

Late-type allergy to the X-ray contrast medium Solutrast® (iopamidol)

HELMUT GALL, HANS PILLEKAMP AND RALF-UWE PETER

Department of Dermatology, University of Ulm, Germany

In the past few years, there have been an increasing number of publications on delayed intolerance reactions, including rashes, following the use of X-ray contrast media. We report a patient in whom infiltrated erythema of the face and generalized maculopapular rashes occurred on 2 occasions, within 1 day, following the use of the X-ray contrast medium Solutrast® (iopamidol) for coronary angiography. The allergological investigations for clarification included prick tests and patch tests using a series of contrast media, as well as individual intravenous provocation tests. We found the cause to be a late-type allergy to the active substance iopamidol contained in the contrast medium Solutrast®. We found a concomitant cross-reactivity to the contrast media iopromid and iomeprol. All 3 contrast media represent the monomeric, non-ionic type.

Key words: adverse drug reactions; maculopapular rashes; non-ionic X-ray contrast media; Solutrast® (iopamidol); late-type allergy; cross-reactivity. © Munksgaard, 1999.

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Drug intolerance is an undesirable and potentially damaging reaction to a medicament used in therapeutic doses. In the past few years, there has been an increase in the number of reports of delayed intolerance reactions after the use of X-ray contrast media, which have occurred later than 1 h and within 48 h of administration (1–4). These have included: influenza-like symptoms, headaches, nausea and vomiting, and also rashes. We report a patient in whom a generalized maculopapular rash occurred on 2 occasions, within 1 day, following the use of an X-ray contrast medium. We found the cause to be a late-type allergy to the active substance iopamidol contained in the contrast medium Solutrast®.

Case Report

A 60-year-old male patient suffered from arterial hypertension and pectanginous complaints. For this reason, a heart catheter examination was performed in 1989 in the Medical Hospital of the University of Ulm, using about 200 ml of the contrast medium Solutrast® (iopamidol). Coronary angiography showed the picture of 3-vessel disease with high-grade circumflexed stenosis, which was successfully dilated. 1 day after the examination using contrast medium, an infiltrated erythema of the

face occurred, together with a generalized maculopapular rash. The skin symptoms receded within 1 week under local treatment with a corticosteroid ointment. On account of further pectanginous symptoms, a check-up angiography also using Solutrast® was performed in 1992. Within 1 day, a generalized maculopapular rash again developed, which receded within a few days under intravenous treatment with dimethindene and prednisolone-21-hydrogen succinate. Medication for treatment of the coronary heart disease and hypertension, metoprolol tartrate, ramipril, hydrochlorothiazide and acetyl salicylic acid, was continued. The patient was referred to us in 1997 for clarification of the rashes.

The allergological tests performed included patch tests (reading after 2 and 3 days) as well as prick tests (immediate reading after 20 min and late reading after 2 and 3 days) with an iodine block (potassium iodide solution at the concentrations 2, 20, 200 and 500 mg/ml) and a contrast medium series (Solutrast®, Ultravist®, Imeron®, Biliscopin® and Urografin®). Finally, intravenous provocation tests were also performed with Biliscopin®, Imeron® and Solutrast® (5 ml in each case at the dilutions 1:1000, 1:100, 1:10 and undiluted) staggered by 20 min (modified according to 5). The test results are shown in Table 1.

Table 1. Summary of the allergological tests with the contrast medium series

Medicament	Patch test D3	Prick test D3	Intravenous provocation
iodine block	—	—	
Biliscopin®	—	—	negative
Urografin®	—	—	
Solutrast®	+++	++	positive
Ultravist®	+++	++	
Imeron®	++	++	positive

Table 2. Test results with the individual components of the contrast media

Patch test	D2	D3
Solutrast® components		
iopamidol 0.61 g/ml	++	++
trometamol 1 mg/ml	—	—
Na-Ca EDTA 0.4 mg/ml	—	—
Imeron® components		
iomeprol 0.61 g/ml	+	+
trometamol 1 mg/ml	—	—
Ultravist® components		
iopromid 0.62 g/ml	++	++
trometamol 2.42 mg/ml	—	—
Na-Ca EDTA 0.1 mg/ml	—	—

The patch tests and the prick tests with the iodine block and the contrast media Biliscopin® and Urografin® produced negative results, whereas the 2 and 3 day readings of the patch tests and the 2 and 3 day late readings of the prick tests gave positive results for the contrast media Solutrast®, Ultravist® and Imeron®. The intravenous administration of Biliscopin® produced no reaction, whereas on administration of Imeron® and Solutrast®, infiltrated erythema of the face and generalized maculopapular rashes occurred on the following day.

