Shanghai Archives of Psychiatry, 2017, Vol. 29, No. 6

•CASE REPORT•

Senile Depression with Somatization Symptoms and Insomnia is Diagnosed as Multiple System Atrophy: A Case Report

Ling YUE[1#], Hai YU[2#], Guanjun LI[1], Shifu XIAO[1,*]

Summary: Patients who have senile depression with somatization symptoms are commonly encountered in clinical practice. The present case reports on a patient with senile depression who was repeatedly hospitalized and had somatic symptoms. Although the patient recovered after the first hospitalization, she suffered from a relapse one year later. As we followed up, due to the neurological findings and the response to treatment, we found that the patient is in line with the diagnoistic criteria for multiple system atrophy (MSA). The process of diagnosis and treatment of this case reminds us that clinicians need to consider differential diagnosis for refractory senile depression, especially in those patients with prominent somatization. In this case, rapid eye movement sleep behavior disorder (RBD) serves as a characteristic feature of the organic mental disorder.

Key word: senile depression; multiple system atrophy; case report; rapid eye movement sleep behavior disorder

[*Shanghai Arch Psychiatry.* 2017; **29**(6): 314-319. doi: http://dx.doi.org/10.11919/j.issn.1002-0829.216111]

1. Case history

The patient was a 66 year old divorced female, native of Shanghai, who had been admitted to the geriatric ward of Shanghai Mental Health Center 3 times with complaints of physical discomfort. This discomfort had been present for 2 years and was accompanied mainly with weakness of both lower limbs, and negative cognitions.

A review of the medical history revealed that the patient had no evidence of weakness as of July 2013, especially in the lower extremities. These symptoms worsened and the patient was no longer able to do housework. The patient had undergone multiple examinations in multiple departments of a local general hospital, but no physiological abnormal was discovered. However, the patient still believed she was seriously ill, and had a variety of physical discomforts, manifested as palpitations, stomach pain, shortness of breath, etc. These symptoms continued to get worse and the patient became reluctant to go out. By this time she had a depressive mood with loss of appetite, insomnia, and weight loss. The patient came to our outpatient department for the first time in January 2014 and was considered as having “neurasthenia”. The patient was treated with sertraline 50mg qd and zolpidem tartrate 10mg qn, but these were not efficacious. One morning in February 2014, the patient attempted suicide by cutting her wrist with a kitchen knife in her own room. After surgery and blood transfusion treatment, the patient was admitted to our hospital in April 2014 for the first time and diagnosed with “depression”. The patient was treated with sertraline 75mg/d, mirtazapine 30mg/d, lorazepam 0.5mg bid and Modified Electroconvulsive Therapy (MECT), and was discharged a month later after it she had achieved a certain level

[1]Shanghai Mental Health Center, Shanghai Jiao Tong University, Shanghai, China

[2]Huashan Hospital, Fudan University, Shanghai, China

*correspondence: Shifu Xiao. Mailing address: No 600, South Wanping Road, Xuhui District, Shanghai, China. Postcode: 200030. E-Mail: xiaoshifu@msn.com

#equal contributions to the paper

of recovery. The patient was in good mood and her physical discomfort disappeared. She felt like she did in the past, full of energy.

The patient's mirtazapine was reduced to 15 mg/d in August 2014, and soon the weakness in both feet became worse. Starting in February 2015, her discomfort in the waist and abdomen occurred again, felt like a stone pressing on those areas, with general weakness, and she could not lift her feet. The outpatient doctor she saw increased mirtazapine to 30 mg/d, but there was still no obvious effect. So in February 2015, the patient was admitted again with a provisional diagnosis of "recurrent depression". The patient was treated with duloxetine 60mg/d, mirtazapine 30 mg/d and MECT, and discharged from the hospital about 2 months later when symptoms relieved.

The patient complained of a far weaker curative effect from her second hospitalization compared with her first hospitalization. Weakness in both lower limbs was not completely relieved, and later these symptoms became worse. Six months later, the patient became depressed again, lacked confidence and was not willing to communicate with others. At this point, taking into account that the patient had complained of lower limb weakness, it was recommended that she seek consultation in a neurology department. Outpatient physical examination record noted the following: increased muscular tension in both lower extremities, which was considered as a potential sign of Parkinson's disease. The patient was prescribed Madopar 0.5# tid for treatment. The symptoms did not relieve a month later, so the patient was again admitted to our hospital in November 2015 with "recurrent depression".

The patient had a 5-year history of hypertension, with blood pressure that was under control, but she denied presence of other illnesses. The patient said she was usually cheerful before this illness began to occur. Although divorced, she had a harmonious relationship with her children and ex-husband. She denied a family history of psychiatric abnormalities and other genetic illnesses.

