

Low negative predictive value of skin tests in investigating delayed reactions to radio-contrast media

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Delayed reactions to radio-contrast media (RCM) with positive skin tests are rare. We report the study of a series of 15 patients who presented delayed reactions to RCM, with an analysis of the clinical features and the results of standardized drug skin tests. Patch tests were performed with RCM and iodized antiseptics (IAs). If negative, prick tests were performed, followed by intradermal tests (IDTs), then intravenous administration under hospital surveillance. The main clinical features were maculopapular rashes or a macular rubella-like rashes. Patch tests were positive with RCM in 2 of 15 cases and with IAs in 4 of 15 cases. All the prick tests were negative. IDTs were positive at 24 h in 8 of 15 cases. 5 of 12 patients had a non-severe relapse of the rash upon receiving an RCM despite clearly negative skin tests with the readministered RCM. Visipaque[®] cross-reacted with Iopamiron[®], Iomeron[®], Telebrix[®], Omnipaque[®], Xenetix[®] and Hexabrix[®]. Omnipaque[®] cross-reacted with Hexabrix[®] and Iopamiron[®]. IDTs with delayed readings are of better value than patch tests in such patients. The readministration of RCM with negative IDTs must be performed with progressive amounts under hospital surveillance. Cross-reactions between various classes of RCM are frequent. The responsible epitopes are unknown. Iodine itself could be involved.

Key words: cross-reactions; cutaneous adverse drug reactions; drug skin test; intravenous administration; iodine; iodized antiseptics; radio-contrast media. © Blackwell Munksgaard, 2004.

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Iodized radio-contrast media (RCM) have been used since 1929 for radiological examinations. Toxic reactions are related to a direct toxicity on the vascular endothelium and their high osmolality. Toxic adverse reactions are frequent although decreasing since the use of the RCM of the 3rd generation, but true allergic reactions are rare. Allergic adverse reactions can be immediate with anaphylactoid reactions or delayed. The latter are usually defined as reactions that occur more than 1 h, but less than 7 days, following the RCM injection. The most common side effects are flushed face, pain at the site of injection, nausea, vomiting and flu-like illness. Renal insufficiency, pulmonary oedema due to rapid expansion of the intravascular volume or cardiac disorders are less frequent. A few cases have been published previously concerning positive patch tests or delayed positive intradermal tests (IDTs) performed with RCM in such patients (1–8). We report a study on 15 patients presenting with a delayed reaction after receiving an injection of RCM, with an analysis of the clinical character-

istics, the results of skin tests and the negative predictive value of the tests.

Patients and Methods

15 patients, 11 female and 4 male (mean age 55.4 years, from 37 to 78 years old), have been retrospectively included after developing an adverse skin reaction, with a very probable imputability in one case and a probable imputability in 14 cases of RCM, according to the Moore et al. criteria (9). All these patients were referred from October 1998 to April 2003. The responsible RCM were Visipaque[®] (iodixanol) (Nycomed Laboratory, Paris, France) in 11 cases, Iomeron[®] (iomeprol) (BYK Laboratory, Le Mée-sur-Seine, France) in 1 case, Xenetix[®] (iobitridol) (Guerbet Laboratory, Roissy-Charles-de-Gaulle, France) in 1 case, Hexabrix[®] (ioxaglate) (Guerbet Laboratory) in 1 case and Omnipaque[®] (iohexol) (Nycomed Laboratory) in 1 case.

Immunoallergological investigations were carried out 6 weeks to 8 months after resolution

of the adverse reaction. Patch tests were performed with 7 different RCM. The classes were the ionic tri-iodized monomer class of RCM with Telebrix[®] (ioxitalamate) (Guerbet Laboratory), the ionic hexa-iodized dimer class of RCM with Hexabrix[®] (ioxaglate), the non-ionic tri-iodized monomer class of RCM with Iopamiron[®] (iopamidol) (Schering Laboratory, Lys-lez-Lannoy, France), Iomeron[®] (iomeprol), Xenetix[®] (iobitridol), Omnipaque[®] (iohexol) and the non-ionic hexa-iodized dimer class of RCM with Visipaque[®] (iodixanol). Patch tests were performed with the pure injectable products, put on the upper back using Finn Chambers[®] on Scanpor[®] tape (Epitest Ltd oy, Tuusula, Finland) or Hayes Chambers (Chemotechnique, Malmö, Sweden), according to internationally accepted methods used in patch testing for studying contact dermatitis. Patch tests were also performed with the European standard series and iodized antiseptics (IAs) were also tested: povidone-iodine 10% and 1% aq., povidone 10% aq., iodized alcohol pure and iodoform 5% petrolatum. In the more recent cases, we also tested iodine potassium (2 patients).

