

Case of recurrent cerebral haemorrhage in an older adult man who uses dimethylsulfoxide (DMSO) for self-management of low mood and pain

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SUMMARY

We present the case of a man in his 70s who had suffered two separate frontal lobe haemorrhages in the context of using dimethylsulfoxide (DMSO) to manage his low mood. The known pathophysiology of DMSO renders it a likely causative agent of the recurrent intracerebral haemorrhages. This case highlights the need for clinicians to robustly enquire about a patient's use of over-the-counter medications, of non-prescribed supplements and other substances, as part of the history. In addition, the case highlights the potential for highly debilitating adverse effects from using DMSO.

BACKGROUND

Dimethylsulfoxide (DMSO) is a colourless, odourless liquid. The medical uses of DMSO have generally fallen in to three functional categories encompassing tissue/organ preservation, penetration-enhancing solvent excipients and active pharmaceutical agents, primarily anti-inflammatory.¹ DMSO has been available on the online market; with reported but unsubstantiated benefits of use in arthritis. Some studies have shown that DMSO has toxic effects; for instance, it can induce red blood cell haemolysis, reducing platelet (PLT) activities and decreasing PLT aggregation levels, inhibiting the growth of EAhy926 cells, preventing cell progression from G1 phase to S phase and elevating apoptosis rates. Additionally, it has been reported that DMSO can cause an intracerebral bleed.²

People often use DMSO for arthritic joint pain, for speeding up wound healing, treating eye conditions such as cataract and glaucoma and for lowering intracranial hypertension. DMSO is usually taken by mouth or used topically over the skin and in rare occasions intravenously.³

Through our case report, we wish to reflect on one of the potentially fatal side effects of DMSO—the ability to induce an intracerebral haemorrhage.

CASE PRESENTATION

The patient is a man in his 70s who lives alone with a medical history of two intracerebral haemorrhages (initially left-sided frontal intracerebral haematoma in 2018 and a right-sided frontal intracerebral haemorrhage in 2019); each individually affecting the left and right frontal lobes. Otherwise, the patient had enjoyed good physical health and worked in an active outdoor profession up until the second haemorrhage.

The residual deficits following the previous haemorrhages were neuropsychiatric and predominantly arose following bilateral frontal lobe damage; including anhedonia, mild perseverance, a lack of executive function and symptoms of depression. The patient's motor and sensory functions were preserved and the patient was discharged home with a package of care and follow-up within the primary care sector with Neurology input. In 2020, the patient was admitted to hospital with confusion of acute onset and a CT scan of the patient's brain revealed a further haemorrhage within the left frontal lobe. The patient had a history of mild depression and held health beliefs that were not consistent with the western medical model. The patient declined to use conventional antidepressant medication prescribed by the general practitioner (GP); instead using DMSO that he purchased from the internet; believing this to be helping his mood. This was contrary to his GP's advice and concerns raised by his family. The patient described having used DMSO for at least 2 years prior to the first intracerebral haemorrhage. The patient was admitted to hospital by ambulance after having telephoned a relative and appeared to be confused. The patient's relative was duly concerned and alerted the ambulance service. On arrival to the patient's home, the ambulance crew noted that there was evidence that the patient had used DMSO; despite the advice from his GP and other medical professionals to stop using it.

The patient displayed symptoms consistent with a frontal brain injury including marked perseverance; as evidenced by compulsively walking around the ward and pulling alarms in a repetitive manner. There was a marked deficiency of executive function as well as hostility and agitation; consistent with a change in personality. Social disinhibition was also a feature during the patient's admission.

INVESTIGATIONS

In 2018, the patient had his first intracerebral bleed. His head CT scan showed large 4 cm×3.3 cm×3 cm left frontal intracerebral haematoma with some subarachnoid extension.

After 6 months, the patient had brain MRI and magnetic resonance angiography (MRA) as a follow-up to exclude any underlying causes for the bleed. MR angiography was reported as normal by the neuroradiologist and there was no evidence of



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Figure 1 CT of the head.

cerebral amyloid angiopathy (CAA) pathology demonstrated no evidence of arteriovenous malformation.

