Paranoia and slowed cognition

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Mr. K, age 45, is paranoid, combative, and agitated. Two weeks ago he sustained chemical abrasions at home. What could be causing his altered mental status?

CASE Behavioral changes

Mr. K, age 45, is brought to the emergency department (ED) by his wife for severe paranoia, combative behavior, confusion, and slowed cognition. Mr. K tells the ED staff that a chemical abrasion he sustained a few weeks earlier has spread to his penis, and insists that his penis is retracting into his body. He has tied a string around his penis to keep it from disappearing into his body. According to Mr. K's wife, he went to an urgent care clinic 2 weeks ago after he sustained chemical abrasions from exposure to cleaning solution at home. The provider at the urgent care clinic started Mr. K on an unknown dose of oral prednisone.

Mr. K's wife reports that her husband had a dysphoric episode approximately 6 months ago when his business was struggling but his mood improved without psychiatric care. Mr. K's medical history includes episodic sarcoidosis of the eyes, skin, and lungs. In the past these symptoms remitted after he received oral prednisone.

ED clinicians consider neurosarcoidosis and substance-induced delirium in the differential diagnosis (***Table, page 44***).[1] A CT scan of the head fails to show lesions suggestive of neurosarcoidosis. Chest radiography does not reveal lesions suggestive of lung sarcoids and Mr. K has no skin lesions.

Mr. K is admitted to the psychiatric inpatient unit for acute stabilization, where he remains aggressive and combative. He throws chairs at his peers and staff on the unit and is placed in physical restraints. He requires several doses of IM haloperidol, 5 mg, lorazepam, 2 mg, and diphenhydramine, 50 mg, for severe agitation. Mr. K is guarded, perseverative, and selectively mute. He avoids eye contact and has poor grooming. He has slow thought processing and displays concrete thought process. Prednisone is discontinued and olanzapine, titrated to 30 mg/d, and mirtazapine, titrated to 30 mg/d, are started for psychosis and depression.

Mr. K's mood and behavior eventually return to baseline but slowed cognition persists. He is discharged from our facility.

What is the most likely diagnosis for Mr. K?

a) major depressive disorder with psychotic features
b) delusional disorder
c) substance-induced psychotic disorder
d) substance-induced mood disorder
e) substance-induced delirium

The authors' observations

Cortisone was first used to treat rheumatoid arthritis in 1948 and corticosteroids

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How would you handle this case?

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Table

DSM-IV-TR criteria for substance-induced delirium

A. Disturbance of consciousness (ie, reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention
B. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia
C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day
D. There is evidence from the history, physical examination, or laboratory findings of either 1) or 2) 1) The symptoms in criteria A and B developed during substance intoxication 2) Medication use is etiologically related to the disturbance

Source: Reference 1

Clinical Point

Symptoms of steroid dementia include impaired verbal memory and spatial thinking but normal procedural memory

have been linked to multiple neuropsychiatric complications that have been broadly defined as steroid psychosis. This syndrome includes reversible behavioral manifestations such as hypomania, irritability, mood reactivity, anxiety, and insomnia in addition to more severe symptoms such as depression, mania, and psychosis.[2] Although mild cognitive deficits have been noted in patients taking corticosteroids, most published cases have focused on steroid-induced psychosis.

In 1984, Varney et al[3] noted a phenomenon they called "steroid dementia" in 6 patients treated with corticosteroids. On first evaluation, these patients presented with symptoms similar to early Alzheimer's dementia—impaired memory, attention, and concentration. Three patients initially were diagnosed first with Alzheimer's dementia until their symptoms spontaneously improved when steroids were reduced or discontinued. Although their presentation resembled Alzheimer's dementia, patients with steroid dementia had a specific cognitive presentation associated with corticosteroid use. Symptoms included impaired verbal memory and spatial thinking but normal procedural memory. These patients showed intact immediate recall but impaired delayed recall with difficulty tracking conversations and word finding. Overall, patients with steroid dementia showed a predominance of verbal declarative memory deficits out of proportion to other cognitive symptoms. These symptoms and recent corticosteroid exposure differentiated steroid dementia from other forms of dementia.

In a later article, Varney reviewed electroencephalography (EEG) and CT findings associated with steroid dementia, noting bilateral EEG abnormalities and acute cortical atrophy on CT.[4] Steroid dementia largely was reversible, resolving 3 to 11 months after corticosteroid discontinuation. Additionally, Varney noted that patients who had psychosis and dementia had more severe and longer-lasting dementia.

TREATMENT Progressive decline

Mr. K is college educated, has been married for 15 years, has 2 children, age 9 and 11, and owns a successful basketball coaching business. He has no history of substance abuse, legal issues, or violence. He reports a good childhood with normal developmental milestones and no history of trauma.

In the 6 months after his initial psychiatric admission, Mr. K sees various outpatient providers, who change his psychotropics multiple times. He also receives 4 courses of prednisone for ocular sarcoidosis. He is admitted twice to other psychiatric facilities. After he has paranoid interactions with colleagues and families

of the youth he coaches, his business fails.

After his third psychiatric inpatient hospitalization, Mr. K becomes severely paranoid, believing his wife is having an affair. He becomes physically abusive to his wife, who obtains a restraining order and leaves with their children. Mr. K barely leaves his house and stops grooming. A friend notes that Mr. K's home has become uninhabitable, and it goes into foreclosure. After Mr. K's neighbors report combative behavior and paranoia, police bring him in on an involuntary hold for a fourth psychiatric hospitalization (the second in our facility).

