
Adverse Allergic Reaction to Technetium-99m Methylene Diphosphonate

Jay A. Spicer, David F. Preston, and Ronald L. Stephens

Departments of Diagnostic Radiology and Medicine, Divisions of Nuclear Medicine and Clinical Oncology, University of Kansas, College of Health Sciences and Hospital, Kansas City, Kansas

Adverse allergic reactions to radiopharmaceuticals are rare but have been documented in the literature. This report presents data consistent with a definite adverse reaction to the radiopharmaceutical [^{99m}Tc]MDP.

J Nucl Med 26:373-374, 1985

Since 1982, there have been two relatively comprehensive articles published which have dealt with drug radiopharmaceutical interactions or radiopharmaceuticals involved in adverse reactions (1,2). The article by Cordova et al. (2) is of particular interest because it lists the number of adverse reactions involving radiopharmaceuticals that have been reported to the United States Pharmacopoeia (USP), the Society of Nuclear Medicine (SNM) and the Food and Drug Administration (FDA) since 1976. This report shows that only three technetium-99m (^{99m}Tc) radiopharmaceuticals have been involved in all reported reactions, one of which is [^{99m}Tc]methylene diphosphonate ([^{99m}Tc]MDP). Of the 22 reported reactions to MDP, 12 were listed as probable, eight as possible, and two as unlikely. We feel the following case report can be listed as a definite reaction to MDP.

CASE REPORT

A 60-yr-old white female had a comedo-type ductal carcinoma of the breast in 1980, which resulted in a left mastectomy. By April of 1983, multiple lung metastases were apparent on chest x-ray. On April 4, 1983 she underwent a bone scan with MDP which revealed multiple metastases to thoracic and lumbar spine and right ischium. Forty-eight hours later she noted a scratchy sore throat and a puritic, raised, erythematous rash which persisted for 3-4 days. It was not of such severity that it was initially mentioned to her physician. The presence of the puritic erythematous rash with ulcerated erythematous

pharynx was documented by her husband, a college professor and careful observer. She was taking 5-FU, doxorubicin hydrochloride, cyclophosphamide, dexamethasone, tamoxifen (10 mg b.i.d.), and haloperidol. She experienced a remarkable regression of her tumor.

On January 18, 1984 brain metastases were identified by computerized tomography. She was taking diphenylhydantoin (300 mg q.h.s), dexamethasone (4 mg q.6 h.), tamoxifen (10 mg b.i.d.), and megestrol acetate (40 mg. p.o.q.i.d.) was started. On January 18, a left ventricular ejection fraction of 65% was found. The red cells were tagged using cold stannous pyrophosphate. No symptoms were reported by the patient. On February 16, 1984 a repeat MDP bone scan was performed showing new metastatic lesions to bone. Forty-eight hours later she developed a sore throat, generalized maculo papular rash, which was puritic and erythematous. She developed conjunctivitis and a hyperemic ulcerated pharynx consistent with the diagnosis of erythema multiforme. All medications were discontinued and prednisone was begun. The rash cleared slowly over 3-4 days. Because of the symptoms, the patient made a special appointment with the oncologist and stated that the rash and symptoms were very similar but much worse than the April 1983 reaction.

DISCUSSION

Allergic reactions to radiopharmaceuticals are rare. Our initial impression was that some factor other than MDP must be the cause of the allergic reaction. The patient described had only one known allergic reaction in the past, that to morphine. As noted, the patient had been on several chemotherapy drugs and had received whole brain radiation without any report of any kind of reaction. No i.v. iodinated contrast was administered during the 2 wk prior to either bone scan. In both in-

Received Sept. 4, 1984; revision accepted Dec. 12, 1984.
For reprints contact: Jay Spicer, MS, Dept. of Diagnostic Radiology, University of Kansas Med. Ctr., 39th & Rainbow, Kansas City, KS 66103.

stances, multiple other doses had been dispensed to other patients without any reported reactions (five other patients on April 4, 1983 and six other patients on February 16, 1984.) This patient was neither the first nor the last to receive a dose on either date, thus any kind of pyrogenic or nonsterile reaction can be ruled out.

The first bone scan was performed using a kit from a different manufacturer than the second scan. The second scan utilized a kit containing no stabilizing agent, while the first kit used did contain a stabilizer, thus eliminating the possibility of a reaction to the stabilizer. The cardiac ejection fraction used a pyrophosphate (PYP) agent and no allergic reaction was noted by the patient or her physician. Evaluation of both the MDP and the PYP kits revealed the only difference in formulation was the fact that one was phosphonate (MDP) and the other an inorganic phosphate (PYP).

The time delay noted (48 hr postinjection) is consis-

tent with the report of Cordova et al. (2), indicating a 4–24 hr and longer time lag before the development of a rash. The rash development was also the most common allergic reaction reported for MDP. We cannot implicate any previous diagnostic study or drug which may have sensitized this patient to MDP.

An evaluation of the data presented indicates that, in our opinion, the allergic reaction was definitely caused by the organic phosphate, MDP.

REFERENCES

1. Hladik WB, Nigg KK, Rhodes BA: Drug-induced changes in the biological distribution of radiopharmaceuticals. *Semin Nucl Med* 2:184–218, 1982
2. Cordova MA, Hladik WB, Rhodes BA: Validation and characterization of adverse reactions to radiopharmaceuticals. *Noninv Med Imag* 1:17–24, 1984