15 months later, the patient had his second intracerebral bleed and his head CT revealed a new localised haemorrhage in the right frontal lobe measuring maximum 4 cm diameter.

On the last admission, a new large 4 cm×3.3 cm×3 cm left frontal intracerebral haematoma with some subarachnoid extension was found on his head CT scan (figure 1).

Blood tests such as C-reactive protein (CRP), urea and electrolytes, liver function test and clotting profile were unremarkable.

DIFFERENTIAL DIAGNOSIS

Hypertension

Hypertension is considered to be the most common cause of intracranial haemorrhage. It usually affects basal ganglia (mainly putamen), thalamus, pontine and cerebellum. During all the three intracerebral bleeds, the patient's blood pressure was found to be within the normal range and he has never been diagnosed with hypertension. Additionally, all of the three incidences

occurred within the frontal lobe which is an uncommon area for a hypertensive intracerebral bleed.⁴

Tumour

Many studies showed that brain tumours can present with acute intracranial bleeds.⁵⁻⁷ The patient's medical records indicate that he did not experience any symptoms consistent with malignancy. Additionally, all the investigations and scans failed to detect any tumour or malignancy.

Cerebral amyloid angiopathy

CAA is considered as the third most common cause of spontaneous intracerebral haemorrhage after hypertension and subarachnoid aneurysmal haemorrhage.⁸ CAA is a deposition of amyloid beta peptide in blood vessels of the brain and usually affects the small and medium size vessels. CAA is a degenerative vasculopathy that is classically associated with lobar intracerebral or sulcal haemorrhage.⁸ This patient suffered recurrent frontal lobar bleed. Furthermore, the prevalence of CAA increases with age with autopsy studies suggesting a prevalence of about 30% in 60-year to 69-year olds and over 50% in the age range from 70 to 89 years. The age of this patient fits perfectly into the higher prevalence range.⁹ Although a definitive diagnosis of CAA can only be made by post-mortem biopsy, neuroimaging especially MRI sequence of gradient echo and susceptibility-weighted imaging are useful in detecting microbleeds and deposition of iron on the brain cortex (cortical superficial siderosis).^{10 11} However, this patient had multiple brain scans including CT and MRI, but there was no evidence to support the diagnosis of amyloid angiopathy.^{4 10 12}

Trauma

Although the patient had a history of an unwitnessed fall in July 2019, the immediate scans did not show any signs of acute intracerebral injury and there was no evidence of any neurological sequelae.

TREATMENT

The neurosurgical team had made the decision that surgical intervention was not indicated and therefore conservative management was commenced. The patient's blood pressure was monitored and the systolic pressure was physiologically and consistently lower than 130 mm Hg. Consistent with recommendations and best practice for patients who have had a stroke, nutrition and hydration were monitored and optimised.¹³ The patient's swallow was not impaired and therefore he was able to eat and drink without restriction. As with all patients presenting with a brain haemorrhage, physical rehabilitation was considered. However, the patient displayed symptoms consistent with a frontal brain injury including marked perseverance, deficiency of executive function as well as intermittent hostility and agitation. With the patient's history of depressive disorder and previous successful treatment with mirtazapine, we restarted the mirtazapine on the patient's admission. Unfortunately, the patient was not able to engage in a conversation about his mental state or about the reinstatement of mirtazapine; owing to his cognitive deficit and it was thus restarted in his best interests after discussion with the MDT. While objective measures for affective disorder such as the Brief Assessment Schedule Depression Cards (BASDEC) were considered, the patient's cognitive impairment did not render them appropriate in terms of attaining reliable diagnostic information. Blood tests revealed no biochemical or

