When Psychiatric Disease is Not What it Seems: History Taking Uncovers Steroid-Induced Delirium Following Intra-Articular Injections

CLARE NIMURA, BA; ZACHARY SHAW, MD; SARAH FREEMAN, MD

KEYWORDS: Delirium; hallucination; psychosis; corticosteroid injection; geriatric

BACKGROUND

Acute neuropsychiatric symptoms in older adults are often multifactorial and diagnostically challenging. This case describes an 87-year-old woman with mild cognitive impairment who developed episodic insomnia and hallucinations following intra-articular corticosteroid injections for osteoarthritic pain. While neuropsychiatric adverse effects are well recognized with systemic corticosteroids, they can also occur after local administration, particularly in older adults with baseline cognitive impairment.[1,2]

Corticosteroids are widely used anti-inflammatory agents delivered via systemic or local routes, including intra-articular injections for osteoarthritis. Although intra-articular therapy is generally considered safe, systemic absorption can occur, occasionally leading to adverse effects.[3,4] Neuropsychiatric manifestations range from mood changes and sleep disturbance to delirium with hallucinations and delusions, with heightened risk in older adults due to pharmacokinetic variability, age-related blood-brain barrier changes, and polypharmacy.[5,6] Symptoms may emerge within days of exposure, sometimes after a single injection. Acute delirium and hallucinations following intra-articular corticosteroid injections have been reported in older adults, though the incidence of these neuropsychiatric complications is uncertain and underrecognized.[2,7,8]

When evaluating acute psychotic symptoms, it is important to distinguish delirium from psychotic disorder. As defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), criteria for substance/medication-induced psychotic disorder include prominent hallucinations or delusions developing during or shortly after medication exposure, symptoms not better explained by a primary psychotic disorder, and disturbances that do not occur exclusively during delirium. Functional impairment or distress is also required, and persistence of symptoms beyond typical medication half-life may suggest an independent psychotic disorder.[9]

This case highlights the importance of considering intra-articular corticosteroid exposure as a potential trigger for acute delirium with prominent hallucinations and delusions in older adults and underscores the importance of a complete history.

CASE PRESENTATION

An 87-year-old woman with mild cognitive impairment, a prior diagnosis of a recurrent unspecified delusional disorder, hypothyroidism, and osteoarthritis presented from her assisted living facility with acute insomnia and auditory and visual hallucinations. Her medication history included levothyroxine, atorvastatin, vitamin D3, and famotidine. Notably, she had received two intra-articular corticosteroid knee injections one day prior to symptom onset. Her daughter reported that she was found wandering the halls of her assisted living facility overnight, conversing aloud and responding to apparent internal stimuli; she had not slept for approximately 36 hours by the time she presented to the hospital. During this period, she also made several phone calls to her daughter with confabulation regarding recent events. Prior to presentation, she was in her usual state of health and performing all activities of daily living independently.

On admission, she was afebrile and hemodynamically stable. She was alert and oriented to person and time but disoriented to place and recent events; there was no evidence of auditory or visual hallucinations at the time of initial evaluation. Her thought process was linear and goal-directed, without delusions. Physical examination revealed no neurological deficits. A complete blood count, metabolic panel, thyroid function tests, and urinalysis were unremarkable, and a CT scan of the head was normal. Urine toxicology screening and ammonia level had been negative on prior similar admissions but were not obtained during this hospitalization.

Further history from the patient's daughter revealed that over the preceding year, she had experienced similar episodes every few months, characterized by acute, transient auditory and visual hallucinations and delusional beliefs that others were overly infatuated with her, with spontaneous resolution of symptoms and complete return to baseline mental status within 48 to 72 hours. Several episodes were

empirically treated with antibiotics for presumed urinary tract infection, though no consistent infectious etiology was identified. She underwent extensive outpatient evaluation by geriatric psychiatry, neurology, and neuropsychology, including comprehensive laboratory testing, electroencephalography, brain MRI, and vision screening, all of which were unrevealing. She was ultimately diagnosed with mild cognitive impairment with suspected unspecified episodic delusional/psychotic disorder and started on quetiapine.

