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Hyperthermia after Metrizamide Myelography

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Metrizamide is a water-soluble, nonionic, iodinated contrast agent that has gained general acceptance for myelography. We present a patient who developed severe hyperthermia several hours after and apparently related to metrizamide myelography. To our knowledge, no similar complication has been described before [1–7].

Case Report

A 68-year-old man with carcinoma of the prostate was seen with increasing neck pain, right shoulder paresthesias, and a pathologic compression fracture of the C5 vertebral body. After a C1–C2 puncture, 8 ml of metrizamide in a concentration of 300 mg I/ml was injected intrathecally in fractions under fluoroscopic control. The patient moved excessively during the procedure because of his severe neck pain. Fluoroscopic screening showed that a large amount of contrast material spilled intracranially along the clivus up to the suprasellar cisterns. The myelogram demonstrated an anterior extradural mass at the C5 level, with moderate obstruction to the caudad flow of the metrizamide. The patient was then stood nearly upright on the tilt table for 3–5 min, after which no metrizamide could be seen fluoroscopically in the intracranial or cervical regions. At the conclusion of the procedure, the patient complained only of a mild headache. Prophylactic oral anticonvulsant therapy with phenytoin (Dilantin) was begun because of the relatively large intracranial spill of metrizamide. The patient was instructed to remain still in bed with his head raised 20°–30° for the next 8 hr.

About 5 hr after the procedure, the patient developed a temperature of 40°C. Eleven hr after the myelogram, it rose to 41°C and rapidly peaked at 42.5°C. During this severe hyperthermic episode, the patient became comatose, had a respiratory arrest, and required intubation. Cooling measures were begun immediately, and the patient's temperature quickly came down to 40°C and was normal 24 hr after the myelogram. He awoke without detectable neurologic abnormality when his temperature returned to normal. An apparently traumatic lumbar puncture 8 hr postmyelography showed bloody cerebrospinal fluid (CSF) with an appropriate red cell–white cell ratio, normal glucose concentration, and a protein concentration of 188 mg/dl. Cultures were negative from CSF, blood, urine, sputum, and a chronic leg sinus tract secondary to old osteomyelitis.

Radiation therapy to the cervical spine was started, and the patient was discharged from the hospital about 1 week after admission without any further complaints or complications.

Discussion

Hyperthermia may be secondary to excess heat production, impairment of the heat dissipating mechanism, or loss of central nervous system control of body temperature. Excessive production of heat can be seen with the use of certain drugs that increase body activity (amphetamines, hallucinogens), strenuous exercise, infection, hyperthyroidism, and malignant hyperthermia [8–12]. In malignant hyperthermia, various anesthetic agents are thought to activate an underlying metabolic defect, which results in violent muscle contractions. Large amounts of heat are produced, raising the body temperature at a rate as high as 1°C every 5 min [13]. Impairment of the heat-dissipating mechanism occurs with sweat-gland dysfunction, drugs such as anticholinergic agents that inhibit sweating, hot and/or humid environment, obesity, cardiovascular disease, and extremes of age [8–13]. Loss of central nervous system control of body temperature usually results from hypothalamic lesions but occasionally from an abnormality of the brainstem or spinal cord [14].

Laboratory animal experiments point to the complex and poorly understood hypothalamus as the principal thermostat of the body. Cells involved with temperature control in the anterior hypothalamus have primarily a receptor function. They receive information from afferent neural pathways, bacterial pyrogens, and other substances in blood, as well as blood temperature itself [15]. In the posterior hypothalamus cells receive and integrate the thermal information from the anterior hypothalamus and then relay stimuli to the peripheral nerves that initiate shivering, sweating, vasoconstriction, and other heat-regulatory maneuvers [16]. Since warm receptor cells are more numerous than cold receptor cells in the anterior hypothalamus, a destructive lesion involving the entire anterior hypothalamus in laboratory animals will result in hyperthermia [15]. A selective lesion of the medial anterior hypothalamus, where most cold receptor cells are located, produces hypothermia [14]. A lesion of the posterior hypothalamus, where signals for both heat production and dissipation originate, usually produces a poikilothermic animal, that is, the body temperature fluctuates with the ambient temperature [17].

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In humans, lesions of the hypothalamus may also lead to thermoregulatory disorders. Postoperative hyperthermia that clears in a few weeks is not an uncommon problem after surgery around the third ventricle [18]. Tumors, especially craniopharyngiomas [19, 20], vascular accidents [21], trauma [22], agenesis of the corpus callosum [23], Wernicke disease [24], and infection [25] have all been reported to cause persistent thermal regulatory disorders [26–29]. Phenothiazine drugs, apparently acting on the posterior hypothalamus, can render patients poikilothermic, and hyperthermic deaths during heat waves have been reported in patients taking phenothiazine medications [30–33].

