

Case Conference

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2010/8/10

Discussion

Outline

- Differential diagnosis of hyperthermia
- Drug-induced movement disorders
- Neuroleptic malignant syndrome

Differential diagnosis of hyperthermia

- Hyperthermia: BT > 37.5°C
- Fever: induced by cytokine activation during inflammation

Differential diagnosis of hyperthermia

External	Environmental exposure
Infection-related	Sepsis, encephalitis, brain abscess, meningitis, typhoid fever, tetanus
Malignancy-related	Tumor fever, pheochromocytoma
CNS-related	Hypothalamic stroke, status epilepticus, cerebral hemorrhage
Drug-related	Malignant hyperthermia, neuroleptic malignant syndrome, serotonin syndrome, alcohol and sedative-hypnotic withdrawal, salicylate and lithium toxicity, sympathomimetic toxicity, anticholinergic toxicity, dystonic reactions....
endocrine	Thyroid storm
Other	catatonia

Modified from *Uptodate*

Drug-induced movement disorders

- Dystonic movements
- Akathisia
- Tardive dyskinesia
- Neuroleptic malignant syndrome
- Rabbit syndrome
- Serotonin syndrome

Dystonic movements

- Dystonic: 張力障礙
- Intermittent or sustained **muscle spasm**
 - Head: oculogyric muscle → forced upward gaze
 - Neck → torticollis
 - Tongue → dysarthria
 - Paraspinal muscle → opisthotonus (角弓反張)
- Most common in young males
- Typically occur **soon** after beginning or increasing the dose of FGA

Akathisia

- 靜坐不能
- Antipsychotic and antidepressant medication
- Subjective:
 - Muscle tension
 - Difficulty finding a comfortable body position
 - Inability to stop moving
- Objective:
 - Rocking from foot to foot while standing
 - Frequently crossing and uncrossing the legs when seated
 - pacing
- Sleep disturbance
- May provoke violent action

Tardive dyskinesia

- many months or years after taking antipsychotic drugs
- No matter with or without continued medication use
- Varied movement
 - Face, mouth, lips
 - Tongue thrusting, chewing movements, lip smacking, eye blinking
 - Choreoathetoid movement: writhing finger motions
 - Truncal dyskinesia, respiratory dyskinesia

Rabbit syndrome

- Uncommon
- Rapid chewing movement similar to those made by rabbits
- The tongue is spared.

Serotonin syndrome

- Combination of ≥ 2 serotonergic medications by different mechanisms
- Restlessness
- **Myoclonus**
- Hyperreflexia
- Diaphoresis
- Shivering or tremor
- autonomic changes: **fever, mental status changes**

Serotonin syndrome

- Clinical triad
 - Mental-status changes
 - Autonomic hyperactivity: e.g. fever
 - Neuromuscular abnormalities: myoclonus

Neuroleptic malignant syndrome

- Potentially fatal complication of antipsychotic medication
 - 10%!
- The most severe end of a spectrum:
 - Antipsychotic-induced parkinsonism
 - Extrapyrimal syndrome with fever
 - Fulminant NMS

Neuroleptic malignant syndrome

- Clinical presentation
 - Muscle rigidity
 - Elevated temperature ($\geq 38^{\circ}\text{C}$)
 - ≥ 2 of the following symptoms:
 - Diaphoresis, tachycardia, elevated or labile BP
 - Dysphagia, incontinence
 - Tremor
 - Changes in the level of consciousness
 - Mutism
 - Leukocytosis
 - Laboratory evidence of muscle injury
 - Liver enzyme elevation

NMS: 4 clinical syndromes

- **Hyperthermia**
- Altered mental status
 - Mutism, delirium, coma...
- Skeletal muscle rigidity: lead-pipe rigidity
- Autonomic dysfunction:
 - Tachycardia, hyper-or hypotension, diaphoresis

Neuroleptic malignant syndrome

- Pathophysiology
 - Hypodopaminergic state
 - Fluctuation in dopamine binding
 - Different level of dopamine dysregulation:
 - Corpus striatum \rightarrow muscle contraction and rigidity \rightarrow heat generation \rightarrow conscious disturbance
 - Hypothalamus \rightarrow impaired heat regulation
 - Spinal cord \rightarrow autonomic dysfunction
 - Mesocortical dopamine tract \rightarrow fluctuation in mental status
 - Familial clusters of NMS: A1 allele of D_2 receptor

Neuroleptic malignant syndrome

- Provocative factors
 - Concurrent medical and neuropsychiatric issues
 - Dehydration, Psychomotor agitation
 - Psychiatric diagnosis and history
 - Mood disorders, Preexisting catatonia, **History of NMS**
 - Medications
 - **Acute parenteral antipsychotics**
 - High potency FGAs (e.g. haloperidol)
 - Concurrent lithium treatment
 - High dose of an antipsychotic
 - Dosing increases or **intermittent noncompliance**
 - Demographics
 - **Male gender**, Younger age

Treatment of NMS

- Early identification
 - Antipsychotics should be immediately D/C
- Supportive interventions
 - IV hydration
 - BT control
 - Ventilator support
 - dialysis
- Dopamine agonist, muscle relaxants, electroconvulsive therapy (ECT)
- Antipsychotics: 1-2 weeks after symptoms resolve
 - Consider alternative agent (e.g. SGA) from low dose

Treatment of NMS

Intervention	Dosing
Amantadine	200-400 mg/d PO
Bromocriptine	2.5 mg BID or TID PO or 45 mg/d
Levodopa/carbidopa	50-100 mg/d cIF
ECT	
Dantrolene	1 mg/kg/d IV for 8 days, then PO for 7 days
BZD	1-2 mg IM as test dose; if effective, switch to PO
Supportive measures	IV hydration, cooling blankets, ice packs....

Reference

- Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. LWW; 2009
- Uptodate