Case Report
Psychosis in Dementia with Lewy Bodies:
Assessment, investigations and treatment with clozapine

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Clinical history and examination
Mr B, a 72 year old married man was referred by his general practitioner to the old age psychiatry memory clinic. He presented with recent onset short term memory problems and a fine hand tremor (not ‘pill-rolling’ in nature).

At initial assessment it was noted that he had a 9 month history of progressive short term memory problems, disorientation to time and difficulty using household items, such as the telephone. A few months earlier his cognition had worsened while suffering from a urinary tract infection (UTI), which was consistent with an associated delirium. Although Mr B recovered from the physical effects of his infection, his cognition did not return to his baseline prior to the UTI. His cognition fluctuated between periods of frank confusion and lucidity.

He also reported a 3 week history of well-formed visual hallucinations, including seeing people and insects in his home. Mr B was insightful regarding his perceptual disturbance, acknowledging that these experiences were out of keeping with reality. He was easily reassured by his family and did not find these experiences distressing.

As well as a peripheral tremor, Mr B also presented with other parkinsonian symptoms including poor mobility with a slow and shuffling gait. He experienced difficulty navigating turns and corners when walking, which resulted in recurrent falls. His ability to perform his daily activities was also affected; in particular his family noted that he performed tasks more slowly.

Mr B developed new onset urinary incontinence. Symptoms of gait disturbance, urinary incontinence and cognitive impairment can be indicative of normal pressure hydrocephalus (NPH). This is a condition in which there is dilatation of the cerebral ventricles but normal cerebro-spinal fluid (CSF) pressure on lumbar puncture. If treated quickly, cognitive impairment caused by NPH might be reversible, emphasising the importance of excluding this diagnosis. Cases of NPH can be divided into idiopathic and those that are secondary to mechanical obstruction of CSF flow across the meninges. This can be caused by conditions such as meningitis, subarachnoid haemorrhage or trauma. Treatment is by a ventriculo-peritoneal shunt and is more likely to be effective when the condition is secondary to an obstructive cause.
Mr B was usually fit and healthy, with no significant past medical history or vascular risk factors. He was not prescribed any regular medications. He was a non-smoker and drank alcohol in moderation. He reported no past psychiatric history and no family history of cognitive or functional psychiatric disorders.

Prior to retirement he worked in the insurance industry. He actively participated in sports.

He continued to drive a car and reported no concerns or accidents whilst driving. He lived in his own home with his wife.

While undergoing assessment for cognitive decline, Mr B began to suffer from ‘black-outs’. He was found unresponsive at home by his wife but unfortunately no further information was available regarding the nature of these ‘black-outs’. It was not clear whether the episodes were a feature of his dementia syndrome in the form of transient loss of consciousness. Mr B spent a short time on a general medical ward and was noted to have mitral and tricuspid regurgitation. Mr B also had a lesion on his right adrenal gland – which was later found to be a benign neoplasm. This was thought to be unrelated to both his black-outs and cognitive impairment. After a further episode of transient loss of consciousness, it was suspected that they were epileptic seizures and treatment with lamotrigine was initiated.

Investigations
Mr B scored 23/30 on the Mini Mental State Examination (Folstein et al., 1975) and 59/100 on the Addenbrooke’s Cognitive Examination (Mioshi et al., 2006). He lost points on orientation, attention, recall and visuo-spatial construction. He was noticeably slow in completing the tasks.

A magnetic resonance imaging scan was organised upon receiving this referral as part of the ‘one stop shop’ model and this showed generalised atrophy which was slightly more prominent in the medial temporal lobes. There was no evidence of small vessel disease or infarcts. The ‘one stop shop’ memory service allows referred patients to undergo comprehensive assessment, including cognitive testing, occupational therapy assessments and a medical review, all within the same attendance at outpatient clinic. Any investigations which are deemed necessary, such as an ECG, blood tests and imaging, are arranged prior to this appointment so that the results are available for review.

