

CARDIAC ARREST: AN UNUSUAL SIDE-EFFECT OF INTRAVENOUS ORNIDAZOLE*

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Nitroimidazoles have been used alone or in combination with other antibacterial agents in the treatment of brain abscess. They are associated with certain adverse reactions related primarily to the gastrointestinal tract and central nervous system. But, as far as we know, cardiac arrest due to ornidazole has not been reported in the literature.

In this study, we presented a case in which cardiac arrest occurred as an unusual side-effect of intravenous ornidazole administered to a ten-year-old girl suffering from brain abscess. *Key words:* ornidazole, cardiac arrest.

Anaerobic microorganisms such as Bacteroides, Fusobacteriums and Gram (+) cocci are the agents responsible for brain abscess in 85-88 percent of cases. In patients with congenital cyanotic heart disease, the incidence of brain abscess is 2-6 percent, and infections caused by multiple microorganisms are frequent¹. In addition, microaerophilic and anaerobic streptococci can cause up to 45 percent of brain abscesses.

In the treatment of brain abscess, 5-nitroimidazoles have been used alone or in combination with other antibacterial agents because of their bactericidal activity and perfect penetration into cerebrospinal fluid. The nitroimidazoles have some adverse reactions related primarily to the gastrointestinal tract and central nervous system. In this study, we report an unusual adverse reaction to ornidazole, that to our knowledge, has not been documented in the literature.

Case Report

A ten year-old girl was brought to the hospital for evaluation of vomiting and headache of ten days' duration. Her past history revealed that she had been under

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medical supervision for a condition that had been diagnosed as congenital heart disease (dextrocardia and double outlet right ventricle of the transposition type) when she was two and a half years old.

Physical examination revealed bilateral grade 2 papilledema, left-sided facial paresis of the central type and left hemiparesis. The cranial computerized axial tomography revealed a 5 × 5 cm abscess located in the right frontal lobe. The patient underwent surgery immediately, and the abscess was aspirated through a burr hole.

Treatment consisted of benzyl penicillin G combined with chloramphenicol and ornidazole (Biteral[®], Roche) 20 mg/kg/day in three divided doses (i.v. infusion in 50 cc fluid in 30 minutes or longer). No other medication was given to the patient. Alpha-hemolytic streptococci, beta-hemolytic streptococci, *N. meningitidis* and anaerobic Gram (+) rods (unidentified) were cultured from the surgical specimen. The determination of alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, calcium, phosphate, blood urea nitrogen, uric acid and creatinine concentrations were found to be within normal limits.

On the 13th day of therapy, the patient's body temperature rose to 39 °C, and dyspnea and increased cyanosis were noted two hours after the administration of benzyl penicillin G and ornidazole. Since we thought this was an adverse reaction to benzyl penicillin G, it was discontinued. Although all the symptoms promptly disappeared six hours after the first reaction, identical signs and symptoms were observed during the infusion of ornidazole, and in addition, cardiac arrest occurred. Chloramphenicol was not administered. Cardiac rhythm returned to normal within 30 seconds as a result of cardiac massage and the establishment of adequate ventilation with ambu. The blood pressure was 110 mm Hg systolic and 80 mm Hg diastolic. Flushing, urticaria or other signs of allergic reactions were not observed. Ornidazole therapy was discontinued.

Discussion

The nitroimidazoles, particularly metronidazole, tinidazole and ornidazole are used to treat many serious infections caused by Gram (+) and Gram (–) anaerobic bacteria and protozoa (*T.vaginalis*, *E.histolytica*, *G.lamblia*). It is also given prophylactically. However, some well-known dose-dependent adverse reactions, which disappear shortly after treatment is discontinued, have been associated with the use of these drugs²⁻⁶.

Many reports document the adverse effects of metronidazole and tinidazole, while there are very few concerning the side-effects of ornidazole. In a report from Australia, thirty-six suspected reactions to tinidazole were presented and ten of them were considered to be due to hypersensitivity reactions. Reported manifestations include generalized urticaria, facial, periorbital or laryngeal edema,

hypotension, bronchospasm and dyspnea⁴. In our patient, only fever, irregular respiration, increased cyanosis and dyspnea were noted. There were no dermatologic signs.

In a study from Norway, high-dose tinidazole administered intravenously to one patient caused unconsciousness lasting 10 seconds followed by a spasm in one arm. In addition a drop in systolic blood pressure was observed in this patient, however, the total IgE level was normal. This reaction was not considered a type I allergy, but a direct toxic reaction to the drug⁵. Furthermore, tachycardia and bradycardia were observed in four of five cases receiving Tiberol[®] (ornidazole) tablets. In one of these cases, there was persistent atrial flutter and extrasystoles, but because these patients were taking multiple medication, the exact cause was not specified and, therefore, not reported (Roche, personal communication, 24 April 1989).

After a search of the literature, we discovered that fever was a rare reaction to this drug, and that no case had been reported in which cardiac arrest had occurred. The cardiac arrest that occurred in our patient is considered by us to be a direct toxic effect of the drug.

REFERENCES

1. Patrick CC, Kaplan SL. Current concepts in the pathogenesis and management of brain abscesses in children. *Pediatr Clin North Am* 35: 625, 1988.
2. Webster LT Jr. Drugs used in the chemotherapy of protozoal infections. In Gilman AG, Goodman LS, Rall TW, Murad F (eds.). *The Pharmacological Basis of Therapeutics* (8th ed). New York: Pergamon, 1990, pp 1008-1021.
3. Scully BE. Metronidazole. *Med Clin North America* 72: 613, 1988.
4. McEwen J. Hypersensitivity reactions to tinidazole (Fasigyn). *Med J Australia* 1: 498, 1983.
5. Aase S, Olsen AK, Roland M, et al. Severe toxic reaction to tinidazole. *Eur J Clin Pharmacol* 24: 425, 1983.
6. Roe FJ. Safety of nitroimidazoles. *Scand J Infect Dis (Suppl)* 46: 72, 1985.

