used as an alternative to midazolam (Table 1).

Table 1 24hours Continuous Subcutaneous Infusion Regime

	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8-9	Day 10-12
Midazolam	10mg	10mg	10mg	15mg	20mg	40mg	50mg	50mg
Morphine			5mg	5mg	5mg	15mg	15mg	15mg
Levomepromazine					12.5mg	37.5mg	50mg	50mg
Keppra						750mg	750mg	1g

Five days after her admission, she developed tonic-clonic seizures and was therefore commenced on levetiracetam 750mg via subcutaneous infusion, which was increased to 1g due to further seizure activity the previous night. We have highlighted in table 1 the rapid daily adjustments to the pharmacological regime used in order to effectively manage her symptoms, particularly myoclonic jerks/abnormal movements and distress. Ultimately, she was requiring higher dose SC midazolam (50mg/24 hours) and SC levomepromazine (50mg/24 hours) via syringe driver. We made no change to the driver for the last 3 days as she remained comfortable and settled. She passed away 10 days post admission, with her family and nursing staff at her side.

Discussion

sCJD, as discussed, is a rapidly progressive, ultimately fatal disease. According to the National Prion Unit,[1] 'typically there is an insidious onset followed by a very rapid decline' as seen in this case. The average life expectancy from onset is 12 months,[3] but was unfortunately much shorter at only 4 months for our patient who appeared to have a particularly aggressive form. Given there is no effective curative treatment, the prognosis currently remains very poor. The focus is therefore on symptom control and support within a multi-disciplinary team (MDT), the very essence of good palliative care.

Psychological support for the patient (if cognitively able) and the family is essential, given the speed of deterioration and the nature of the disease as it strips away cognitive function much like an accelerated dementia, but with all the other neurological changes including dysphasia to also contend with. In addition, death often follows swiftly after diagnosis, a mere 12 days in this case, leaving very little time for processing and adjustment. Unfortunately for Ms M, on admission to the hospice her cognitive and communication abilities had deteriorated to such an extent that family support/counselling for her was not possible. However, we could still provide valuable support in terms of how we cared for her, including the use of calming non-verbal communication. Furthermore, we provided family support/counselling and spiritual support for her partner which were vitally important to help cope with the terrible shock, distress and sense of loss. We also initiated advanced care planning discussions from the outset, in order to help Ms M's partner, prepare both mentally and practically. This included discussion of the treatment escalation plan with the family and we were all in agreement that Ms M would be for hospice only care, focusing on her comfort and dignity.

As regards symptom management, Ms M presented with a whole array of rapidly changing symptoms. Quibell and Gunn[4] in their recent study of 6 CJD patients who were referred to hospital palliative care, state that symptoms tended to occur in the following order of frequency: 'Myoclonus, pain, agitation/startle, visual problems, dystonia, emotional distress, respiratory distress, communication issues, swallow/feeding issues, nausea, constipation, respiratory secretions, seizures'. These were all also evident in our case, to a greater or lesser extent. For us, the most challenging symptom set to manage and therefore what we will focus on in this report was that of the emotional lability with associated episodes of extreme and inconsolable distress, agitation and restlessness which occurred both day and night. Thompson et al.[5] discuss the importance of non-pharmacological interventions stating 'the involvement of suitably trained and experienced caregivers and the care of patients

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in appropriate, calm, and containing settings seem to be particularly valuable'. We also found this to be effective, particularly initially, as noted in the section above. It also emphasises the importance of the MDT approach. Thompson et al.[5] go on to say 'for more severe psychotic symptoms or agitation, short courses of antipsychotic medication appear to be effective in some cases.' The National Prion Unit[1] also state: 'Olanzapine, which has its maximum receptor blocking activity against 5HT2 receptors, can be helpful'. As noted, Ms M was admitted already on regular olanzapine as initiated by the National CJD Research & Surveillance unit. Thompson et al.[5] continue 'benzodiazepines may be an appropriate option in the later stages of disease, where psychotic features often coexist with significant neurological disability and other distressing symptoms, such as myoclonus', with Wei et al.[5] also noting the benefit for myoclonus. The National Prion Unit[1] also note 'Agitation and anxiety are frequent symptoms in patients with CJD. Often the patient can't settle and paces around ... Benzodiazepines such as diazepam, which act on benzodiazepine receptors associated with gaba receptors, are effective anxiolytic drugs and can promote sleep'. Finally, Wall et al.[6] found that 'The medications most often associated with benefits, in the opinion of the treatment teams, included anxiolytic class medications and antipsychotic medications.' They went on to say 'the benefits observed from medications in the anxiolytic class may be due to their relatively rapid onset as well as the sedative and anticonvulsant effects. Benzodiazepine medication … was relatively successful when the patient exhibited myoclonus, sleep disruption, agitation, and symptoms consistent with anxiety'.

We found that midazolam did prove to be helpful with Ms M, and indeed was the medication we used first line for distress and myoclonus, and formed the basis of the syringe driver medications, to which others were then added. We found that midazolam on its own was partially effective, but the addition of levomepromazine at times, and particularly with the addition of morphine, seemed to provide more effective symptom control. Given the communication difficulties, the beneficial effect of the morphine could have been due to neuropathic type pain/heightened sensitivity which Ms M was otherwise unable to convey.

Overall, it seems that it was the calm, multi-faceted approach of the supportive care along with the timely responses to the rapidly changing and complex array of symptoms that proved to be most helpful. This case suggests that palliative care in a hospice environment can be particularly beneficial to both patient and their loved ones in managing this distressing disease.

Conclusion

Given that currently there are only very limited studies on palliative care in CJD, the value of case reports in these rare cases becomes greater. Certainly, in caring for Ms M, we found guidance from the National Prion Unit,[1] advice from the National CJD Research & Surveillance Unit at Edinburgh and the handful of available research studies, including case studies, to be very helpful. The key points from our experience managing a patient with sCJD, was the importance of the holistic, palliative MDT approach, with non-pharmacological input just as important as pharmacological. As the disease progressed to the terminal stages, the symptoms we found particularly challenging to manage were the episodic and overwhelming episodes of distress, agitation and restlessness. We found that a combination of midazolam (1st line), levomepromazine and morphine was the most effective. Finally, psychological support is vital in cases that carry such a devastating prognosis, to help the patient where possible and their families/friends navigate through this emotional journey, with often very little time for adjustment. Ultimately, we hope that in turn, this study may add a little more to the small body of research into this rare, but important area.

Acknowledgments

None

Conflicts of interest

The authors declare that there are no conflicts of interest.

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