The clinical history was suggestive of dementia with Lewy bodies (DLB) and thus functional imaging in the form of a DaTscan (type of SPECT scan) was considered. DaTscan uses a radioactive ligand which binds to the dopamine transporter molecule. This can provide evidence of the presence or absence of dopamine transporters and therefore loss of nigrostriatal neurones as seen in Parkinson’s disease or dementia with Lewy bodies. However, it was decided that the clinical picture was sufficient to make a diagnosis in the absence of functional imaging.

Diagnosis
Approximately 3 months after initial referral, a diagnosis of DLB (McKeith et al., 1996) was made. The main feature required for a diagnosis of DLB is progressive cognitive impairment (McKeith et al., 1994). This may comprise visuo-spatial and executive dysfunction initially and not necessarily include extensive memory problems in the initial stages. Two of the following core symptoms are also required for a probable diagnosis of DLB and one is required for possible DLB (McKeith et al., 1995);
(a) fluctuating cognition, with variations in attention
(b) recurrent visual hallucinations, which are typically well formed
(c) spontaneous motor features of Parkinsonism

Supportive features of DLB are neuroleptic sensitivity, repeated falls, syncope, transient loss of consciousness, systematised delusions and hallucinations in other perceptual modalities. Mr B’s presentation met the above criteria for a diagnosis of probable DLB, given his progressive cognitive impairment alongside all three of the core symptoms. He also had supportive features in the form of repeated falls and suspected transient loss of consciousness.

Treatment
Rivastigmine was initiated as first line treatment in accordance with National Institute for Health and Clinical Excellence (NICE) guidance for treatment of Parkinson’s disease dementia/Lewy body dementia. Unfortunately, Mr B did not tolerate this even at the lowest dose; therefore, he underwent a trial of galantamine (Wild et al., 2003). Mr B did not receive treatment for his parkinsonian symptoms.

Progression in the community
Mr B remained well in the community for approximately 1 year. After which he began to experience visual hallucinations in the form of seeing people and insects around the home. He also developed delusions of morbid jealousy, believing that his wife was having an affair and he began to accuse her of such. These beliefs were very persistent and intense and they resulted in significant arguments and marital disharmony. Mr B also presented with sexual disinhibition and an increased libido. Due to the intensity of Mr B’s symptoms of morbid jealousy it was felt that he posed a risk of physical harm towards his wife.

Mr B’s physical health was reviewed and no organic cause was found for his psychotic symptoms. Therefore, quetiapine was initiated and increased to 50mg twice daily. After a trial without galantamine, his hallucinations worsened and the medication was re-started. Due to a poor response to treatment and increasing risk of physical harm and sexually inappropriate behaviour towards his wife, Mr B was admitted to a psychiatric inpatient ward.

Clozapine trialled
After discussion with Mr B and his family, clozapine at a dose of 6.25mg once daily was initiated. Over the course of 6 weeks this was increased to 25mg once daily. Quetiapine was reduced and stopped. Approximately 3 weeks after initiating clozapine, Mr B’s psychotic symptoms started to reduce in both frequency and intensity.

This improvement continued and at the time of discharge from hospital, Mr B had minimal visual hallucinations and no delusional beliefs. He had good insight into his perceptual disturbance and was not distressed by the experiences. Two months post discharge, Mr B remained well with improvement in his level of functioning.

Conclusion
There are very few studies about the use and efficacy of clozapine in the treatment of DLB. Some case studies report benefits from clozapine for the treatment of neuropsychiatric symptoms in Lewy body disease (Chacko et al., 1993). Majic et al (2010) report the success of using high dose clozapine in conjunction with levodopa. Conversely, some studies suggest that extra-pyramidal side effects and confusion are associated with the use of clozapine (Widman et al., 1997).
Psychosis in DLB remains challenging and difficult to treat. Further studies to determine the efficacy of various medications, including clozapine, are required.

References


NICE. *Supporting People with Dementia and their Carers in Health and Social Care* (modified Oct 2012)  (www.nice.org.uk accessed 24/07/13)


Consent

Consent was given by the patient to publish this report.