When patch tests with the RCM were negative, prick tests were performed with the pure injectable products with the same 7 RCM, followed by IDTs. IDTs were carried out according to the guidelines for performing drug skin tests of the European Society of Contact Dermatitis (10). We injected 0.4 ml of sterile dilutions of the 7 RCM on the external aspect of the arms from 10^{-4} to 10^{-1} of the commercialized form of the RCM. With 5 of 7 of the RCM, IDTs were also performed with the pure form except for Visipaque[®] and Hexabrix[®]. All the IDTs were performed under hospital surveillance for 24 h. When it was possible to find an RCM with negative skin tests, intravenous administration with this RCM was carried out with 1/100 of the dose required for radiological examination. Then, if this was well tolerated 2–24 h later, an injection was made with 1/10 of the dose required. A pure dose would be injected only for the radiological examination.

According to a method previously described (11), lymphocyte activation tests (LATs) were performed for 3 patients (case nos 11, 12 and 15) with Hexabrix[®], Visipaque[®], Omnipaque[®] and Iopamiron[®]. All results were negative.

Results

None of the 15 patients had a history of contact allergy to IAs. 2 had a history of atopic dermatitis. 5 had a history of contact dermatitis (nos 3, 6, 7, 12 and 15) with positive patch tests to balsam of Peru (*Myroxylon pereirae* resin) (3 cases: nos 3, 6 and 7), nickel sulfate (2 cases: nos 7 and 12),

potassium dichromate, cobalt chloride or fragrance mix. 5 patients had a history of cutaneous adverse reaction (nos 6, 7, 10, 11 and 13), to betalactam antibiotics in 3 cases (nos 6, 10 and 11), with IDT positive in 1 case (no. 10) to Augmentin[®] (amoxicillin, clavulanic acid) and Clamoxyl[®] (amoxicillin), in 1 case to Tahor[®] (atorvastatin) (no. 13) and in 1 case to Magne B6[®] (magnesium/pyridoxin) with positive patch tests to pyridoxine (no. 11).

The clinical features of the delayed reactions due to RCM were a maculopapular rash (Fig. 1) in 5 cases, a macular rubella-like rash (Fig. 2) in 5 cases, pruritus in 1 case, a widespread itchy erythema associated with deep oedema in 1 case, pompholyx associated with a lip oedema in 1 case, a maculopapular exanthema with facial oedema in 1 case and a flushed face with localized eczema on the arms (Table 1). The mean delay of the onset of the skin reactions was 26 h (6–72 h) after the RCM injection. The mean duration of the rash was 4.8 days (1–20 days). For all patients, no other substances were imputable. Topical corticosteroids and antihistamines were prescribed in only 6 cases. Neither systemically administered corticotherapy nor norepinephrine were required. The radiological examinations necessitating the injection of the responsible RCM were coronarography (5 cases), computed tomographic scan (5 cases), arteriography (3 cases), intravenous urography (1 case) and angiography. These examinations were required for coronaropathy (2 patients), myocardial infarction, cardiac failure, heart transplant surveillance, stenosis of the renal artery, melanoma (2 patients), leg ulcers (2 patients), urinary infection, slipped disk, thrombosis of the femoral artery and pulmonary embolism. The underlying disease was not stated in 1 case.

Histological examination were performed in 5 patients. In 3 patients presenting with a rubella-like rash, slight keratinocyte alteration and slight

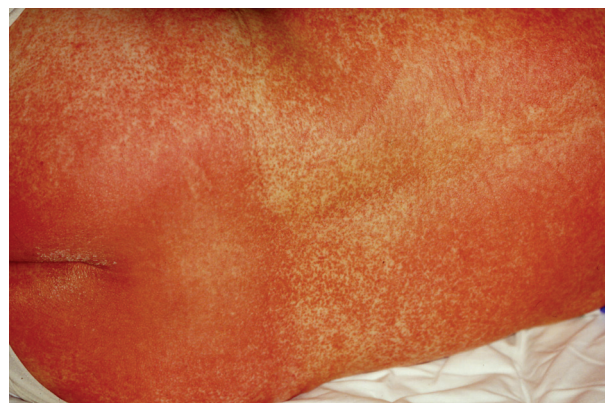


Fig. 1. Maculopapular rash due to Visipaque[®].

