

REVERSIBLE MILD COGNITIVE IMPAIRMENT - A CASE REPORT

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SUMMARY

With an increased general practitioner and public awareness, patients are being referred on to Memory Clinics earlier and Mild Cognitive Impairment (MCI) is often a conclusion of the assessment. The function of memory clinics is to facilitate early and accurate diagnosis of dementia and its management. Mild Cognitive Impairment is an organic condition which in significant proportion of cases, progresses to Dementia. In Bedfordshire and Luton, patients with MCI are followed up at nine months to yearly intervals and detailed neuropsychological assessments are carried out to monitor cognitive functions in order to detect dementia early and plan care at an early stage in line with the NICE guidance CG42.

An interesting patient presented to the Memory Clinic. He suffered from bipolar disorder with age of onset after 50 years. He was successfully treated with a combination of antidepressants, antipsychotics and lithium carbonate. He started complaining of memory difficulties and the initial memory assessment concluded that he had MCI. He was followed up by the clinical psychologist at memory assessment services at yearly intervals. There were no active cognitive interventions done by the psychologist. In the meanwhile the patient developed Parkinson's disease and was treated successfully with levodopa. Following this, neuropsychological tests demonstrated a significant improvement in cognitive functions. The patient was assessed as having recovered from mild cognitive disorder.

In this article the authors discuss the possible differential diagnosis and causative factors for the presentation of MCI in this patient. Furthermore the possible reasons for recovery are explored. This also raised interesting questions as to the pharmacological management of mild cognitive disorder secondary to neurological conditions and as to how the course of mild cognitive disorders could be modified by effective interventions.

Key words: dementia - Mild Cognitive Impairment – MCI - bipolar disorder - Parkinson's disease - levodopa

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INTRODUCTION

With increase in the ageing population the prevalence of dementia is on the rise worldwide (Alzheimer's disease International 2008). Services worldwide focus on early identification and management of dementias. This led to identification of a stage of memory impairment not amounting to dementia. There have been various terminologies used to describe this stage including benign senescent forgetfulness; Age associated memory impairment and cognitive impairment with no dementia (Petersen 2004). Mild cognitive impairment as a nosological entity came into vogue since Peterson started researching the field. According to him patients with mild cognitive impairment fulfil the following criteria:

- Complaint of subjective memory impairment;
- No apparent cognitive deficits or dementia features;
- Normal activities of daily living;
- Objective deficits in neurocognitive function (Petersen et al. 1997).

Since then the concept of MCI has extended to include not only memory impairment, but also impairment of other cognitive domains not amounting to dementia. MCI has been classified into single domain or multi domain MCI. Based on the cognitive domain affected MCI could be classified into amnesic or non-amnesic type. These are of aetiological value i.e. amnesic MCI is more suggestive of Alzheimer's disease

and non-amnesic MCI is usually due to vascular or other pathologies. There are studies focussing on the type of Mild Cognitive Disorder and their progression to Dementia a conversion rate of 10% per year and approximately 60-65% of people with mild cognitive impairment develop clinical dementia during their life (Busse et al. 2006).

There are also very few studies which focus on the patients who recovered from MCI. Current research focuses on factors promoting recovery from MCI, as modifying these factors could delay the progression or prevent the development of Dementia. This also brought to the limelight that MCI could be static or progressive. In the progressive form of MCI a significant proportion of cases progress to Dementia. NICE guidance CG42 'Dementia: Supporting people with dementia and their carers in health and social care' (NICE 2006) recommends that once identified, patients with MCI are followed up at nine months to yearly intervals and detailed neuropsychological assessments are carried out to monitor cognitive functions in order to detect dementia early and plan care at an early stage.

CASE SUMMARY

Our patient is a 62 years old Caucasian gentleman, living with his wife, unemployed for the past eight years. His first contact with psychiatric services was at the age of 53 years. He developed a moderate depressive episode following the death of his mother.

