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Diagnosis of Cerebellar Cognitive Affective Syndrome and Patient Management: Case Report and Literature Review

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cerebellar cognitive affective syndrome, ccas, schmahmann syndrome, fluoxetine, third generation antipsychotics

ABSTRACT
Cerebellar Cognitive Affective Syndrome (CCAS), also known as Schmahmann syndrome, is a disorder involving deficits in executive function, spatial cognition, language, and affective regulation resulting from cerebellar damage. This syndrome presents a significant clinical challenge due to its diverse symptomatology, which can include anxiety, depression, euphoria, emotional lability, as well as executive, attentional, and visuospatial deficits. The management of CCAS, especially in children, is complicated by limited data and a lack of controlled studies. This report details the case of a 13-year-old girl with a history of epilepsy and post-ictal intellectual disability who developed impaired coordination, severe aggressiveness, and behavioral disorders, leading to a diagnosis of CCAS. Treatment with a combination of Fluoxetine, a serotonin reuptake inhibitor, and Aripiprazole, a third-generation antipsychotic, resulted in significant improvements in the patient's emotional regulation, social functioning, and cognitive abilities. This case suggests that the combination of Fluoxetine and third-generation antipsychotics may be a promising therapeutic strategy for managing CCAS in pediatric patients. Our findings emphasize the importance of early diagnosis to avoid misdiagnosis and ensure effective treatment. Nonetheless, more research is needed to evaluate the long-term effectiveness and safety of these therapies and to develop robust, evidence-based guidelines.

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INTRODUCTION

The cerebellum has long been recognized as a key structure for motor control. However, this traditional view has been substantially revised in recent years, with growing evidence highlighting the cerebellum's critical role in cognition and emotion. Consequently, the cognitive and psychiatric manifestations of cerebellar lesions, collectively known as Cerebellar Cognitive Affective Syndrome (CCAS), have gained clinical relevance (Schmahmann & Caplan, 2006). CCAS is characterized by impairments in executive functions (e.g., planning, set-shifting, verbal fluency, abstract reasoning, working memory), spatial cognition, and linguistic processing, typically resulting from damage to the cerebellum, particularly the posterior lobe. Moreover, when lesions involve the vermis, individuals with CCAS often exhibit significant affective dysregulation (Schmahmann & Caplan, 2006; Alan et al., 2024).

A related condition, Cerebellar Mutism Syndrome (CMS), shares several features with CCAS. CMS is characterized by reduced speech or mutism, alongside neurological, behavioral, and cognitive impairments, and is most frequently observed in the pediatric population following surgical resection of posterior fossa tumors (Yildiz et al., 2010). Although CMS and CCAS represent a continuum of symptoms, CCAS is more commonly reported in adults. Notably, a link between vermis abnormalities and affective disorders has been observed in children with conditions such as vermal agenesis and post-operative posterior fossa syndrome (Yildiz et al., 2010).

While numerous cases of CCAS have been reported in adults, the literature on children

and adolescents remains limited. This scarcity of evidence means there is insufficient data to firmly establish the efficacy of specific psychopharmacological treatments for this syndrome. However, some reports suggest that Zolpidem may be a promising treatment for pediatric CMS (Shyu et al., 2011). Conversely, case reports in adults have indicated potential therapeutic benefits for CCAS symptoms from various agents, including Fluoxetine, Lithium, Donepezil, Aripiprazole, Quetiapine, Modafinil, and Dextromethorphan/Quinidine (Bhatia et al., 2016; Pesic et al., 2014; Nishida et al., 2019; Yap et al., 2012; Rodriguez, 2017; Molinari et al., 2019; Caplan & Daly, 2012).

In this context, we report the case of a pediatric patient who presented with clinical symptoms and neuroimaging findings indicative of CCAS. We also discuss the use of fluoxetine in combination with a third-generation antipsychotic, which resulted in significant clinical improvement.

CASE REPORT

A 12-year-old girl was referred to the emergency room of Dr. Kariadi Hospital from Purwodadi Hospital due to a complex condition that could not be managed locally. The patient's history was notable for significant psychosocial stressors. She lived with her mother and grandparents in a single household. From the age of 10, the patient was frequently exposed to parental conflict, often witnessing arguments between her father and mother. She typically internalized these experiences, remaining silent and reluctant to confide in anyone, including her mother, for fear of adding to her mother's burden. This situation occurred almost daily and deeply affected the patient, particularly when she saw her mother crying. The patient also frequently witnessed her father becoming angry with her grandfather, who often intervened during parental disputes.