Table 1. Clinical features of the delayed reactions due to radio-contrast media (RCM)

Number	Sex	Age (years)	Clinical features	Responsible RCM	Delay of onset (h)
1	Female	47	Rubella-like rash	Iodixanol (Visipaque [®])	72
2	Male	53	Maculopapular rash	Iodixanol (Visipaque [®])	24
3	Female	73	Rubella-like rash	Iodixanol (Visipaque [®])	24
4	Male	61	Rubella-like rash	Iodixanol (Visipaque [®])	72
5	Female	70	Rubella-like rash	Iodixanol (Visipaque [®])	7
6	Female	78	Maculopapular rash	Iodixanol (Visipaque [®])	24
7	Female	66	Maculopapular rash	Iodixanol (Visipaque [®])	6
8	Female	49	Maculopapular rash	Iodixanol (Visipaque [®])	48
				Ioxaglate (Hexabrix [®])	24
9	Female	45	Lip oedema with pompholyx	Iodixanol (Visipaque [®])	24
10	Male	59	Pruritus	Iodixanol (Visipaque [®])	6
11	Female	37	Deep oedema and erythema	Iodixanol (Visipaque [®])	6
12	Female	45	Maculopapular rash	Iobitridol (Xenetix [®])	72
13	Female	43	Rubella-like rash	Iomeprol (Iomeron [®])	18
14	Female	56	Maculopapular rash and facial oedema	Iohexol (Omnipaque [®])	7
15	Male	49	Facial flush, arm eczema, headache, conjunctivitis	Not stated	6

upper dermal lymphocytic perivascular infiltration, with a small number of eosinophilic polymorphonuclear cells, were observed. Direct immunofluorescence was negative. In 2 patients with a maculopapular rash, histological examinations gave similar results, with more prominent lymphocytic dermal infiltration than was observed in the rubella-like rash, with diffuse dermal oedema without vasculitis, and also with spongiosis and exocytosis of inflammatory cells in the epidermis. Direct immunofluorescence was negative.

Skin test results are summarized in (Table 2) 2 of the 15 patients tested had positive results on patch tests performed with RCM.

Patch tests with IAs were positive in 4 of 15 cases, all with povidone-iodine (with negative patch tests to povidone), iodized alcohol in 3 cases and with potassium iodine in 1 of 2 patients tested. 3 of 4 patients had no history of intolerance to IAs (Table 3) In 1 patient, povidone-iodine was applied on the site of injection of Visipaque[®]. 3 days later, an erythematous plaque developed on this site, a widespread macular erythematous rash, not involv-

ing the neck and face, occurring over the next few days. The rash disappeared after 1 week with topical corticosteroids. We emphasize that in 1 case (no. 11), patch tests with IAs and RCM were positive despite treatment with immunosuppressive drugs, i.e. cyclosporin A and prednisolone prescribed for a heart transplant. The same patient also had positive patch tests to Hexabrix[®] (ioxaglate), Telebrix[®] (ioxitalamate) (Fig. 3), Iomeron[®] (iomeprol) and Iopamiron[®] (iopamidol).

Prick tests with IAs were negative in the 3 patients tested. Prick tests with RCM were negative in all 15 patients tested.

IDTs were negative on immediate readings but positive on delayed readings at 24 h in 8 of 15 cases (Fig. 4).

When results were negative on day 1 reading, we did not observe any later positivity of the IDT during the following week. IDTs were positive with only 1 RCM in 4 patients, with 2 RCM (1 case), with 3 RCM (2 cases) and with 4 RCM (1 case) (Table 2). In the 8 patients with positive delayed IDT, the initial clinical features of the cutaneous adverse drug reaction (CADR) were a maculopapular rash in 2 cases, a macular rubella-like rash in 2 cases, pruritus (1 case), widespread erythema with deep oedema (1 case), a flushed face with arm eczema associated with headache and conjunctivitis (1 case) and maculopapular exanthema with oedema of the face (1 case).