He was treated with antidepressants, CBT and bereavement counseling and he recovered partially. He suffered from two more episodes of depression characterised by suicidal attempts. He also presented with obsessional symptoms. As the response to medication was inadequate he was treated with a course of Electro-Convulsive Therapy (ECT) (6 ECTs) at the age of 57 years. This led to transient improvement of his symptoms. The following year his depressive symptoms worsened and he was treated as an inpatient with another course of ECT. Considering the non-response to antidepressants and presence of agitation lithium therapy was initiated. A diagnostic re-evaluation helped to make a diagnosis of bipolar disorder. This also brought to light the family history of bipolar disorder in his father as well as his great grandfather. As his symptoms of agitation and irritability continued Quetiapine was added to the existing treatment regimen. Following this his suicidal behaviour subsided and his mood stabilised. He was 59 years old at that time. On follow up reviews the patient started complaining of tremors of the hands and forgetfulness. He was assessed thoroughly by the psychiatrist and a neurological opinion was sought. The initial neurological diagnosis was drug induced Parkinsonism probably Quetiapine induced. As the patient and his wife continued to complain of memory difficulties he was referred to the memory assessment services. The patient suffered from short term memory impairment and lack of motivation. There was no history suggestive of other cognitive difficulties. He did not suffer from cerebrovascular accidents. He underwent routine dementia screen including blood tests, CT scan of the brain as well as Neuropsychological assessment. He was diagnosed as suffering from MCI in the year 2011 i.e. at the age of 60 years. He was followed up by the memory assessment services at yearly intervals.

As the patient's tremors continued to worsen he was referred to a neurologist at the age of 62 years. He underwent DAT scan which was not conclusive of Parkinson's disease. However considering the presentation a diagnosis of probable Parkinson's disease was made and the patient was treated with levodopa. This not only led to improvement in the Parkinsonian symptoms, but also significantly improved his cognitive functions. The conclusions suggest that the patient has recovered from mild cognitive disorder.

Past Medical History included viral meningitis at the age of 38 years, treated successfully without a sequelae, hypertension and diabetes mellitus.

Current Medication included:

- Bisoprolol,
- Quetiapine,
- Priadel,
- Metformin,
- Lofepamine,
- Atovastatin,

- Lansoprazole,
- Aspirin,
- Gliclazide.

Findings in the Neuropsychological assessment

The patient completed a range of tests sensitive to patterns of cognitive impairment in people with dementia which included

- Wechsler Test of Adult Reading (WTAR)
- Graded Naming Test (GNT)
- Verbal Fluency Test (letter and category)
- Trail Making Test A and B
- Repeatable Battery for the Assessment of Neuropsychological Status (R-BANS) which included tests for
 - Immediate Memory;
 - Delayed Memory;
 - Visuospatial and Constructional abilities;
 - Attention

The patient's pre-morbid intellectual functioning, as estimated by the Wechsler Test of Adult Reading (WTAR), fell within the Average range. Scores on the other tests administered during the assessment were compared to this expected level of functioning to ascertain areas where a loss in functioning may have occurred.

Salient findings in the Neuropsychological assessment Reports

At the age of 60 years: Significant deterioration in memory, attention, verbal fluency, cognitive flexibility and visual search. Slight deterioration in visuospatial skills and naming. This pattern of performance may be related to underlying low mood or possibly an organic basis for decline.

At the age of 61 years: Some improvement in performance since the previous assessment, specifically in naming and both letter and semantic fluency. Findings suggest that cognitive difficulties pertain to his current diagnosis of Bipolar Affective Disorder rather than an underlying degenerative process. A medical review may be warranted to review the diagnosis. During the medical review the diagnosis of MCI was confirmed.

At the age of 62 years: Evidence of deficits in the functional domains of attention, although immediate attention remains intact. Marked improvements in memory, significant improvement in language functioning. At this time, the current neuropsychological assessment does not conclude a diagnosis of Mild Cognitive Impairment and is not consistent with an underlying degenerative process. It would appear that deficits in attention and perceived memory problems may relate to underlying low mood and/or Parkinson's disease.

Table 1. Summary and comparison of neuropsychological functions over three years period

Test/Subtest/ Age	60 years	61 years	62 years (with levodopa therapy)
Immediate Memory	Impaired**	Impaired**	Average
Delayed Memory			
Verbal Memory			
List Recall	Impaired**	Impaired**	Average
Story Recall	Impaired**	Borderline**	Borderline**
Visual Memory			
Figure Recall	Impaired**	Impaired**	Average
Language Functioning			
Naming (GNT)	Low Average*	Average	Very Superior
Letter Fluency (FAS)	Impaired-Borderline**	Borderline**	Low Average*
Category Fluency (Animals)	Impaired**	Borderline**	Average
Attention			
Attention			
Digit Span	Impaired**	Impaired**	Average
Coding	Impaired**	Impaired**	Impaired**
Sustained Attention (Trails A)	Impaired**	Impaired**	Impaired**
Divided Attention (Trails B)	Impaired**	Impaired**	Impaired**
Visuospatial & Constructional	Low Average*	Low Average*	Very Superior

