

Serotonin syndrome or NMS? Clues to diagnosis

Ryan Kimmel, MD

Disease course, lab findings, vital signs, and a physical exam can help distinguish serotonin syndrome and NMS

Symptoms of serotonin syndrome and neuroleptic malignant syndrome (NMS) are similar—mental status changes, autonomic dysfunction, and neuromuscular abnormalities—making the syndromes difficult to differentiate. However, therapeutic interventions and the mortality rates associated with these syndromes are widely divergent.

Because many medication regimens for treatment-resistant mood disorders modulate both serotonin and dopamine systems, psychiatrists must be prepared at any time to recognize either syndrome and quickly initiate appropriate treatment. For this, we rely on disease course, lab findings and vital signs, and the physical exam.

Clinical course

Serotonin syndrome symptoms can develop within minutes to hours after the administration of an agent that increases central serotonergic tone, such as a selective serotonin reuptake inhibitor. After rapid onset, serotonin syndrome symptoms may improve or even resolve within <24 hours. NMS, on the other hand, can develop days to weeks after the administration of a dopamine antagonist—such as an antipsychotic—and may take 3 to 14 days to resolve.

Labs and vital signs

The triad of fever, leukocytosis, and increased creatine kinase (CK) are associated with NMS. Hyperthermia is present in at least 90% of cases,¹ although, some definitions of NMS list fever as a sine qua non. Leukocytosis and elevated hepatic transaminases are reported in at least 75% of NMS cases and increased CK in >90% of cases.^{1,2} These signs may be present in serotonin syndrome but are less common.

Although the pathophysiology of NMS is unclear and literature is limited, some case series report iron deficiency in >95% of cases.³ If this finding were replicated on a larger scale, iron deficiency might be a sensitive, rapid, and inexpensive test to help diagnose atypical NMS presentations. Larger studies are needed before clinicians can rely on this laboratory finding to diagnose NMS.

Physical exam findings

Neuromuscular manifestations also can help distinguish serotonin syndrome from NMS. Physicians often and rightly associate muscle rigidity with NMS. This finding also is present in approximately one-half of serotonin syndrome cases, however. Hyperreflexia and myoclonus, if present, may suggest serotonin syndrome.

References

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2. Rosebush P, Stewart T. A prospective analysis of 24 episodes of neuroleptic malignant syndrome. *Am J Psychiatry.* 1989;146:717-725.
3. Rosebush P, Mazurek M. Serum iron and neuroleptic malignant syndrome. *Lancet.* 1991;338(8760):149-151.

Dr. Kimmel is an acting assistant professor, department of psychiatry, University of Washington, Seattle.

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