In 12 cases, we intravenously administered increasing concentrations of one of the RCM that had negative results on skin tests. A relapse of the CADR was observed in 5 of 12 cases. The mean delay of onset of the relapse of the CADR after the IDT was from 6 to 24 h.

The clinical features of these relapses were the same as those observed during the initial CADR. As we injected a small concentration of RCM in

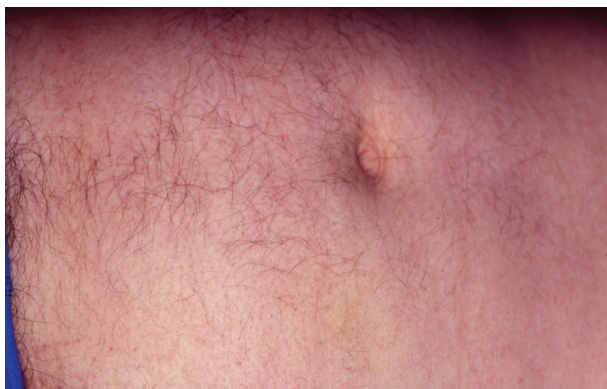


Fig. 2. Macular, rubella-like rash due to Visipaque[®].

Table 2. Results of skin tests and intravenous readministration of radio-contrast media (RCM)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Visipaque [®]															
Patch tests	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Prick tests	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
IDT	–	–	–	–	–	–	–	+d	–	+d	+d	–	–	–	–
Administration	+d	+d	NT	NT	NT	+d	NT	NT	NT	NT	NT	NT	NT	NT	+d
Hexabrix [®]															
Patch tests	–	–	–	–	–	–	–	–	–	–	+	–	–	–	–
Prick tests	–	–	–	–	–	–	–	–	–	–	NT	–	–	–	–
IDT	–	–	–	–	–	–	–	–	–	–	NT	–	–	–	–
Administration	–	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	+d	NT
Telebrix [®]															
Patch tests	–	–	–	–	+	–	–	NT	–	–	+	–	–	NT	–
Prick tests	–	–	–	–	NT	–	–	NT	–	–	NT	–	–	NT	NT
IDT	–	NT	+d	NT	NT	NT	–	NT	–	+d	NT	–	–	NT	NT
Administration	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Xenetix [®]															
Patch tests	–	–	–	–	–	–	–	NT	–	–	–	–	–	NT	–
Prick tests	–	–	–	–	–	–	–	NT	–	–	–	–	–	NT	NT
IDT	–	–	–	–	NT	–	–	NT	–	–	+d	+d	–	NT	NT
Administration	NT	–	–	NT	NT	NT	NT	NT	NT	–	NT	NT	–	NT	NT
Iomeron [®]															
Patch tests	–	–	–	–	–	–	–	NT	–	–	+	–	–	NT	NT
Prick tests	–	–	–	–	–	–	–	NT	–	–	NT	–	–	NT	NT
IDT	–	–	+	–	–	NT	–	NT	–	+d	NT	–	–	NT	NT
Administration	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Omnipaque [®]															
Patch tests	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Prick tests	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
IDT	–	–	–	NT	–	–	NT	–	–	–	+d	–	–	+d	+d
Administration	NT	NT	NT	NT	–	NT	NT	–	–	NT	NT	NT	–	NT	NT
Iopamiron [®]															
Patch tests	–	–	–	–	–	–	–	NT	–	–	+	–	–	NT	–
Prick tests	–	–	–	–	–	–	–	NT	–	–	NT	–	–	NT	–
IDT	+d	–	+	–	–	–	NT	NT	–	+d	NT	–	–	NT	+d
Administration	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	–	NT	NT	NT

+, immediate positive reaction; +d, delayed positive reaction; administration, intravenous readministration of RCM; IDT, intradermal tests; NT, not tested.

most of the cases, the ADR was slighter than the initial one.

2 of 7 patients with negative tests to all the RCM had a relapse of the CADR during rechallenger with the RCM that had induced the initial CADR.

3 of 8 patients who had a positive reaction on skin tests with some RCM had a relapse of their CADR during the administration of an RCM that had shown negative results on skin tests.