The most likely cause of hyperthermia in our patient was interference with the thermoregulatory function of the hypothalamus. Its occurrence 5 hr after spinal intrathecal injection of metrizamide, when the intracranial subarachnoid concentration of metrizamide could be expected to be relatively high [34], strongly incriminates metrizamide diffusion into the hypothalamus as the cause of the hyperthermia. Since injection of various substances into the hypothalamus in experimental animals can cause disturbances in temperature regulation [15–17, 35, 36], and brain penetration from CSF by metrizamide has been demonstrated [34], one can postulate similar penetration of metrizamide from the suprasellar cisterns into the hypothalamus in our patient. The metrizamide then most likely caused the described hyperthermia by acting as a depressant or inhibitor on the warm receptor cells of the anterior hypothalamus. Transependymal absorption from the third ventricle into the hypothalamus is less likely because only small amounts of metrizamide normally flow into the third ventricle after myelography and also because the cerebral ventricles with their ependymal lining appear to tolerate metrizamide better than does the brain surface [37, 38].

The differential diagnosis in our patient included aseptic meningitis and an infectious source of the fever. An infectious source of the fever was believed to be unlikely because of negative blood, urine, CSF, sputum, and leg sinus tract cultures. Fever of an infectious origin usually does not rise to 42.5°C unless it involves the central nervous system, that is, infectious meningitis, and even then such an elevation would be very unusual. Other possible causes of hyperthermia, such as drugs (other than metrizamide), which may increase heat production or cause interference with heat dissipation, were excluded clinically.

Aseptic meningitis can be seen after metrizamide myelography as well as after injection of other myelographic and foreign material into the CSF. Its incidence is reported to be as high as one in 1000 metrizamide myelographies [39]. Clinically, aseptic meningitis is manifested initially by headache and nausea or vomiting followed by fever and signs of meningeal irritation. One-third of the patients with aseptic meningitis after metrizamide myelography develop mental changes such as various dysphasias, lethargy, and disorientation, but not coma [39]. CSF findings are characterized by marked leukocytosis, initially polymorphonuclear but in 5–7 days mononuclear; mild elevation of protein; lowering of glucose; and, most importantly, negative stain and culture for bacteria. The symptoms usually begin 8–16 hr after the myelogram and clear 1–5 days later [40]. There is no specific treatment for aseptic meningitis. The rapid appearance of symptoms, a temperature of 42.5°C, coma, and no definite CSF leukocytosis in our patient make aseptic meningitis a very unlikely diagnosis.

Many review articles indicate that most complications and side effects of metrizamide are mild and self-limited [1–7]. Our case of severe hyperthermia after metrizamide myelography was life-threatening and had to be correctly recognized and treated as a dire emergency.

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REFERENCES

1. Baker RA, Hillman BJ, McLennan JE, Strand RE, Kaufman SM. Sequelae of metrizamide myelography in 200 examinations. *AJR* **1978**;130:499–502
2. Bertoni JM, Schwartzman RJ, Van Horn G, Partin J. Asterixis and encephalopathy following metrizamide myelography; investigations into possible mechanisms and review of the literature. *Ann Neurol* **1980**;9:366–370
3. Hauge O, Falkenberg H. Neuropsychologic reactions and other side effects after metrizamide myelography. *AJNR* **1978**;3:229–232
4. Oftedal S, Kayed K. Epileptic effects of water soluble contrast media. *Acta Radiol [Suppl]* (Stockh) **1973**;335:45–56
5. Skalpe IO. Adverse effects of water-soluble contrast media in myelography, cisternography and ventriculography. A review with special reference to metrizamide. *Acta Radiol [Suppl]* (Stockh) **1977**;355:359–370
6. Sortland O, Lundervold A, Nesbakken R. Mental confusion and epilepsy following cervical myelography with metrizamide. A report of a case. *Acta Radiol [Suppl]* (Stockh) **1977**;355:403–406
7. Gelmers HJ. Adverse side effects of metrizamide in myelography. *Neuroradiology* **1979**;18:119–123
8. Austin MG, Berry JW. Observations on one hundred cases of heatstroke. *JAMA* **1970**;161:1525–1529
9. Clowes GHA, O'Donnell TF. Heat stroke. *N Engl J Med* **1974**;291:564–566
10. Knochel JP. Environmental heat illness. *Arch Intern Med* **1974**;133:841–864
11. Stine RJ. Heat illness. *Ann Emerg Med* **1979**;8:154–160
12. Stitt JT. Neurophysiology of fever. *Fed Proc* **1981**;40:2835–2842
13. Nelson TE, Flewellen EH. The malignant hyperthermia syndrome. *N Engl J Med* **1983**;309:416–418
14. Hardy ID. Posterior hypothalamus and the regulation of body temperature. *Fed Proc* **1973**;32:1564–1571
15. Plum FR, Van Uitert R. Nonendocrine diseases and disorders of the hypothalamus. In: Reichlin S, Baldessarini RJ, Martin JB, eds. *The hypothalamus*. New York: Raven, **1978**:429–440
16. Meyers RD. Temperature regulation. In: Haymaker W, Anderson E, Navta WJH, eds. *The hypothalamus*. Springfield, IL: Thomas, **1969**:506–520
17. Branch EF, Burger PC, Brewer DL. Hypothermia in a case of thalamic infarction and sarcoidosis. *Arch Neurol* **1971**;25:245–255