Review of records and additional history revealed a consistent temporal relationship between psychotic episodes and intra-articular corticosteroid injections. Each prior episode had occurred within days of an injection, and associated neuropsychiatric symptoms consistently resolved within several days with or without medical intervention. Given this temporal relationship, her advanced age, baseline cognitive impairment, and the recurrent, transient nature of her symptoms, her presentation most likely represented delirium with prominent hallucinations and delusions, rather than a primary late onset delusional disorder. She did not meet DSM-5 criteria for a substance/medication-induced psychotic disorder, as her psychotic symptoms occurred exclusively in the context of delirium rather than as an isolated or persistent psychotic syndrome. The inpatient psychiatry consultation service concurred with this assessment. By the morning after admission, her mental status had returned to baseline without intervention; she was alert and oriented to person, place, and time, with intact recall of events during hospitalization.

At discharge, recommendations were made to the outpatient geriatric psychiatry team to consider dose reduction or discontinuation of standing antipsychotic therapy, and to her outpatient orthopedic provider to limit future intra-articular corticosteroid injections by reducing either injection frequency or the number of joints treated concurrently.

DISCUSSION

This case illustrates the value of thorough medication history. The differential diagnosis for acute delirium with hallucinations and delusions in older adults is broad and includes metabolic or endocrine derangements, infection-related delirium, primary CNS infections, substance intoxication or withdrawal, dementia-related neuropsychiatric symptoms, primary psychiatric disorders, medication-induced psychotic disorder, and medication-induced delirium.[1,2] In this patient, a comprehensive metabolic, endocrine, and infectious evaluation was unrevealing, excluding significant metabolic or infectious etiology. A urine toxicology screen would have strengthened the assessment for substance involvement, although urine toxicology screens obtained in earlier presentations were negative, lowering suspicion for substance involvement.

The recurrent, transient nature of her symptoms initially raised concern for a late-onset primary psychotic disorder; however, detailed history revealed a consistent temporal relationship with intra-articular corticosteroid injections. Neuropsychiatric complications of corticosteroids include insomnia, mood changes, mania, and delirium with hallucinations and delusions, occurring in up to 18% of patients receiving systemic corticosteroids.[10-12] Intra-articular injections can also result in clinically significant systemic absorption,[3,4] and several case reports describe steroid-induced delirium or hallucinations following local injections in older adults.[2,7,8] Pharmacokinetic studies demonstrate that systemic absorption after intra-articular corticosteroid injection can be both rapid and prolonged. Methylprednisolone acetate, for example, reaches peak plasma levels at approximately four hours post-injection, with detectable levels persisting for at least 96 hours,[13] whereas triamcinolone acetonide extended-release formulations produce lower peak concentrations but sustained exposure for up to 20 weeks.[14] Risk factors for neuropsychiatric complications include high corticosteroid dose, number of joints injected, solubility of the preparation, advanced age, baseline cognitive impairment, and polypharmacy.[1,15] This phenomenon remains underreported, leading to likely misattribution of symptoms to primary psychiatric illness, minor metabolic derangements, or asymptomatic bacteriuria.

Management of delirium begins with recognition and discontinuation of possible offending agents. While supportive measures are first line treatment, short-term antipsychotic therapy may be considered if symptoms are severe or pose a safety risk to the patient or others, but should be used cautiously in older adults due to potential adverse effects.[11,16] In this case, careful history and interdisciplinary collaboration prevented misdiagnosis and unnecessary chronic antipsychotic therapy and antibiotic therapy. Recognition of the potential for intra-articular corticosteroid injections to precipitate delirium with hallucinations and delusions is increasingly important as the use of these injections increases among older adults.[17,18]

CONCLUSION

Systemic absorption of intra-articular corticosteroids can precipitate acute delirium with prominent hallucinations and delusions in older adults, particularly those with cognitive impairment or polypharmacy. Failure to recognize these episodes may result in inappropriate psychiatric diagnoses and unnecessary antipsychotic therapy. This case underscores the importance of considering all forms of corticosteroid exposure as potential triggers for acute delirium and highlights the critical role of thorough history and careful clinical evaluation in identifying modifiable medication-related etiologies.