At age 11, the patient experienced conflict with school peers because of her active involvement in competitive races. On several occasions, a peer encouraged others to ostracize her. The patient felt powerless and kept her feelings to herself, not wanting to burden her parents. At that time, she denied persistent sadness or psychotic symptoms, such as formless auditory hallucinations. The patient grew very close to her grandparents, seeking stability amid her mother's constant sadness.

Regarding social background, the patient was an only child in a household marked by long-standing parental conflict. Her father worked as a sports teacher and was often away from home, while her mother was an elementary school teacher. The family dynamics deteriorated as the father appeared increasingly irresponsible regarding domestic affairs and provided inconsistent financial support. Consequently, the patient was primarily cared for by her mother and grandparents. Despite reported good social interactions with peers, she experienced bullying related to her competition successes. There was no prior medical history of febrile seizures, epilepsy, head injuries, or substance use.

In the period leading up to her illness, the patient exhibited behavioral changes, including communication difficulties and increased aggressiveness and irritability, particularly towards her mother. This was a notable change from her previously described temperament as a good-natured and even-tempered child. She began displaying emotional outbursts towards her mother, sometimes without apparent provocation, and demonstrated regressive, age-inappropriate behaviors.

Two weeks prior to admission, the patient developed a severe global headache but could still perform usual activities; she had no fever but vomited twice. She was initially taken to a midwife and received medication, without improvement. Thirteen days before admission, she reported more frequent dizziness and began appearing confused; her activities became limited. Behavioral changes emerged, such as walking without her slippers. Ten days before admission,

the patient continued to experience dizziness, slept excessively, and became unable to perform daily activities; she vomited twice and began wetting the bed. She was then taken to Purwodadi Hospital.

Eight days before transfer to Dr. Kariadi Hospital, the patient had a seizure at Purwodadi Hospital. Following this seizure, she developed frequent bedwetting, had inadequate communication, and became unable to speak or follow commands. Due to the lack of improvement, she was referred to Dr. Kariadi Hospital.

During her stay at Dr. Kariadi Hospital, the patient had two further seizures within 24 hours and was admitted to the Pediatric Intensive Care Unit (PICU) under the care of the Pediatric Neurology team. A comprehensive diagnostic workup was performed, including a Contrast CT-Scan, Lumbar Puncture, Mantoux test for TB, Complete Blood Count, and Neurological Examination. The leading diagnosis was Cerebellitis, possibly of autoimmune origin. A psychiatry consultation was obtained, and an initial diagnosis of Organic Psychosis was made. However, following a deeper assessment utilizing the Montreal Cognitive Assessment - Indonesian version (MoCA-Ina), which revealed severe cognitive decline, the diagnosis was refined to Cerebellar Cognitive Affective Syndrome (CCAS).

During hospitalization, the patient was started on Aripiprazole 2.5 mg/24 hours to control agitation and Fluoxetine 10 mg/24 hours to address mood symptoms. Over time, she demonstrated reduced aggression and impulsivity, along with increased awareness of her actions. The patient currently exhibits no neurological, cardiac, or gastrointestinal side effects and has maintained adherence to her outpatient treatment regimen.

Fig. 1 MRI Contrast reveals a hyperintensity lesion in the left cerebellar hemisphere. Findings are consistent with Encephalitis and Cerebellitis, differential diagnosis includes infectious acute cerebellitis versus immune-related acute cerebellitis.