Patient no. 2 had a non-tolerated readministration of Visipaque[®]. The progressive readministration of an other RCM (Xenetix[®]), which also had negative results on skin tests, was well tolerated. A second IDT with Visipaque[®] was performed after relapse of the ADR, but remained negative.

Either in their clinical history or in the results of skin tests, cross-reactions were observed between Visipaque[®] and other RCM in 7 cases, respectively, in 5 cases with non-ionic tri-iodized

monomer RCM: Iopamiron[®] (5 cases), Iomeron[®] (3 cases), Xenetix[®] (1 case), Omnipaque[®] (2 cases); with Hexabrix[®], which is an ionic hexa-iodized dimer RCM, in 2 cases and with Telebrix[®], which is an ionic tri-iodized monomer RCM, in 4 cases.

We also observed cross-reactions between Omnipaque[®] and Hexabrix[®] in 2 cases and between Omnipaque[®] and Iopamiron[®] in 1 case.

As controls, we used the results obtained from the same skin tests with RCM performed on 13 patients suspected of having an immediate reaction to RCM. At the end of the investigation, no patient was sensitized. In these control patients, we obtained negative results on patch tests (13 cases), prick tests (11 patients), IDT with Visipaque[®] (8 cases), Hexabrix[®] (7 cases), Iopamiron[®] (7 cases), Xenetix[®] (7 cases), Omnipaque[®] (7 cases), Iomeron[®] (5 cases) and Telebrix[®] (5 cases).

The LATs were negative.

Table 3. Results of patch tests and prick tests with iodized antiseptics

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Povidone-iodine (1 and 10% aq.)															
Patch tests	+	-	-	-	+	-	+	-	-	-	+	-	-	-	-
Prick tests	NT	-	NT	NT	NT	-	NT	NT	-	NT	NT	NT	NT	NT	NT
Povidone 10% aq.															
Patch tests	-	-	-	-	-	-	-	NT	-	-	NT	-	-	NT	-
Prick tests	NT	-	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Iodized alcohol pure															
Patch tests	+	-	-	-	+	-	-	-	-	-	+	-	-	-	-
Prick tests	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Iodoform 5%															
Patch tests	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Potassium iodine															
Patch tests	NT	NT	NT	NT	NT	NT	+	NT	NT	-	NT	NT	NT	NT	NT
Pet.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Alcohol 95%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

+, immediate positive reaction; NT, not tested.



Fig. 3. Positive patch test with radio-contrast media (Telebrix®) in patient no. 11.

Discussion

The frequency of late ADR to non-ionic RCM is not well documented, though it may occur in 2–31% of cases (12, 13). They are more frequent in young adults, women, patients with an allergic history, drug allergy, previous reaction to RCM,

diabetes mellitus, renal disease, cardiac and liver disease (12–15) and in patients treated with interleukin-2 (IL-2) (16).

From our results in this small number of patients, we did not observe a high frequency of atopic history, but 8 patients had a previous history of delayed cellular hypersensitivity with either contact allergy or systemic CADR. In most cases, skin reactions are mild or moderate, and severe delayed reactions are very rare (13).

Our study is the only one where all the onset delays are stated. The mean delay of onset was 26 h, ranging from 6 to 72 h. In previously published studies, the mean delay of onset was 4.9 days (range some hours to 10 days) (17) and 6 h (range 1 h to 7 days) (18). Cutaneous features frequently found in delayed reactions to RCM are maculopapular exanthema, angioedema, flush, itching or urticaria (3). Other clinical features include headache, itching, fever, gastrointestinal symptoms or arm pain (18).

In our patients, we report for the first time the occurrence of delayed pompholyx or pruritus, with positive delayed IDT in both cases (nos 10 and 15).

We emphasize that 2 types of widespread erythematous rashes can occur, a papular, more severe one termed a maculopapular rash (Fig. 1) and a slighter one, macular, sometimes itchy and very transient that we call a rubella-like rash (Fig. 2). The skin eruption in maculopapular rashes is very similar to that observed in maculopapular rashes due to drugs, e.g. amoxicillin, pristinamycin or diltiazem. In contrast, the rubella-like rash is less severe.

We do not know whether the mechanisms are the same in these 2 clinical forms as they are unknown, but histological examinations performed during the CADR in patients with either a maculopapular rash (2 cases) or a rubella-like rash (3 cases) showed similar lymphocytic perivascular dermal infiltration. However, infiltration seemed to be more severe in the maculopapular rashes, being accompanied by keratinocyte alterations and spongiosis which were not found in the rubella-like rashes. Some previous reports also mentioned a dermal perivascular T-cell infiltrate in erythematous rashes due to RCM (5–8).

