



Multiple System Atrophy (MSA-C) Presenting with Cognitive Affective Cerebellar Syndrome and Psychosis

Kognitif Affektif Serebellar Sendrom ve Psikoz Bulguları ile Ortaya Çıkan bir Multisistem Atrofi (MSA-C) Olgusu

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Summary

Besides its well-established motor functions, the modulatory role of cerebellum in the neural networks subserving cognition and emotion has been supported by several lines of evidence obtained from neuroanatomical investigations, functional neuroimaging and clinical research. Damage to cerebellar posterior lobe and vermis may lead to a cognitive affective cerebellar syndrome primarily comprising cognitive disorders characterized by executive dysfunctioning, language and visuospatial impairments in addition to disorders of affect and other psychiatric impairments. Cognitive and affective symptoms have often been reported in neurodegenerative cerebellar diseases while psychotic symptoms occur less frequently. In this article, we describe an extraordinary case of multiple system atrophy (MSA-C), who presented with cognitive affective cerebellar syndrome and psychotic symptoms before cerebellar ataxia was evident. The wide variety of symptoms observed in this case underlines the critical role of cerebellum in modulation of networks engaged in cognition, affect, thought and perception, and provides further evidence regarding the contribution of cerebellar dysfunction to several neuropsychiatric symptoms. (Turkish Journal of Neurology 2013; 19:107-10)

Key Words: Multiple system atrophy, cerebellum, cognitive affective cerebellar syndrome, psychosis

Özet

Serebellumun iyi bilinen motor fonksiyonlarının yanında kognisyon ve emosyon ile ilişkili şebekelerdeki kritik modülatör rolü nöroanatomik inceleme, fonksiyonel nörogörüntüleme ve klinik araştırmalardan elde edilen yeni kanıtlarla desteklenmektedir. Serebellar posterior lob ve vermis lezyonlarını takiben ortaya çıkan kognitif affektif serebellar sendrom primer olarak yürütücü fonksiyonlar, dil ve vizuospasyal işlevleri kapsayan kognitif bozuklukların yanı sıra duygulanımın da etkilendiği çeşitli psikiyatrik bozuklukları içerir. Dejeneratif serebellar hastalıklarda kognitif ve affektif semptomlar sıklıkla görülürken psikotik belirtiler oldukça nadirdir. Bu yazıda serebellar ataksi belirginleşmeden kognitif affektif serebellar sendrom ve psikoz bulguları ile ortaya çıkan sıra dışı bir multisistem atrofi (serebellar alt tipi, MSA-C) olgusu psikotik davranış ve serebellar patoloji ilişkisi yönünden incelenmiştir. Bu olguda görülen zengin semptomatoloji serebellumun kognisyon, affekt, düşünce ve algıya dair bilgilerin işlenmesinde kritik bir rol oynayabileceğini işaret etmekte ve serebellar disfonksiyonun bazı nöropsikiyatrik semptomların altında yatabileceği bilgisini desteklemektedir. (Türk Nöroloji Dergisi 2013; 19:107-10)

Anahtar Kelimeler: Multisistem atrofi, serebellum, kognitif affektif serebellar sendrom, psikoz

Introduction

The traditional view that ascribes cerebellum a functionality limited only to balance and the coordination of motor activity has been challenged in the past 30 years (1). The growing body of evidence pointed out that in addition to its well-known motor functions, it also plays a critical role in regulating cognitive functions that serves as a key structure combining and regulating information from different channels. In 1991, Schmahmann first discuss that cerebellar dysfunction may cause dysmetria in addition

to motor findings (2). This condition that takes place especially following the posterior lob of cerebellum (lobule VI and Crus I and Crus II of lobule VII) and vermis damage was named 'cognitive affective cerebellar syndrome' by Schmahmann and Sherman in 1998 (3). This syndrome, aside from affecting primarily the cognitive functions including executive, language and visuospatial functions, it also gives rise to affective symptoms such as emotional blunting, passivity, personality changes, behavioral disorders and rarely psychosis (3, 4, 5)

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The cerebellar subtype of multisystem atrophy (MSA-C) is a sporadic and progressive synucleinopathy characterized primarily by cerebellar findings and autonomic disorder and secondarily by parkinsonism and corticospinal findings. The diagnostic criteria for MSA-C were revised in the last consensus statement published by Gilman et al. in 2008 (6). While the cognitive and affective symptoms are common in patients with MSA-C (5, 7), psychosis is very rare in patients without obvious extrapyramidal findings (8, 9). In this report, an MSA-C case with unusual clinical symptomatology where the cognitive, affective and psychotic disorders preceded cerebellar ataxia is presented.