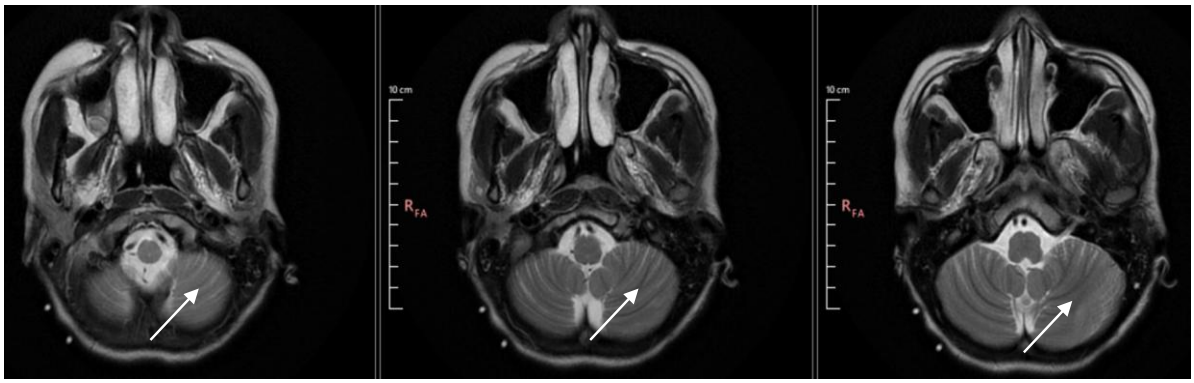

Fig. 1 MRI Contrast appears to be *a hyperintensity lesion* in the left hemisphere of the cerebellum. Encephalitis and Cerebellitis, dd/ *infectious acute Cerebellitis* dd/ *immune – related acute Cerebellitis.*

RESEARCH METHOD

Research Design

The type of research used is included in literature research or literature review (*literature review, literature research*) which is carried out by collecting, evaluating, reviewing and critically analyzing ideas, knowledge, and findings written in an *academic-oriented literature*), and formulate contributions, both theoretically and methodologically, to a topic related to research, namely the diagnosis of Cerebellar Affective Cognitive Syndrome (CCAS) and its management. This literature research uses a *systematic literature review* approach.

Data Source

A comprehensive literature search was conducted across *PubMed* and *Google Scholar* databases to dig up existing information about the influence of the cerebellum on cognition and its relationship to Schmahmann syndrome. This search covers the time of each database up to January 2023.

Initial search strategies were limited to the terms "cerebellar affective cognitive syndrome" and "management of cerebellar affective cognitive syndrome" due to limited research on these conditions. Articles were selected based on an exploration of the influence of psychopharmacotherapy in relation to Schmahmann syndrome.

Following the guidelines of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA), the search strategy is described in Figure 1. From the initial search, 54 articles were identified. After the removal of similar data, 32 articles were screened initially. Based on a review of titles and abstracts, 14 articles were excluded because they did not fit the objectives of this study. Thus, 18 articles were then continued to be taken, then eight articles were deleted because they were not supportive in writing. Therefore, 10 articles proceed to the feasibility evaluation, all of which are integrated into the final review. All 10 articles are described in the Table. 1 for further clarity.

Of the 10 articles selected for detailed analysis, the average article presented in the form of case report studies or clinical observations and Literature Review. Observational studies comparing the advantages of psychopharmacotherapy are difficult to find in this search.

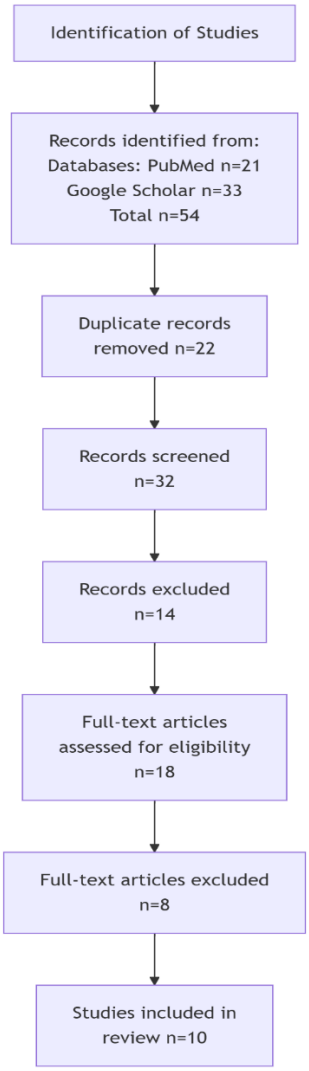

Fig. 2 Schmahmann syndrome, PRISMA Guidelines – Literature Review 2020, *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA)

Discussion

As discussed earlier, there is nothing ambiguous about the role of the cerebellum as its role in the motor system. As with the brain system, most of our knowledge of the cerebellum comes from the underlying symptoms of damage and abnormalities. There are severe movement abnormalities that can be produced by damage to the cerebellum, it is rare to notice the appearance of a pathology related to behavioral changes and disorders in the cerebellar. In the last two decades, the role of the cerebellum in regulating cognition and affectation has been used as a focus of study. Deficits in patients are noted in executive function, which consists of memory impairment (e.g., lack of arithmetic counts), changes in executive function, verbal fluency, problem-solving, multitasking, planning, scheduling and organizing activities (Wright et al., 2016; Schmahmann & Sherman, 1998).

