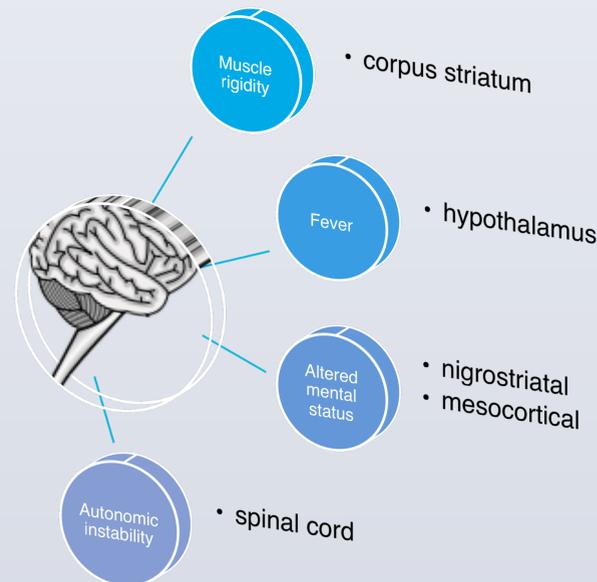




Introduction

- We present a case of an adolescent male with inherited developmental delay and a third ventricle colloid cyst who, following treatment with a first generation antipsychotic, developed a form of neuroleptic malignant syndrome (NMS) characterized by muscle rigidity but not hyperthermia.
- Our patient’s case highlights the importance of having a low threshold for making the NMS diagnosis in children, particularly in those with underlying brain abnormalities, who may be at *a priori* higher risk. It also illustrates that while NMS is typically thought to include both rigidity and fever, the pediatric syndrome may present with only one of these symptoms.



Case Presentation

- “M” was a 17 year old Mexican male who moved to the United States with his parents prior to age ten. In the summer of 2014, he presented to the psychiatric ER of a large county hospital with a several week history of increasing aggression towards his father at home.
- He had recently been psychiatrically hospitalized at an outside facility (his only prior inpatient stay), and had been discharged just one week previously.
- His parents, who were somewhat poor historians, related that M had been given “a shot” at the outside hospital. This calmed him down for “a few days,” but his aggression soon returned and he was subsequently brought to our ER.
- M’s parents said he had no history of mental illness prior to the recent aggression. They did, however, describe him as intellectually “a little slow,” and on clinical exam he was notably microcephalic.
- A 2007 operative report showed that M had been treated surgically for bilateral cryptorchidism. The surgeon noted in passing that M had “some genetic syndrome with developmental delay.”
- Furthermore, a 2007 MRI brain showed a third ventricle colloid cyst, and later records showed that M had an EEG in 2011 following two seizure-like episodes.
- On clinical exam the morning after he was brought in, M was “extremely agitated, punching windows and kicking at staff.” At the time he was tachycardic, with a heart rate of 130 bpm.
- M received a 3mg intramuscular dose of haloperidol, and later that day he was given a second dose.

- The following morning, M was tremulous, diaphoretic, rigid, and confused, although he was not febrile. He was subsequently transferred to the hospital’s medical ER.
- Lab work showed a mild leukocytosis consistent with NMS, though the lack of hyperthermia led an ER physician to conclude that M did not meet “NMS criteria.”
- When CK returned that evening, however, it was very elevated at 19394. Elevated CK is found in ~90% of children and adolescents with NMS.
- M was transferred to another facility for inpatient stabilization.

Discussion

- NMS is a rare complication of psychotropic treatment that is potentially fatal. It has four cardinal features: muscle rigidity, hyperthermia, altered mental status, and autonomic instability.
- NMS is classically, and most often, seen in patients treated with first generation antipsychotics, but it has also been reported in association with second generation antipsychotics, antidepressants, and stimulants.
- Although the pathogenesis of NMS has not been clearly elucidated, its proximal cause is probably sudden and significant blockade of central dopamine receptors. Medications implicated in NMS all have an effect, either direct or indirect, on dopaminergic tone.
- At the level of the corpus striatum, dopaminergic blockade can lead to muscle rigidity. At the level of the hypothalamus, it can lead to fever. At the nigrostriatal and mesocortical levels, it can lead to altered mental status, and at the spinal cord it can lead to autonomic instability.¹
- Underlying brain abnormalities, either congenital or acquired, are thought to raise NMS risk, perhaps by making the central nervous system less able to tolerate shifts in dopaminergic tone.
- Although NMS was first described in the 1960s, no consensus has been reached regarding its formal definition. In 1994, DSM-IV TR included “research criteria” for NMS, according to which both fever and rigidity were necessary to make the diagnosis. This requirement was criticized on the grounds that it may not have been inclusive enough, particularly in children and adolescents.
- Fever and rigidity, considered independently, are common but not universal in NMS. A 1999 review of published NMS cases (n = 77) found that fever was described in 73% and rigidity in 75%.²
- A 2009 review of NMS in children treated with second-generation antipsychotics (n = 23) found that *both* fever and rigidity were present in only 48% (n = 11) of cases.³
- Thus, depending on which central dopaminergic pathways are affected, NMS may present with different combinations of its four cardinal features.
- In recognition of this, DSM-5 defines NMS less strictly, in qualitative terms.

Conclusions

- Any combination of the four cardinal features of NMS (rigidity, hyperthermia, altered mental status, and autonomic instability) in a child or adolescent treated with a medication known to affect dopaminergic tone should raise suspicion for the diagnosis.
- Serum CK, which is elevated in upwards of 90% of children and adolescents with NMS, may be a useful confirmatory test.
- NMS may be a particularly important consideration in children who have underlying brain abnormalities: congenital, acquired, or both.

References

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