Physical examination revealed a slow gait, increased muscular tension in both lower limbs, and normal muscular strength in the limbs without static tremor. Upon mental status examination, the patient was seen to be down in spirits, with a number of body discomforts, particularly fatigue (she said "my two feet are very heavy"), a tight feeling in her waist and abdomen, low self-esteem, feelings of helplessness, and negative ideas like" It's better to die ". But she also said that if she had strength, her mood would be much better.

After the patient was admitted to the hospital, a full examination was done and results were found to be within normal limits. Head MRI showed: 1. Multiple ischemic foci at bilateral frontal and parietal lobe, and corona radiata. 2. Brain atrophy. Neuropsychological tests showed: Mini-mental State Examinatlon (MMSE) score of 20, Hamilton Depression Scale (HAMD) score of 46, Hamilton Anxiety Scale (HAMA) score of 38. To make a comparison with her first hospitalization when MMSE score was 18, HAMD-17 score was 40, and HAMA score was 35. Combined with the patient's clinical manifestations and neurological symptoms, we decided to consult with the neurology department of Huashan hospital (Shanghai, China). Consultation physical examination showed: increased muscle tension in the left upper limb and both lower limbs, lower extremity hyperreflexia, and Babinski sign (+). Vertical position of blood pressure changed: supine blood pressure was 132/80; standing blood pressure was 115/65mmhg. The inquiry revealed that the patient had rapid eye movement sleep behavior disorder (RBD) and sphincter dysfunction at the same time. The patient complained of constant nightmares that were full of nervous and terrorism related content. In her dreams she was sometimes hunted and would often wake up screaming uncontrollably, waking up her son who lived two doors down. This situation had been going on for several years, long before the onset of depression. Sphincter dysfunction manifested as constipation. In addition, an additional problem was also discovered during the interview: the patient had been taking Madopar after meals, which was reducing the absorption and efficacy of her medication. Due to the data from all previous examinations the patient was given a diagnosis of multiple system atrophy (MSA) by the neurology team. Spinal cord lesions could not be excluded. She was given the following recommendations: 1. thoracic MRI scan (T4 as the center); 2. Madopar 1/2# tid (before meals); 3. polysomnography (PSG); 4. monitoring of blood pressure; 5subsequent follow-up visit at the neurology department. According to the consultation advice, Madopar was administrated before meals, and examination was done to exclude spinal cord disease. Three days later, the patient reported that lower limb weakness had improved significantly and her mood subsequently improved as well. A week later the patient was discharged from the hospital.

2. Discussion

This is a case of late-onset depression, initially manifested in typical somatic symptoms. After her first hospitalization, and treatment with antidepressants and MECT, the patient achieved full remission. However, over the long-term she had several depressive relapses. Though her clinical treatment and diagnosis initially started with depression, the real underlying issue was a neurodegenerative disease – MSA.

MSA is a sporadic neurodegenerative disease. It is common in adulthood and is frequently seen in those 50 to 60 years old (mean age of onset, 54.2 years old). Epidemiological surveys shows that the incidence of MSA in people over 50 years old is about 3/10 million,[1], and there is no complete epidemiological data in China. MSA is characterized by varying degrees of autonomic

nerve dysfunction, and symptoms poorly responsive to levodopa including Parkinsonism symptoms, ataxia, and pyramidal signs.[2] It is easily found sleeping disorders in MSA patients, RBD is the most common type of them which is even as the prelude to MSA. RBD is currently considered to be a red flag for MSA, characterized by vivid and terrifying dreams with increased simple or complex behavior in the sleep stage of rapid eye movement. At present, polysomnography (PSG) is often used in the diagnosis of RBD, and it is found that the incidence of RBD in MSA is as high as 90-100%.[3] Iranzo studied 67 cases of MSA[4] and found that 100% of the patients had symptoms of RBD, of which 52% had RBD symptoms appear earlier than Parkinson symptoms, cerebellar symptoms and autonomic nervous system symptoms, an average of 7-year earlier. RBD plays an important role in the early diagnosis of MSA. Neuroprotective treatment can be used as early as possible to improve the course of disease.

RBD is often the first sign of early alpha synuclein neurodegeneration in brainstem structures, suggesting the occurrence of early Parkinson's disease, multiple system atrophy and dementia with Lewy body,[5] but these subtle symptoms are easily ignored. A retrospective study by Howell et al. showed that within ten years, approximately 50% of spontaneously RBD patients would develop Parkinson's syndrome.[6] Ultimately, 81% - 90% of RBD patients progressed to neurodegenerative diseases. So early detection of RBD is clinically significant. Studies have shown that about 88% of patients with RBD can be diagnosed by clinical manifestations, but those patients with poor cognitive ability will hardly report RBD symptoms.[7] Therefore, psychiatrists are advised to clarify symptoms during the clinical interview. A straightforward case of insomnia may turn out to be RBD after more information is uncovered. Using PSG and other examination instruments is importance for the early diagnosis of RBD and the possibility of neurodegenerative diseases. In addition, it is important to collect relevant medical history for patients' partners who share the same bed. Early intervention for RBD can help avoid injury to patients themselves and their sleeping partners.