Furthermore, deficits in visuospatial cognition including the disintegration between copying and conceptualizing the drawn image can also occur in this condition. Disorders in language such as agrammatism, mild anomia, and dysprosody. Finally, there is a deficit condition in emotions, which includes a decrease in affective or failure to inhibit impulses (often appearing such as inappropriate humorous comments, impulsive actions, and abusive

speech). Regressive and childish behavior can also occur in some patients, up to obsessive-compulsive traits in some of the population, and abnormal laughing or crying conditions (Schmahmann, 2007).

This current modality of Cerebellar Affective Cognitive Syndrome (CCAS) shows a good and comprehensive basis for knowing the functional condition of the cerebellum, and is able to illustrate precisely the mechanisms by which the cerebellum modulates cognition and affect. Errors in diagnosis can lead to ineffective treatment, and as clinicians it is necessary to recognize CCAS. The ability to accurately diagnose this syndrome can contribute to the improvement of the patient's condition, as well as education to the family regarding the appropriate diagnosis and treatment, including the selection of an appropriate rehabilitation program. The focus of rehabilitation programs is on executive function training, speech and language therapy, visuospatial function, and psychological function improvement. In addition, the need for management that targets the regulation of emotions and behavior, is able to improve the overall quality of life in individuals with cerebellar disorders (Schmahmann, 2007).

Pharmacological management can play an important role in the treatment of CCAS. Our patients recorded improvements related to emotional dysregulation as well as behavioral and cognitive function when administering Fluoxsetin and Aripiprazole. Further research is needed to establish evidence of effective pharmacological management for this syndrome. We also recognize that each case of CCAS is unique and different for each individual, due to underlying factors. In this case report, we have attached various case reports that describe various management regimens that have been proven to have benefits in improving symptoms according to different etiologies. Some of the pharmacological agents used in this case report include Aripiprazole, Quetiapine, and Valproic Acid.

By now we are very familiar with the role of Aripiprazole in patients with agitation conditions, as well as its role in mental disorders in children such as Autism Spectrum Disorder (ASD), Attention and Hyperactivity Disorder (ADHD), schizophrenia and obsessive-compulsive disorder. Our clinical consideration for administering Aripiprazole and Fluoxetine to this patient is based on their role in modulating glutamate in the cerebellar nucleus that regulates the excitatory impulses of these neurotransmitters. The most likely therapeutic mechanism of memantine action is through non-competitive antagonism at the N-methyl-D-aspartate (NMDA) receptor. By binding to NMDA receptors, memantine blocks pathological activation, excitation, and overstimulation by the amino acid glutamate, preventing damage to those receptors while maintaining their normal synaptic function and physiological activity. We speculate that this mechanism of action helps reduce aggressive behavior and improve cognitive function in our patients, resulting in favorable outcomes (Choi et al., 2017; Fukuyama et al., 2018).

Pharmacological Agents Used in Various Case Reports for CCAS Management

In a study conducted by Yap et al. in 2012 entitled "Treatment of Cerebellar Cognitive Affective Syndrome with Aripiprazole", an 18-year-old patient with grade I choroid plexus papilloma in the posterior fosa that extends through the Luschka foramen was given an intervention in the form of aripiprazole 4-7 mg accompanied by nonpharmacological therapy including rehabilitation. Patients experience symptoms of difficulties with balance and coordination, weight loss, academic difficulties, and personality changes that begin 2 years before presentation. Post-therapy findings showed improvements in orientation, memory, and executive function, as well as changes to very bright but limited affective effects visible within 24 hours of starting aripiprazole. The content and syntax of speech are improved but remain simple and descriptive.

Caplan and Daly in 2012 reported a case titled "Dextromethorphan/Quinidine for the Management of Cerebellar Cognitive Affective Syndrome: A Case Report" with the administration of dextromethorphan/quinidine in patients with inferior posterior cerebellar artery stroke. Although specific symptoms were not available, posttherapy findings showed rapid improvement in behavioral symptoms related to deficits in executive function, spatial organization, personality, and language.

Shyu et al. in 2011 in "Novel Use of Zolpidem in Cerebellar Mutism Syndrome" reported a case of patients with classical medullablastoma in the vermis area with small nodules in the left hemisphere area located far from the primary tumor. The patient experiences symptoms in the form of silence, irritable behavior, and ataxia. After the administration of zolpidem, there was an improvement in symptoms where the patient was able to focus more on the surrounding objects and was able to name 5 parts of the body. About 14 days later, the patient began to be able to speak with a single word, and continued to improve after 1 month of zolpidem treatment. There are still residual neurological symptoms in the form of mild ataxia gait.