Case

The patient who is a 45-year-old, right-handed male consulted in our dementia polyclinic with disequilibrium and forgetfulness complaints. It was reported that the symptoms started when he was 31 years old and that he was laid off from his job as a textile worker due to the decreasing quality of his craftsmanship and increased clumsiness. It was reported that the patient, who used to be an exemplary family man, first developed severe insomnia, mild disequilibrium, forgetfulness and behavioral disorders and then used domestic violence towards his spouse and children, getting increasingly reckless and sometimes running away from home to different cities. During that time, the patient was reported to start a business in commerce but experienced severe organizational problems in the workplace, and eventually went bankrupt for giving away most of his merchandise without compensation. His history indicated that he was admitted to a psychiatric service due to the emergence of stealing habits and bouts of jealousy, colorful visual hallucinations involving human forms and aggressive demeanor. It was reported that the patient benefited moderately from the medical treatment but his disequilibrium worsened. By 36 years of age his complaints also included autonomic symptoms

such impotence and incontinence. After making 2 suicide attempts in this period, it was learned that the patient was admitted to psychiatric care for 6 more times until he was 38. The patient who was experiencing REM sleep behavior disorder did not have daytime over-sleepiness but reported to overeat a single type of food (especially bread) unless he was stopped by his family.

The patient's medical history was unremarkable. There was no familial history of neurological conditions. Information about his alcohol and substance use was not obtained. At a first look, his overall appearance was unkempt, his personal care was overlooked and his affective state was child-like, especially considering the inappropriately timed laughs, which, according to reports, were also accompanied by untimely crying although not as often. Systemic inspection did not reveal any remarkable findings. The patient's speech was severely dysarthric and monotonic. While the eye movements were unconstrained in every direction, nystagmus was present in both horizontal and vertical planes. The motor system and reflexes were normal. The cerebellar tests showed clumsiness: prominent bilateral dysmetria and dysdiadochokinesia were present. No signs for Parkinsonism were found in extrapyramidal system examination. Myerson's sign was positive. The evaluation for autonomic nervous system involvement showed orthostatic hypotension (130/80 mmHg lying down, 90/60 mmHg standing up after 3 minutes) along with incontinence. Experiencing postural instability and truncal ataxia, the patient could take a few steps without support after expanding his balance area.

In the mental state examination, his time and location orientation was partially impaired but his personal orientation was intact. In the attention tests, his digit span was narrowed (3 forward – 2 backward) and he could not count the months and the days backwards. A secondary type memory impairment where encoding is impaired was detected. The patient's visuospatial deficit was pronounced and his verbal fluency was reduced; his abstraction skill was partially and his planning and reasoning skills were severely impaired (Figure 1). The patient scored 19 out of 30 in mini mental state examination.

In cranial magnetic resonance (MR) imaging, axial slices of T2-weighted volumes showed hot cross buns in the pons which are often observed in MSA patients, and advanced atrophy in both cerebellar hemispheres, vermis, pons and middle cerebellar peduncles (Figure 2). The fourth ventricle was expanded in width. These findings were accompanied by mild cerebral atrophy.

For the ataxia treatment, the patient was started on 3600 mg/day piracetam but his ataxia did not show meaningful improvements. His visual hallucinations stopped completely and his delirium and agitation improved remarkably after the addition of 600 mg/day quetiapine to his treatment regimen.

Discussion

Our case possibly meets the MSA-C diagnostic criteria when the symptoms are considered (6). In accordance to the diagnostic criteria, the symptoms of the disease are defined as disequilibrium, clumsiness and behavioral disorders after 30 years of age, before the addition of autonomic dysfunctions urinary incontinence, impotence and orthostatic hypotension to the list. In this sporadic case without a familial history of disease, a cerebellar syndrome

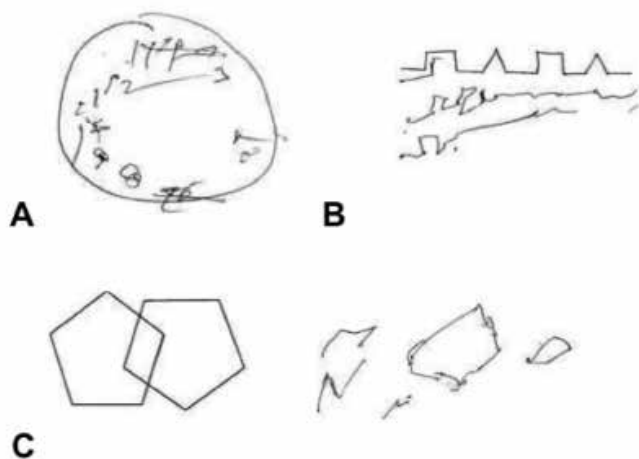


Figure 1: (A) Shows the patient's drawing of a clock and (B) Luria's alternating series. (C) When asked to copy intersecting pentagons, the patient drew the shapes seen on the right.

including dysarthria, extremity ataxia, postural instability and ataxia gait was detected. In the structural imaging, aside from the expansion of the 4th ventricle, atrophy in pons and middle cerebellar peduncle which are typical for MSA-C, the presence of severe and diffuse atrophy involving vermal region which is often associated with affect and psychosis, and the cerebellar hemisphere posterior lobes which are indicated in cognitive functions, is noteworthy. The concurrent start of the cerebellar findings with the cognitive decline and psychosis appears to support a causal relationship in this case. The psychosis developing secondary to the cerebellar damage has previously been indicated in combination with vermis tumor (5), cerebellar malformations (10), cerebellar trauma (11) and degenerative cerebellar diseases (primarily spinocerebellar ataxias) (12,13). However, even though cognitive affective cerebellar syndrome is often seen with executive dysfunctions, personality changes and affective symptoms in degenerative cerebellar diseases, psychosis is rarely manifested. Especially in the multisystem atrophy patients with dominant cerebellar ataxia, psychosis which is a component of mental involvement, is rarely seen and only a few cases were reported (8, 9).