What deserves consideration is the relationship between MSA and depression, and why the patient with a final diagnosis of MSA was first presenting with a typical depressive disorder. First of all, research has shown that MSA combined with depression is common. A study from China found that MSA comorbid with depression reached 65.6%[8]; whereas the rate in another study outside of China was 43%[9], and with the exacerbation of MSA, the incidence of emotional disorders increased. The mechanism is not clear. It is possible that the neurodegenerative diseases affect the synthesis or metabolism of emotion related neurotransmitters.[10] It can be seen that depression can be present throughout the whole course of MSA. There are both psychological factors and organic factors that can cause these pathological changes to mood. When reviewing the depressive symptomology in this case, especially the occurrence of suicidal behavior before the first hospitalization, it is difficult to ascertain whether MSA inherently includes depressive symptoms or the depression is a separate, yet comorbid, entity. Therefore, her depressive symptoms cannot be explained by MSA accompanied with depression. But from the longterm analysis, the patient's first "depressive episode" occured 2 years before diagnosis of MSA and was followed by two relapses. With the appearance of MSA symptoms, the depressive mood became more and more serious. There was a temporal correlation between depressive symptoms and the development of MSA. Therefore, we hypothesize that the patient's first depressive episode may have been a prodromal version of MSA. In terms of the evolution of clinical symptoms, the patient's depressive symptoms had their own unusual characteristics. For example, her somatic complaints were always "fixed" - characterized by lower limb weakness and discomfort in the waist and abdomen, aggravating with each passing day, and the patient said, "if my legs were strong, my mood would be much better". It could be that the core issue for the patient was physical discomfort. Therefore, the key to diagnosis would lie in uncovering all the patient's physical symptoms. In this case, in addition to the above mentioned RBD symptoms that were easily overlooked and misdiagnosed as "insomnia", "the symptoms of lower limb weakness" are common complaints that are even more easily overlooked in clinical practice. Although we were unable to identify the patient's somatic illness at that time, the symptoms of "lower limb weakness" gradually increased. And finally, the corresponding neurological signs appeared, manifested as slow gait and increased lower limb muscle tension, which were actually a MSA superimposed Parkinson symptom. This also reminds clinicians that when you found somatic complaints, particularly with elderly patients, careful physical examination of the nervous system needs to be done to avoid misdiagnosis. At first the patient's antidepressant treatment was quite effective. A possible explanation is that in the early stage of MSA, the condition may temporarily improve after neurotransmitters are modulated from the antidepressants. However as MSA progresses, the antidepressant treatment continues to lose its effectiveness. Therefore, the patient's response also partially validated the hypothesis that MSA neurotransmitter unbalance leads to depression.[10] In conclusion, MSA is closely related to depressive symptoms and is difficult to identify in the early stage of MSA, but there are still "clues" that can be found through comprehensive and detailed medical history, physical examination, and close follow-up.

Also worth mentioning is that many clinicians when prescribing Madopar forget to remind patients and family members to take the pills correctly. Pharmacokinetic studies have found that food intake can reduce the speed and extent of levodopa absorption.

[11] When given Madopar after a standard meal, the peak plasma concentration of levodopa decreases by 30%, the peak time is prolonged, and the extent of absorption is reduced by 15%. Therefore, mentioned the correct way to take Madopar can achieve the full effect of treatment.

In psychiatry, especially in geriatric psychiatry, diagnosis and treatment of depression often centers around somatic symptoms. It is important to keep in mind that the 2010 APA guidelines suggest that "elderly people with depressive disorders should be thoroughly examined for somatic symptoms."[11] There are some common "somatic symptoms" in this case, insomnia, constipation, and lower limb weakness. But there was another disease underlying these symptoms. Therefore, psychiatrists need to ask about medical history, carefully identify symptoms, and not neglect neurological and physical examinations so as not to miss organic diseases.

Funding statement

No funding support was obtained for preparing this case report.

Conflict of interest statement

The authors declare that they have no conflict of interest related to this manuscript.

Informed consent

The patient signed an informed consent form and agreed to the publication of this case report.

Authors' contributions

YL and YH wrote the first draft of the case report, and LGJ provided analysis of the patient's medical history, and Xiao Shifu offered guidance for writing.