Molinari et al. in 2019 in the study "Modafinil in the rehabilitation of a patient with post-surgical posterior fossa syndrome: a lesson to be learned" administered modafinil 7 months after the initial surgical action with an increase in the dosage scheme to 100 mg twice daily. Patients showed dominant negativism conditions in the form of flat mood, lack of interaction, and withdrawal, decreased motor activity, and apathy. The condition of not caring about the medical staff, not appearing aggressive, and excessive anxiety. The results of therapy showed a drastic improvement in the patient's mood, motivation, and social interaction. There seems to be an improvement in social conditions both with family and hospital staff. Patients begin to be able to eat and drink on their own after 2 weeks of treatment. There seems to be improved conditions in attention, visuospatial and cognitive. There are no side effects of mania or psychosis on the use of this modafinil.

Nishida et al. in 2019 in "Cerebellar Cognitive Affective Syndrome Improved by Donepezil" reported a case of a 60-year-old patient with right cerebellar hemorrhage with cerebroventricular rupture administered donepezil. Patients experience mild memory impairment and severe brain dysfunction including decreased mental capacity, attention, and executive function. Ten months after donepezil, there were improvements in executive function and memory work, as well as improvements in the Rivermead Behavioral Memory test.

Bhatia et al. in 2016 in "Cerebellar Cognitive Affective Syndrome: A Case Report" reported a 60-year-old patient with extensive atrophy of the cerebellar with depletion of the cerebellar peduncles who were given 20 mg of fluoxetine. The patient experienced a persistent and prolonged sad mood condition, dull affects, anhedonia, difficulty concentrating, feeling hopeless, expectation of death, sleep and eating disorders for approximately 2 months, accompanied by high fever, vomiting and diarrhea. Patients also complained of difficulty speaking and walking, loss of balance and needing help. Improvement was seen after observation within 4 weeks, but no specific symptoms were found.

Peljto et al. in 2014 in "Cerebellar Cognitive Affective Syndrome Presented as Severe Borderline Personality Disorder" reported a case of a 16-year-old patient with partial blockage of the vermis and thromb-encephalosynapsis who were given a combination of fluoxetine 40 mg, olanzapine 15 mg, clozapine 150 mg, clomipramine 100 mg, and lithium carbonate 900 mg. The patient showed instability in affective and self-injurious behavior, and was also diagnosed with Borderline Personality Disorder. The results showed a decrease in suicidal ideation, a more stable affective state, and improved control of self-harm impulses.

Rodriguez in 2017 in "Psychiatry Intervention in Cerebellar Cognitive Affective Disorder: Case Report" reported a 72-year-old patient with bilateral lesions of the cerebellum

who was given 50 mg of quetiapine. Patients show classic symptoms on CCAS even though specific symptoms are not found. The results of therapy showed significant improvements in mood and cognition.

Yildiz et al. in 2010 in "Cerebellar Mutism Syndrome and its Relation to Cerebellar Cognitive and Affective Function: Review of the Literature" mentioned amantadine as an alternative first line for the improvement of apathy symptoms in cerebellar mutism syndrome. However, there is no basis for mentioning that amantadine has been shown to provide improvements to CCAS during the literature search process. Information regarding patient age, specific symptoms, cerebellum disorders, and post-therapy findings were not available.

Cosme-Cruz et al. in "Cerebellar Cognitive Affective Syndrome: A Case Report and Literature Review of Available Treatments" reported a case of a 13-year-old patient with MRI who showed a dysgenesis of the rostrum area and a decrease in the volume of the corpus callosum and inferior agenesis of the vermis. Patients were given memantine 10 mg twice daily and quetiapine 300 mg in the morning and 400 mg in the evening. The patient's condition shows aggressive behavior and often acts of hurting others and difficulty speaking. After therapy, the patient becomes calmer and less aggressive, less impulsive, and able to be aware before taking an action. Patient verbalization also improved and was more expressive.

CONCLUSION

Cerebellar Cognitive Affective Syndrome (CCAS) is a challenging disorder to recognize, particularly in children and adults, as highlighted by this case report documenting successful treatment with a combination of fluoxetine and third-generation antipsychotics, specifically aripiprazole. The observed improvement in mood, cognition, and aggressiveness emphasizes the potential effectiveness of this therapeutic approach. However, there is a critical need for longitudinal studies involving larger patient populations to better understand the long-term effects and optimize treatment strategies. Early and accurate diagnosis remains essential for appropriate management, and further research should focus on validating and expanding therapeutic options for CCAS in diverse and extended cohorts.

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