In the literature, there is only 1 previously published series of 58 patients (17). Patch tests with RCM were positive in 46 of 58 cases. 48 patients had IDT, with delayed positive results in all cases (17). In comparison, we observed positive results on patch tests in only 2 of 15 patients. But in this Akiyama et al. study, the RCM tested, the concentration used for IDT and the results obtained from controls are unknown.

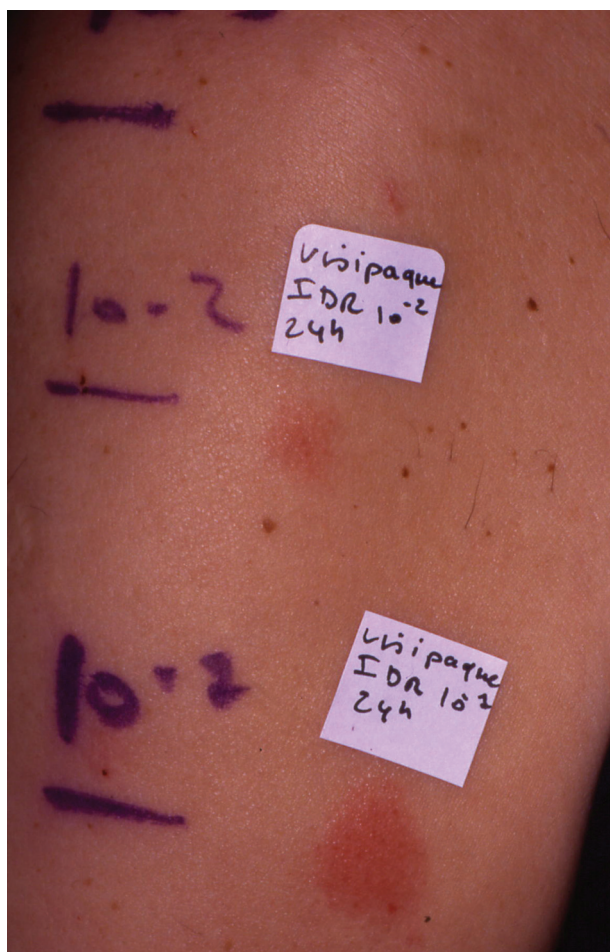


Fig. 4. Delayed positive intradermal tests with Visipaque®.

In other collected case reports, the patch tests were positive for 10 of 10 patients, prick tests positive for 1 of 4 patients and IDT positive for 4 of 5 patients (1–8). In the literature, 28 controls with negative results have been reported (1, 3, 7).

In the literature, patch tests have thus been reported as positive in 56 of 68 cases but in only 2 of 15 of our patients. In the literature, we have found 52 positive IDT in 53 patients tested; but in our series, IDTs were positive in only 8 of 15 patients, though we did not observe any false-positive delayed reaction in 13 controls: with patch tests (13 patients), prick tests (11 patients) and IDT with Visipaque® (8 patients), Hexabrix® (7 patients), Iopamiron® (7 patients), Iomeron® (5 patients), Xenetix® (7 patients), Omnipaque® (7 patients) and Telebrix® (5 patients).

Prick tests seem to have a low value in investigating delayed reactions to RCM.

For the first time, we report reactivation of the initial rash elicited by IDT with RCM.

During the hours following IDT, 2 patients (nos 6 and 15) had reactivation of the CADR, but at a lower intensity than the initial reaction. These symptoms disappeared in 48–72 h.

LATs do not seem to be of much value in investigating delayed reactions to RCM as they were all negative in our patients.

The responsible mechanisms, clinical features, histological findings and high frequency of delayed positive results on skin tests, as well as the high frequency of delayed reactions to RCM in patients treated by IL-2 (16), are all in favour of delayed T-cell hypersensitivity.

For the first time, we report the low negative predictive value of drug skin tests in investigating delayed reactions to RCM. 5 of 12 patients had a relapse of the ADR upon receiving an RCM, even with clearly negative skin tests with the readministered RCM.