*mildly below expectation; **well below expectation

Table 2. Criteria for MCI (Petersen et al. 1999)

Memory complaint, preferably corroborated by an informant
Objective memory impairment for age
Normal general cognitive function
Intact activities of daily living
Not demented

DISCUSSION

This patient's presentation was interesting in many ways. His cognitive disturbances could be attributed to many factors. Firstly, he suffered from encephalitis as a middle aged person but recovered successfully. Secondly, at the age of 53 years he started developing affective episodes and was diagnosed as bipolar disorder. Although cognitive disturbances have been described as intrinsic to depressive episodes research has shown that euthymic bipolar patients suffer from stable cognitive deficits including attention deficits, executive function difficulties, impaired verbal memory and psychomotor retardation. In fact, the best predictors of psychosocial functioning in bipolar II disorder were subclinical depressive symptoms, early onset of illness and cognitive deficits related to executive functions. Mood stabilisers and atypical antipsychotics may improve some of these cognitive deficits (Torrent C 2006, Latalova Et.al 2011). Thirdly, our patient received two courses of ECT. His memory symptoms started after a year of receiving ECT treatment. In most patients ECT induced cognitive deficits are reversible. In a small group of patients ECT can result in longstanding and permanent cognitive impairments. (Robertson & Pryor 2006) Lastly, there could have been an influence on his cognitive functioning by his medication.

Our patient started recovering from mood symptoms after the addition of lithium with quetiapine. Lithium may affect cognitive functions in the short term by affecting immediate as well as delayed verbal memory, visual memory, attention difficulties as well as executive dysfunction. Long term therapy with lithium may cause psychomotor retardation without causing significant cognitive impairment (Wingo et al. 2009). Quetiapine has been reported to adversely affect neurocognitive functions in bipolar disorder patients in the acute phase of the illness and early stages of treatment. The long term adverse effects are minimal compared to other second generation antipsychotics. Studies on treatment of patients suffering from first episode of psychosis showed a positive effect of quetiapine on cognitive functions (Dias et al. 2012).

Interestingly studies on patients with mild cognitive impairment and bipolar disorder treated with lithium on long term basis had shown a protective effect against the development of Alzheimer's disease. This could be due to GSK3B inhibition (Forlenza et al. 2011) or telomerase inhibition activity of lithium (Martinsson et al. 2013). The therapeutic role of lithium in MCI and early Alzheimer's disease needs further research.

Our patient started presenting with Parkinsonian symptoms as well as cognitive disturbances as his mood symptoms were controlled. Interestingly levodopa therapy improved his cognitive functions. There is abundance of literature on Mild Cognitive Impairment in Parkinson's disease (PD). MCI was common even in the early stage of PD and the subtype was diverse. Parkinson's patients commonly present with executive function difficulties. There are separate criteria used by researchers in the field of MCI in Parkinson's disease. These give allowance to the impairment in psychomotor activity and slowing (Kim et al. 2008).

Dopamine replacement therapy or use of dopamine agonists is the mainstay in the treatment of Parkinson's disease. Research has shown that in addition to benefits in motor functions patients on Dopaminergic agents may have improvements in cognitive functions. Dopaminergic agents have differential effects on different cognitive functions in Parkinson's disease. In the early stages of PD

Use of dopamine replacement therapy renders a beneficial effect on dorsolateral prefrontal cortex (DLPFC)-related executive functions, including attention, set shifting tasks, working memory and planning; however, it has a detrimental effect on Orbitofrontal cortex (OFC) related executive functions. This can manifest as impairment in decision making. Long term benefits of dopamine on cognitive functions are not clear (Poletti 2012, Molloy 2006).

CONCLUSION

Mild cognitive impairment is an important diagnosis. Most studies view MCI as an intermediate phase in cognitive decline between normal aging and dementia, where monitoring and non-pharmacological approaches play the main role, our experience showed that treatment of underlying psychiatric as well as neurological conditions could lead to recovery from MCI. We need long term studies to assess the therapeutic benefits of various pharmacological agents including dopamine replacement therapy in MCI especially MCI in Parkinson's disease.

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