躯体化症状伴失眠的老年抑郁症诊断为多系统萎缩 1 例

岳玲，俞海，李冠军，肖世富

概述：老年抑郁症患者伴有躯体化症状在临床上非常常见。本病例报告了一例反复住院治疗，伴躯体症状的老年抑郁症患者，虽然在首次住院治疗获得了临床痊愈，但一年后病情复发，经过随访以及神经内科诊治，发现这其实是一名多系统萎缩（multiple system atrophy, MSA）的患者。通过这个病例的诊治过程，提示对于一些反复治疗、疗效欠佳的老年抑郁症患者，尤其对于"躯体化症状"突出的病例，临床医生需要反复思考是否存在基础躯体疾病，仔细寻找器质性病因。而快速动眼睡眠行为障碍（rapid eye movement sleep behavior disorder，RBD）作为一个特征性的脑器质性疾病标志值得精神科医生引起重视

关键词：老年抑郁症； 多系统萎缩； 病例报告； 快速动眼睡眠行为障碍

References

1. Wenning GK, Colosimo C, Geser F, Poewe W. Multiple system atrophy. *Lancet Neurol.*2004; **3**(3): 93-103. doi: http://dx.doi.org/10.1016/S1474-4422(03)00662-8
2. Gilman S, Wenning GK, Low PA, Brook DJ, Mathias CJ, Trojanowski JQ, et al. Second consensus statement on the diagnosis of multiple system atrophy. *Neurology*. 2008; **71**: 670-676. doi: http://dx.doi.org/10.1212/01.wnl.0000324625.00404.15
3. Colosimo C. Nonmotor presentations of multiple system atrophy. *Nature Reviews Neurology*. 2011; **7**(5): 295-298. doi: http://dx.doi.org/10.1038/nrneurol.2011.5
4. Iranzo A, Santamaría J, Rye DB, Valldeoriola F, Martí MJ, Muñoz E, et al. Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. *Neurology*. 2005; **65**(2): 247-252. doi: http://dx.doi.org/10.1212/01.wnl.0000168864.97813.e0
5. Beeve BF. REM sleep behavior disorder：Updated review of the core features, the REM sleep behavior disorder-neurode-generative disease association, evolving concepts, controversies, and future directions. *Ann N Y Acad Sci.* 2010; **1184**(11): 15-54. doi: http://dx.doi.org/10.1111/j.1749-6632.2009.05115.x
6. Howell MJ, Schenck CH. Rapid Eye Movement Sleep Behavior Disorder and Neurodegenerative Disease. *JAMA Neurol*. 2015; **72**(6): 707-712. doi: http://dx.doi.org/10.1001/jamaneurol.2014.4563
7. De Cock VC, Debs R, Oudiette D, Leu S, Radji F, Tiberge M, et al. The improvement of movement and speech during rapid eye movement sleep behaviour disorder in multiple system atrophy. *Brain*. 2011; **134**(3): 856-862. doi: http://dx.doi.org/10.1093/brain/awq379

8. Song DD, Yu YX, Dong QW, Zhang HL, Liu JG, Liu Q, et al. [Assessment of cognitive function, emotions and activities of daily living in patients with multiple system atrophy]. *Zhong Hua Yi Xue Za Zhi*. 2013; **93**(25): 1948-1951.doi: http://dx.chinadoi.cn/10.3760/cma.j.issn.0376-2491.2013.25.004
9. Schrag A, Sheikh S, Quinn NP, Lees AJ, Selai C, Mathias C, et al. A comparison of depression, anxiety, and health status in patients with progressive supranuclear palsy and multiple system atrophy. *Movement Disorders*. 2010; **25**(8): 1077-1081. doi: http://dx.doi.org/10.1093/brain/awq379
10. Yamada H, Kato EH, Morikawa M, Shimada S, Saito H, Watari M, et al. Decreased serum levels of macrophage migration inhibition factor in miscarriages with normal chromosome karyotype. *Human Reproduction*. 2003; **18**(3): 616-620. doi: http://dx.doi.org/10.1093/humrep/deg147
11. American Psychiatric Association. *Treatment of Patients with Major Depressive Disorder, Third Edition*. American Psychiatric Association; 2010

.

Dr. Yue Ling obtained a bachelor's degree in clinical medicine in 2005 from Shanghai Second Medical University and a master's degree in medicine in 2013 from Shanghai Jiaotong University School of Medicine. She is currently a PhD (psychiatry) candidate at Shanghai Mental Health Centre, Shanghai Jiaotong University School of Medicine. Since 2005, she has been working as a psychiatrist at the Shanghai Mental Health Center. Her current research direction is: the pathogenesis and clinical characteristics of cognitive and affective disorders in the elderly.