Learning points

- ▶ Dimethylsulfoxide is increasingly understood to be implicated in adverse events, including intracerebral haemorrhage.
- ▶ Over-the-counter or supplemental medication need to be considered as potential contributing factors to a patient's pathology and need to be enquired about robustly in the history-taking.
- ▶ There are significant psychosocial consequences of frontal brain damage with limited evidence for pharmacological treatment. Often, medication may need to be tried off-license. Consultation with patients and their triangle of care and consideration and discussion of the aims and potential limitations of each medication choice are important.

endocrine parameter that was deranged and hence potentially modifiable in terms of improving the patient's affective state. Furthermore, primary care records were consulted in order to add further information to making a best interests decision around prescribing mirtazapine and the records indicated that the patient had been experiencing symptoms consistent with depressive disorder; including anhedonia, fatigue, tearfulness, disturbed sleep and a lack of appetite for at least 6 weeks prior to his admission. At times, the patient's presentation put him and staff members at risk of physical harm and therefore antipsychotic medication was used in order to try to help with these symptoms. Initially, we treated the symptoms as if they were part of a delirium and haloperidol was used, after following the NICE guidelines for non-pharmacological techniques in terms of managing delirium. The non-pharmacological techniques employed included the use of 1:1 nursing care, a well-lit nursing bay, management of pain and constipation and optimisation of food and fluid intake. Furthermore, day/night orientation was promoted. The diagnosis of delirium was made clinically; aided by the use of the 4AT test. The 4AT test is a short tool for delirium assessment and a score of 4 or above suggests presence of a possible delirium±cognitive impairment. The patient, on assessment, scored the maximum score of 12 and in the absence of previous cognitive impairment, the acute onset of symptoms and the known brain insult, delirium was highly suspected. Haloperidol had little effect on the patient's symptoms. There is a lack of evidence for pharmacological management of psychiatric consequences such as challenging behaviours with frontal brain injuries. The use of antipsychotics remains of research interest,¹⁴ but the selection of an appropriate medication is often guided by clinical judgement and the balance of risk versus potential benefit. Owing to the known prolactinergic effects of amisulpride as well as its sedative profile, we tried amisulpride to manage the perseverant and driven behaviours. However, this had little effect in alleviating the patient's symptoms and was hence converted to risperidone, as this has an evidence base and a license for use in behavioural and psychological symptoms of dementia (BPSD). While we recognised that the patient did not have a diagnosis of dementia, the step-down deterioration in his cognitive function and behaviours consistent with organic disease of vascular origin rendered him suitable to warrant the trial of risperidone.

OUTCOME AND FOLLOW-UP

The risperidone helped with the symptoms of agitation and aggression, but the perseverant behaviour persisted and at times the patient was disinhibited and agitated. In order to meet the patient's care needs safely while allowing the potential for neurorehabilitation, the patient was discharged from the acute hospital to nursing residential care with input from the community older adult psychiatric services to further review the patient's mental state and recovery.

DISCUSSION

To our knowledge, published cases of brain haemorrhage in the context of the use of DMSO are very sparse. A case report published in 2004 presented a 55-year-old man who had presented with three haemorrhagic areas within the brain after ingesting DMSO.¹⁵ In this particular case report, the patient also had metastatic disease within the brain. This is the first published case report that we are aware of that demonstrates brain haemorrhage in an otherwise healthy adult male, where DMSO has been ingested. Clinical guidelines for the management of brain

haemorrhage are comprehensive. However, there is a deficit in guidelines regarding the pharmacological management of frontal brain injury with challenging symptoms such as agitation, aggression and sexual disinhibition. The British Association of Psychopharmacology recommends the use of haloperidol to manage challenging behaviours in the context of delirium and hence this was the initial medication choice in this case.¹⁶ However, haloperidol had little effect on the patient's symptoms and therefore we tried amisulpride off-license with its known sedative profile, and risperidone, as risperidone has an evidence-base and a license for use in BPSD.¹⁷ While we recognised that the patient did not have a diagnosis of dementia, the step-down deterioration in his cognitive function and behaviours consistent with organic disease of vascular origin rendered him suitable to warrant the trial of risperidone.

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