The case presented here is exceptional in the sense that psychosis started when the cerebellar motor findings were still relatively mild and that the neuropsychiatric symptomatology was severe enough to impair functional activity. In our case study, the psychosis involved delirium and hallucinations of the human form, and the patient tried to have conversations with these hallucinations thinking that they are people he knew. These types of vivid and realistic hallucinations were previously reported in MSA patients (14) and they bear clinical resemblance to peduncular hallucinosis. Peduncular hallucinosis may occur as a result of damage to the brainstem reticular formation or thalamus' input pathways, or the inhibitory serotonergic neurons associated with raphe nucleus (15). Cerebellar vermis' connection to reticular formation, raphe nucleus and thalamus (16, 17) satisfy the necessary anatomical

basis for this condition and strengthen the possibility that the hallucinations seen in our case were peduncular hallucinations when the clinical findings are taken into account.

In our case study, the cognitive dysfunction affected more than one cognitive faculty and caused enough damage to disrupt the patient's daily activities. The detailed neuropsychological evaluation studies revealed a cognitive profile in MSA patients where executive functions, reasoning, attention, verbal memory and visuospatial functions were impaired and indicated a spectrum of cognitive disorders ranging between normal cognitive findings and subcortical dementia (7, 18). In addition to the reports showing the relationship between frontal atrophy and the disease duration, there have been case studies where the cognitive disorders became obvious at the onset of the disease (18, 19). In a study where the cognitive and neuropsychiatric findings of synucleinopathies were evaluated, MSA patients performed worse than Parkinson's Disease patients and better than Lewy body dementia patients (20). However, a cognitive impairment severe enough to disrupt daily activities is not common in MSA and dementia is rarely seen (21).

Another finding relating to the emotional regulation disorder in this case study is the pathological laughing and crying behavior. The pathological laughing or crying behavior, described as pseudobulbar affect or emotional incontinence, is a condition where laughing, crying or both are induced in the absence of a stimulus evoking an emotional response. This condition, which indicates problems regulating or coordinating emotional expressions, was reported to be common in MSA-C patients (36%) than normal (22). It is argued that this condition may arise secondary to the disruption of the cerebellar emotional behavior regulation and may caused by the involvement of the corticopontocerebellar pathways neighboring corticobulbar pathways (22).

According to the universal cerebellar transformation hypothesis put forward by Schmahmann in 2000, cerebellum is an important hub modulating the mental activities just as much as the motor activities within distributed neural circuitries (4). Through its anatomical and functional connections to the structures critical in cognition (prefrontal cortex, parietal cortex, anterior cingulate cortex, basal ganglia, subcortical limbic structures, thalamus, hypothalamus, periaqueductal gray matter and the brainstem nuclei that produce monoamine), cerebellum assures that functions are sustained at a basal level (2, 17, 18, 23). The involvement of the non-motor cerebellar parts, therefore, causes emotional disorders and present as cerebellar cognitive affective syndrome (3). In the present case, the existence of these various findings as a result of cerebellar degeneration suggest cerebellum's contribution in thinking, affect, perception and cognition at a neural circuitry level, and also underline the view that cerebellar dysfunction may underlie certain neuropsychiatric symptoms.

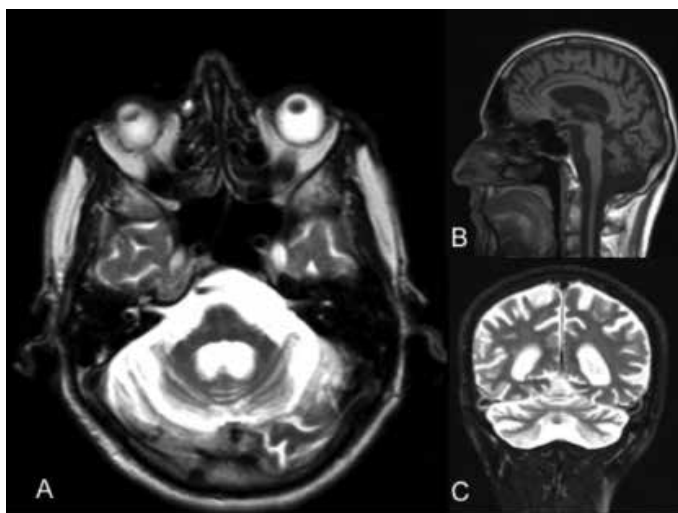


Figure 2: (A) Axial T2, (B) sagittal T1 ve (C) coronal T2 cranial MR slices show visible atrophy in cerebellum, pons and middle cerebellar peduncles as well as expansion in the 4th ventricle. In the axial T2 section, a hyperintensity shaped as “hot cross bun” is seen in pons.

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