These reactions do not seem to be due to active sensitization induced by the skin tests, as the non-tolerated readministration was performed in less

than 10 days after the IDT, which is rather a short time in which to observe active sensitization. Furthermore, in 1 case, the IDT with Visipaque® remained negative even after non-tolerated intravenous administration of Visipaque®.

Usually, RCM are divided into 4 classes according to their chemical structures (Table 4): ionic tri-iodized monomers, ionic hexa-iodized dimers, non-ionic tri-iodized monomers and non-ionic hexa-iodized dimers. They differ in the number of atoms of iodine and the number of carboxylic and hydroxylic functions. They have different physicochemical properties considering their osmolality, viscosity, hydrophilicity, ionic content and pH.

In our patients, cross-reactions between RCM were frequent and observed in 7 of 15 cases.

According to their chemical class, non-ionic tri-iodized monomeric RCM cross-reacted with non-ionic hexa-iodized dimeric RCM in 5 cases, with ionic tri-iodized monomeric RCM in 3 cases and ionic hexa-iodized dimeric RCM in 2 cases. Non-ionic hexa-iodized dimeric RCM also cross-reacted with ionic tri-iodized monomeric RCM in 4 cases and ionic hexa-iodized dimeric RCM in 1 case. Ionic hexa-iodized dimeric RCM cross-reacted with ionic tri-iodized monomeric RCM in 1 case.

Cross-reactions also occurred between RCM and IAs in 3 cases (nos 1, 5 and 11).

In the Akiyama et al. study (17), cross-reactions between non-ionic RCM occurred in 30 of 58 cases, non-ionic RCM cross-reacted with ionic RCM in 1 of 58 cases, and with inorganic iodine in 1 of 25 cases tested. For other authors (1–8), non-ionic tri-iodized monomeric RCM cross-reacted with other non-ionic tri-iodized monomeric RCM in 4 of 9 patients tested (1, 3, 4, 7), with ionic hexa-iodized dimeric RCM in 1 case, with ionic tri-iodized monomeric RCM in 3 cases and with non-ionic hexa-iodized dimeric RCM in 1 case.

Considering all previous reported studies and our results, cross-reactions can occur from 1 chemical

Table 4. Chemical classification of radio-contrast media (RCM)

RCM	Generic name	Commercial name
Ionic tri-iodized monomer	Amidotrizoates	Radioselectan® (Schering Laboratory)
	Ioxitalamate	Telebrix®
Non-ionic tri-iodized monomer	Iomeprol	Iomeron®
	Iopamidol	Iopamiron®
	Iopentol	Ivepaque® (Nycomed Laboratory)
	Iohexol	Omnipaque®
	Ioversol	Optiject® (Guerbet Laboratory), Optiray® (Guerbet Laboratory)
	Iopromide	Ultravist®
	Iobitridol	Xenetix®
	Ioxaglate	Hexabrix®
Ionic hexa-iodized dimer		
Non-ionic hexa-iodized dimer	Iodixanol	Visipaque®

class to another and also with IAs, thus the epitopes involved in these delayed reactions are unknown. A role for iodine itself could even be proposed.

In conclusion, from this first study done with a standardized protocol of drug skin tests, we can still propose beginning with patch tests with RCM, even if they seem of lesser value than in previous papers. Furthermore, there is a lower risk of re-elicitation of the adverse reaction with patch tests than with IDT (2 relapses observed in our patients with IDT).

Prick tests have no value in these patients, but they have to be performed before performing IDT if the reaction has not been well enough defined to diagnose and, consequently, to avoid a severe immediate anaphylactoid reaction.

IDTs are of value with immediate, but most essentially, with delayed readings taken at 24 h. Their specificity seems to be high but remains to be determined with further studies done on a larger number of patients.

Finally, we emphasize that, due to the low predictive value of IDT, negative results on IDT do not permit the immediate readministration of an RCM. It is absolutely necessary to carry out progressive readministration of the RCM under hospital surveillance.

Porri et al. (19, 20) advise premedication with antihistamine and corticosteroid the day before radiological examination in patients who have presented with a delayed reaction to RCM. None of our patients received such premedication. We emphasize that, in 1 of our patients (no. 11), the CADR and positive reactions on skin tests occurred despite long-standing systemic intake of corticosteroids and immunosuppressive drugs prescribed for a heart transplant.

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