

Adverse allergic reaction to ^{131}I MIBG

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Abstract No adverse allergic reactions to iodine-131-metaiodobenzylguanidine (^{131}I MIBG) at a diagnostic dose have been reported in the English literature. This report of a skin eruption in a 35-year-old man after an intravenous injection of ^{131}I MIBG strongly suggests an adverse allergic reaction, and is the first to address such a side effect of ^{131}I MIBG at a diagnostic dose. Erythematous maculopapular eruptions, some of which were contiguous, were seen in a symmetric disposition on the patient's chest walls, elbows, neck and face 18 h after the ^{131}I MIBG injection. Antiallergic treatment resolved the lesions completely. There were no possible causes of the exanthema other than the ^{131}I MIBG injection. Urticaria related to the ^{131}I MIBG injection and caused by type I allergic reaction was suspected, and these findings point to the possible risk

of a hitherto unreported allergic skin reaction to ^{131}I MIBG. We would like to draw the attention of nuclear physicians to this possible drawback of ^{131}I MIBG.

Keywords ^{131}I MIBG · Adverse reactions · Skin eruption · Side effect · Radiopharmaceuticals

Introduction

Adverse reactions to radiopharmaceuticals are rare, the reported frequencies being between 2.1 and 11/100,000 [1–4]. Iodine-131-metaiodobenzylguanidine (^{131}I MIBG) scintigraphy is a well-established method for the detection of pheochromocytoma [5]. The Japan Radioisotope Association [3, 4] reported a total of three cases of adverse reactions to ^{131}I MIBG in 2000 and 2001 in a survey of adverse reactions to radiopharmaceuticals, but no cases have been documented since 2002. However, these cases were based on responses to questionnaires sent to nuclear medicine institutions to establish the incidence of such adverse reactions, and so the details of the adverse reactions were not described. No adverse reactions to ^{131}I MIBG at a diagnostic dose have previously been reported in the English literature, so that this is the first report in which the possibility of an adverse allergic reaction caused by injection of ^{131}I MIBG has been described.

Case report

A 35-year-old man was found to have hypertension in a routine physical checkup that showed his systolic blood pressure to be 160 mmHg. A slightly elevated plasma noradrenaline level of 497 pg/mL (normal range 100–

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450 pg/mL) was also detected. Other vital signs and laboratory results were within normal limits. He had no history of allergic reactions. A diagnostic dose of 20 MBq of ^{131}I MIBG (Fujifilm RI Pharma, Tokyo, Japan) was administered intravenously to detect the possible presence of pheochromocytoma. Before the ^{131}I MIBG injection, the thyroid iodine uptake was blocked with a saturated solution of potassium iodide (KI) (200 mg/d orally, starting before tracer administration and continuing for 4 days). Eighteen hours later, when the patient awoke on the following morning, he noticed a rash with intense itching on his face and chest walls, and so he returned to the hospital. Upon physical examination (24 h after the ^{131}I MIBG injection), erythematous maculopapular eruptions, some of which were contiguous, were seen in a symmetrical disposition on both sides of the chest wall and both elbows, and also on the neck and face, suggesting erythema multiforme due to an allergic reaction (Fig. 1). Except for the ^{131}I MIBG injection, no other possible causes of exanthema, such as a history of unusual food intake, fatigue, sleep disturbance or contact with any chemicals, could be found in this patient's lifestyle or behavior. His vital signs and laboratory results, including the serum level of IgE, were normal. After intravenous and oral administration of hydrocortisone and olopatadine hydrochloride, the exanthema had retreated markedly by the next day, and, after oral administration of loratadine, was resolved completely on the 13th day after the patient first presented. The results of a patch test, a scratch test and a drug-induced lymphocyte stimulation test using KI and non-radioactive ^{127}I MIBG in order to prevent radiation exposure were negative.



Fig. 1 Photograph of the left chest wall shows contiguous erythematous maculopapular eruptions

Discussion

In this case, our interpretation that the patient's symptoms resulted from an allergic reaction to ^{131}I MIBG was based on the sequence of events, his response to antiallergic treatment and the lack of any other reasonable explanation. The patient's dosage of 20 MBq of ^{131}I MIBG (0.108–0.180 mg of iodobenzylguanidine, according to the interview form), which was determined as directed in the interview form was not an overdose, was reasonable for the detection of pheochromocytoma and was in line with those in other reports [3–5]. Although the serum level of IgE and the skin test were normal and negative, these do not eliminate the possibility of a drug's responsibility in drug reactions [6–9]. The ^{131}I MIBG injections contained additives of acetic acid, sodium acetate and sodium chloride. Although hypersensitivity to ethanol metabolite acetic acid, sodium acetate and sodium chloride is reported [10–12], it is extremely rare and has not been investigated sufficiently to the best of our knowledge. These are unlikely to have caused the allergic reaction because the patient had no history of allergic reactions to those substances.

Urticaria is frequently caused by an allergic reaction followed by a polymorphous rash, angioedema and erythema multiforme [13–15]. Erythematous maculopapular eruptions, some of which were contiguous, were seen in our patient. This eruption may have developed from an initial urticaria (not reported by the patient) over the course of half a day since the onset of the latter symptom. His exanthema resolved completely after treatment with anti-allergic agents. These facts strongly suggested allergic skin reactions. The fact that the eruption experienced in this case seemed to be urticaria suggests a type I allergy and the risk of drugs that induce type I allergies. These allergies, unlike other types of allergic reactions, can sometimes induce anaphylactic shock, resulting in serious conditions. The re-injection of the drug that induced a type I allergy is contraindicated. For this reason, it is important to report that this type I allergic reaction appeared after the injection of ^{131}I MIBG. Especially, because this radiopharmaceutical can be massively administered to treat malignant tumors such as malignant pheochromocytoma, any reports of an adverse reaction to this drug should be disseminated.

The currently approved formulations of KI are not known to contain allergens, and our patient's skin test for KI was negative. Be that as it may, it was not possible to disprove the possibility that KI caused the allergic reaction. Nauman et al. [16] reported that 1% of minor rashes were observed on administration of KI as a specific blocker of thyroid radioiodine uptake in Poland after the Chernobyl accident, but no control values for their incidence were

determined. Although our patient was given KI, it is highly unlikely to be the cause of the allergic skin reactions, because he had no history of allergic reactions to gargling with KI and he was administered KI more than 4 days before the rash developed.

The dose of iodine included in a ^{131}I MIBG injection is much smaller than that in iodine CT contrast media. Moreover, most of iodine in this radioactive agent is incorporated in the compound MIBG. Therefore, the eruption observed in this case was definitely not iododerma; accordingly, this appears to be a hitherto unreported allergic skin reaction to ^{131}I MIBG. We here draw the attention of nuclear physicians to a possible adverse allergic reaction to ^{131}I MIBG.

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