18. Cushing H. *Papers relating to the pituitary body, hypothalamus, and parasympathetic nervous system.* Springfield, IL: Thomas, **1932**:36–37
19. Lipton JM, Rosenstein J, Sklar FH. Thermoregulatory disorders after removal of a craniopharyngioma from the third cerebral ventricle. *Brain Res Bull* **1981**;7:369–373
20. Gordy PD, Peet MM, Kahn EA. The surgery of craniopharyngioma. *J Neurosurg* **1949**;6:503–517
21. Kahn EA, Crosby EC, DeJonge BR. Tumors of the hypothalamic region. In: Kahn EA, Crosby EC, Schneider RC, Taren JA, eds. *Correlative neurosurgery*. Springfield: Thomas, **1969**:94–130
22. Miyasaki K, Miyachi Y, Arimitsu K, Kita E, Yoshida M. Posttraumatic hypothalamic obesity—an autopsy case. *Acta Pathol Jpn* **1972**;22:779–802
23. Noel P, Hubert JP, Ectors M, Franken L, Flament-Durand J. Agenesis of the corpus callosum associated with relapsing hypothermia. A clinico-pathological report. *Brain* **1973**;96:359–368
24. Phillip G, Smith JF. Hypothermia and Wernicke's encephalopathy. *Lancet* **1973**;2:122–124
25. Lipsett MB, Dreifuss FE, Thomas LB. Hypothalamic syndrome following varicella. *Am J Med* **1962**;32:471–475
26. Fox RH, Davies TW, Marsh FP, Urich H. Hypothermia in a young man with an anterior hypothalamic lesion. *Lancet* **1970**;2:185–188
27. Appenzeller O, Snyder RD. Autonomic failure with persistent fever in cerebral gigantism. *J Neurol Neurosurg Psychiatry* **1969**;32:123–128
28. Davison C, Selbe NE. Hypothermia in cases of hypothalamic lesions. *Arch Neurol Psychiatry* **1935**;33:570–591
29. Killeffer FA, Stern WE. Chronic effects of hypothalamic injury. Report of a case of near total hypothalamic destruction resulting from removal of a craniopharyngioma. *Arch Neurol* **1970**; 22:419–429
30. Forester D. Fatal drug-induced heat stroke. *Ann Emerg Med* **1978**;7:243–244
31. Maickel RP. Interaction of drugs with autonomic nervous function and thermoregulation. *Fed Proc* **1970**;29:1973–1979
32. Sarnquist F, Larson CP. Drug-induced heat stroke. *Anesthesiology* **1973**;39:348–350
33. Zelman S, Guillan R. Heat stroke in phenothiazine-treated patients: a report of three fatalities. *Am J Psychiatry* **1970**; 126:1787–1790
34. Drayer BP, Rosenbaum AE. Metrizamide brain penetrance. *Acta Radiol [Suppl]* (Stockh) **1977**;355:280–292
35. Kollias J, Bullard RW. The influence of chlorpromazine on the physical and chemical mechanisms of temperature regulation in the rat. *J Pharmacol Exp Ther* **1964**;145:373–381
36. Krupin T, Koloms BA, Klutho L, Webb G, Becker B. Increased intraocular pressure and hyperthermia following administration of substance P into rabbit third ventricle. *Exp Eye Res* **1982**;34:319–324
37. Oftedal S. Intraventricular application of water-soluble contrast media in cats. *Acta Radiol [Suppl]* (Stockh) **1973**;335:125–132
38. Heimburger RF, Campbell RL, Kalsbeck JE, Mealey J, Goodell CL. Positive contrast cerebral ventriculography using water soluble media. *J Animal Studies Confin Neurol* (Basel) **1966**;28:97
39. Slevin D. *Amipaque and aseptic meningitis*, Winthrop Medical Information #82–14. New York City: Winthrop-Breon, **1982**
40. Freeman LM, Blaufox MD, eds. Amipaque. In: *Physicians' desk reference for radiology and nuclear medicine*. Oradell, NJ: Medical Economics, **1979**:173–175

Editor's Note

In response to our query, Winthrop-Breon Laboratories made the following statement concerning reports they have received on hyperthermia after metrizamide myelography.

> Over the past 5 years in over 2 million myelograms, we have received about 20 reports of the occurrence of hyperthermia. We excluded those cases of fever occurring as part of the aseptic meningitis–type syndrome. The degree of fever was mild in two or three cases, 39°C–39.5°C in most, and one patient developed a fever of 40.5°C. The fever lasted 4–6 hr in all cases except one, in which it lasted 24 hr. All reports were of single incidences except two involving four patients, two each at two different hospitals. In about half the reports, fever was the only symptom or sign mentioned. In the other half, other adverse neurologic effects were mentioned, but fever dominated.