During this hospitalization—6 months after the initial ED presentation—the neurology team conducts a repeat medical workup. EEG shows generalized slowing. Head CT and MRI show diffuse cortical atrophy that was not seen in previous imaging. Mr. K has ocular lesions characteristic of ocular sarcoidosis. His mental status examination is similar to his first presentation except that the psychosis and thought disorganization are considerably worse. His cognitive functioning also shows significant decline. Cognitive screening reveals intact remote memory with impaired recent memory. His thinking is concrete and his verbal memory is markedly impaired. His Mini-Mental State Examination score is 27/30, indicating functional capacity that is better than his clinical presentation. Because of difficulty with concentration and verbal processing, Mr. K is unable to complete the Minnesota Multiphasic Personality Inventory despite substantial assistance. On most days he cannot recall recent conversations with his wife, staff, or physicians. He is taking no medications at this time.

Mr. K is restarted on olanzapine, titrated to 30 mg/d, to control his psychosis; this medication was effective during his last stay in our facility. Oral prednisone is discontinued and methotrexate, 10 mg/week, is initiated for ocular sarcoidosis. Based on recommendations from a case series report,[5] we start Mr. K on lithium, titrated to 600 mg twice a day, for steroid-induced mood symptoms, Mr. K's psychosis and mood improve dramatically once he reaches a therapeutic lithium level; however, his cognition remains slowed and he is unable to care for his basic needs.

The authors' observations

Steroid dementia may be the result of effects in the medial temporal lobe, specifically dorsolateral prefrontal cortex, which impairs working memory, and the parahippocampal gyrus.[6,7] The cognitive presentation of steroid dementia Varney et al[3] described has been replicated in healthy volunteers who received corticosteroids.[3] Patients with Cushing's syndrome also have been noted to have diminished hippocampal volume and similar cognitive deficits. Cognitive impairment experienced by patients treated with corticosteroids may be caused by neuronal death in the hippocampus and dorsolateral prefrontal cortex. The etiology of cell death is multifactorial and includes glutamate-mediated excitotoxicity, activation of proinflammatory pathways, inhibited utilization of glucose in the hippocampus, telomere shortening, and diminished cell repair by brain-derived neurotrophic factor. The net result is significant, widespread damage that in some cases is irreversible.[8]

Because of the severity of Mr. K's psychosis and personality change from baseline, his cognitive symptoms were largely overlooked during his first psychiatric hospitalization. The affective flattening, delayed verbal response, and markedly concrete thought process were considered within the spectrum of resolving psychosis. After further hospitalizations and abnormal results on cognitive testing, Mr. K's cognitive impairment was fully noted. His symptoms match those of previously documented cases of steroid dementia, including verbal deficits out of proportion to other impairment, acute cerebral atrophy on CT after corticosteroid treatment, and gradual improvement of symptoms when corticosteroids were discontinued.

continued

Clinical Point

Steroid-induced cognitive impairment may be due to cell death in the hippocampus and dorsolateral prefrontal cortex

Clinical Point

Lamotrigine and memantine may be cognitively protective for patients taking prednisone

Related Resources

- Sacks O, Shulman M. Steroid dementia: an overlooked diagnosis? Neurology. 2005;64(4):707-709.
- Cipriani G, Picchi L, Vedovello M, et al. Reversible dementia from corticosteroid therapy. Clinical Geriatrics. 2012;20(7):38-41.

Drug Brand Names

Diphenhydramine • Benadryl
Divalproex • Depakote
Haloperidol • Haldol
Lamotrigine • Lamictal
Lithium • Eskalith, Lithobid
Lorazepam • Ativan
Memantine • Namenda
Methotrexate • Rheumatrex, Trexall
Mirtazapine • Remeron
Olanzapine • Zyprexa
Prednisone • Deltasone, Meticorten, others

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

How would you manage Mr. K?

a) continue olanzapine and lithium and monitor him closely for changes in mood or cognition
b) continue olanzapine and lithium and add a cognitive enhancer, such as memantine
c) recommend transfer to a long-term care facility

Management recommendations

Educate patients taking steroids about possible side effects of mood changes, psychosis, and cognitive deficits. Close monitoring of patients on corticosteroids is paramount. If psychiatric or cognitive symptoms develop, gradually discontinue the corticosteroid and seek other treatments.

Randomized, placebo-controlled trials of lamotrigine and memantine have shown these medications are cognitively protective for patients taking prednisone.[9]

OUTCOME Long-term deficits

After a 33-day stay in our adult inpatient psychiatric facility, the county places Mr. K in a permanent conservatorship for severe grave disability. He is discharged to a long-term psychiatric care locked facility for ongoing management. Mr. K spends 20 months in the long-term care facility while his family remains hopeful for his recovery and return home. He is admitted to our facility for acute stabilization of psychotic symptoms after he is released from the locked facility. Although no imaging studies are conducted, he remains significantly forgetful. Additionally, his paranoia persists.

Mr. K is poorly compliant with his psychotropics, which include divalproex, 1,000 mg/d, and olanzapine, 30 mg/d. Although he is discharged home with his family, his functional capacity is less than expected and he requires continuous support. Insisting that Mr. K abstain from steroids after the first psychiatric hospitalization might have prevented this seemingly irreversible dementia.

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Bottom Line

Quick identification of steroid-induced mood or cognitive changes is vital for symptom recovery. The primary interventions are to reduce or discontinue corticosteroids, provide supportive care as needed, and monitor for further cognitive changes.