References

1. Manzo C, Serra-Mestres J, Castagna A, Isetta M. Behavioral, Psychiatric, and Cognitive Adverse Events in Older Persons Treated with Glucocorticoids. Medicines. 2018; 5(3):82.
2. Samala RV, Ciocon JO. Steroid-induced hallucination following intra-articular administration: a case report and brief review. J Am Med Dir Assoc. 2011;12(6):451–453.
3. Bilsborough Smith C, Baker D, Botchu R, et al. Corticosteroid injections for non-spinal musculoskeletal conditions: consideration of local and systemic adverse drug reactions. New Zealand Journal of Physiotherapy. 2023;51(1).
4. Stout A, Friedly J, Standaert CJ. Systemic Absorption and Side Effects of Locally Injected Glucocorticoids. PM&R. 2019; 11(4):409-419.
5. Dubovsky AN, Arvikar S, Stern TA, Axelrod L. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics. 2012;53(2):103-115.
6. Parasher A, Bez J. Steroid-induced psychiatric adverse effects: an overview of risk factors, clinical features and management. International Journal of Research in Medical Sciences. 2020; 8(7):2508–2513.
7. Lally L, McCarthy G, Meehan K. Hyperactive delirium following administration of intra-articular corticosteroid. BMJ Case Rep. 2017; bcr2016217483.
8. Robinson DE, Harrison-Hansley E, Spencer RF. Steroid psychosis after an intra-articular injection. Ann Rheum Dis. 2000; 59(11):927.
9. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders* (5th ed.); 2013.
10. Ross DA, Cetas JS. Steroid psychosis: a review for neurosurgeons. J Neurooncol. 2012;109(3):439-447.
11. Huynh G, Reinert JP. Pharmacological Management of Steroid-Induced Psychosis: A Review of Patient Cases. J Pharm Technol. 2021;37(2):120-126.
12. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. Mayo Clin Proc. 2006;81(10):1361-1367.
13. Steer JH, Ma DT, Dusci L, Garas G, Pedersen KE, Joyce DA. Altered leucocyte trafficking and suppressed tumour necrosis factor alpha release from peripheral blood monocytes after intra-articular glucocorticoid treatment. *Ann Rheum Dis*. 1998; 57(12):732-737.
14. Kraus VB, Conaghan PG, Aazami HA, et al. Synovial and systemic pharmacokinetics (PK) of triamcinolone acetonide (TA) following intra-articular (IA) injection of an extended-release microsphere-based formulation (FX006) or standard crystalline suspension in patients with knee osteoarthritis (OA). *Osteoarthritis Cartilage*. 2018;26(1):34-42.
15. Knox EG, Aburto MR, Clarke G, Cryan JF, O'Driscoll CM. The blood-brain barrier in aging and neurodegeneration. Mol Psychiatry. 2022;27(6):2659-2673.
16. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in Older Persons: Advances in Diagnosis and Treatment. JAMA. 2017; 318(12):1161-1174.
17. Kamel SI, Rosas HG, Gorbachova T. Local and Systemic Side Effects of Corticosteroid Injections for Musculoskeletal Indications. AJR Am J Roentgenol. 2024;222(3):e2330458.
18. Koenig KM, Ong KL, Lau EC, et al. The Use of Hyaluronic Acid and Corticosteroid Injections Among Medicare Patients With Knee Osteoarthritis. J Arthroplasty. 2016;31(2):351-355.

Authors

Clare Nimura, BA, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Zachary Shaw, MD, The Warren Alpert Medical School of Brown University, Division of General Internal Medicine, Providence, Rhode Island.

Sarah Freeman, MD, Division of General Internal Medicine, Rhode Island Hospital, Providence, Rhode Island.

Disclosures

This research did not receive external funding.

Ethical Approvals: The patient provided informed consent at the time of hospital admission for the use of de-identified case information for educational and research purposes. No identifying information is included in this report.

Correspondence

Clare Nimura, BA
222 Richmond St.
Providence, RI 02903
Clare_nimura@brown.edu