In order to establish the identity of the actual contact allergen, further patch tests were performed with the individual substances contained in the contrast media Solutrast®, Imeron® and Ultravist®. The tests were carried out at the concentrations stated in the information supplied with the original preparation. The test results are shown in Table 2. Positive reactions were found in each case for the iodine-containing complexes iopamidol, iomeprol and iopromid, whereas the 2 solubilizers trometamol and sodium calcium EDTA were negative.

Histological investigations (biopsies were taken from positive test results)

Patch test reaction to Solutrast® after 3 days: pronounced formation of intraepidermal fibrin-

filled vesicles. Perivascular and interstitial dense lymphohistiocytic infiltrate with individual granulocytes in the upper corium. Conclusion: acute allergic contact eczema.

Prick test reaction to Solutrast® after 2 days: pronounced spongiosis extending to microvesicle formation of lymphohistiocytic cells into the epidermis. Pronounced oedema of the stratum papillare, perivascular lymphohistiocytic infiltrates in the upper corium. Conclusion: well reconcilable with an allergic late-type reaction.

Maculopapular rash following exposure to Solutrast®: distinct oedema, particularly of the lower regions of the epidermis, focal with immigration of lymphohistiocytic cells. Dilation of the capillary vessels in the upper corium with a moderately dense surrounding lymphohistiocytic infiltrate. Conclusion: acute superficial dermatitis, well reconcilable with a drug allergy.

Discussion

X-ray contrast media for intravascular application are obligatory for use in angiography, computer tomography and many other examinations performed in radiographic diagnostics. It has been possible to improve continuously the tolerance of these substances over the past few years. In their large study of 337,647 cases, Katayama et al. (6) were able to show that the immediate side-effects of non-ionic contrast media were reduced by a factor of 4 compared with ionic contrast media. On the other hand, delayed side-effects, mainly skin reactions (3), occurred 2× as frequently with non-ionic contrast media (8.0% compared with 3.8%). The frequency of rashes has been quoted at between 2.4% (3) and 5.5% (2). There are also individual reports of biphasic immediate and late reac-

Iopamidol (Solutrast®)

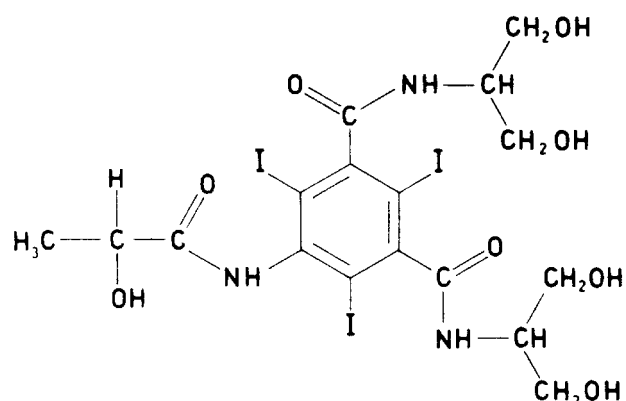


Fig. 1. Chemical structure of iopamidol (Solutrast®).

tions (7, 8). The mechanism of the delayed reaction, particularly of the rashes, has not yet been clarified. Skin tests, provocation tests and histological investigations have so far only been performed sporadically (9, 10).

In the case of our patient, infiltrated erythema of the face and a generalized maculopapular rash occurred on 2 occasions following examinations using the contrast medium Solustrast®. In allergological tests for clarification of the rashes, we were able to demonstrate a late-type allergy to Solustrast®, using patch and prick testing methods with late reading, the findings of which were supported by histology. In the case of Kanzaki and Sakagami (9), a delayed reaction to the contrast medium Isovist® (iotrolan) after 9–12 h was found on prick and intracutaneous tests, in the case of Schick et al. (10), a patch test with Ultravist® (iopromid) was positive. Exposure tests with Solustrast® produced the clinical symptoms of infiltrated erythema of the face and a generalized maculopapular rash. Histologically, the test reaction was well reconcilable with a drug allergy, the histological findings being to a large extent identical with those of other investigators (9, 10). The clinical picture (maculopapular rash), the appearance within 2 days, the positive late-type reaction in the skin tests and the histology, all point towards a drug-induced rash associated with a late-type allergy to Solustrast®. This type of drug rash is typical of the aminopenicillins (11).

In order to establish the identity of the actual contact allergen, further patch tests were performed. Positive reactions were found to the iodine complex, whereas the two solubilizers were negative. Because iodine itself was negative, there is no danger to this patient in applying povidone-iodine to the skin, for example. In this way, we were able to establish a contact allergy to Solustrast® (iopamidol) (Fig. 1), with cross-reactivity to Ultravist® (iopromid) and Imeron® (iomeprol). Iopamidol,

iopromid and iomeprol are all monomeric, non-ionic contrast media.

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Address:

Helmut Gall
Department of Dermatology
University of Ulm
Oberer Eselsberg 40
D-89081 Ulm
Germany