

Acute generalized exanthematous pustulosis induced by iomeprol with cross-reactivity to other iodinated contrast agents and mild reactions after rechallenge with iopromide and oral corticosteroid premedication

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Hypersensitivity reactions to iodinated contrast media (ICM) are rare and occur within 1 hour after infusion, but also up to 7 days later.¹ Delayed reactions may be under-reported, because they may appear after patient discharge.² Reactions are usually mild to moderate, but more severe cases, including generalized acute generalized exanthematous pustulosis (AGEP), have been reported.^{3,4} Patch testing helps in identifying the culprit drug in AGEP,⁵ and may help in choosing an alternative therapy when a new radiological examination involving ICM infusion is required.⁶

CASE REPORT

An 88-year-old patient underwent three radiological examinations requiring intravenous infusion of iomeprol within a few days for

preoperative assessment of aortic stenosis and ischaemic heart disease. Prior medication included furosemide, paracetamol, and simvastatin, all of which were taken for >1 year. At 24 hours after the third injection, the patient was admitted for acute exanthema, with a temperature of 39.9°C (Figure 1A). Numerous pustules were present on the face (Figure 1B), axillary folds, and trunk. Blood tests showed leucocytosis, at 21 g/L, with polymorphonuclear cells at 19 g/L. A skin biopsy showed an intraepidermal pustule with numerous polymorphonuclear cells.

Patch testing was performed 6 months after the occurrence of AGEP. Tests with ioxitalamate (++), iohexol (+++), iomeprol (+++), iobitridol (++), iopamidol (++), ioversol (+++), iodixanol (+++) and iopromide (+) gave positive reactions. A test with amidotrizoate gave a

negative result. Furosemide, paracetamol and simvastatin were not tested.

The attending physicians decided on coronary stenting and endovascular valvuloplasty, including ICM administration of iopromide and a 1 mg/kg dose of oral prednisone starting the day before and ending 4 days after the procedure. An erythematous rash of moderate intensity occurred within 1 day, with no pustules or fever.

DISCUSSION

This case represents definite AGEP with maximum score of 12 according to criteria published in 2001 by Sidoroff et al.⁷ Patch testing showed a strong cutaneous reaction to the culprit ICM but also cross-reactivity with many other ICM agents, except for amidotrizoate, which is used as contrast medium in the urinary tract. There are four different chemical subgroups of ICM: ionic monomers (amidotrizoate, ioxithalamate, and iodamide), ionic dimers (ioxaglate), non-ionic monomers (iohexol, iomeprol, iobitridol, iopamidol, ioversol, iopromide, and iopentol), and non-ionic dimers (iodixanol and iotrolan). The following ICM agents have been reported to induce AGEP: iohexol, iopamidol, iodixanol, ioversol, iobitridol, iopromide, and iomeprol.⁴ Eight of 16 reported cases were patch tested, and seven had positive reactions.⁴ This is a high proportion as compared with other delayed reactions induced by ICM.⁸ Multiple cross-reactivity, as seen in our

patient and in other series,^{6,9,10} is challenging. Three groups of ICM agents have been identified as frequently showing cross-reactivity, but cross-reactions among ICM agents do not follow the current chemical classification.¹¹ In our case, the only negative test result was with an agent not used for coronary artery imaging. However, the patient needed coronary stenting and valvuloplasty, thus requiring further coronarography. For this purpose, iopromide was chosen, because patch testing showed a moderate reaction (+) and because of its low osmolality. However, iopromide and iomeprol share a close chemical structure, and cross-reactivity with iomeprol has been reported in only one patient with iopromide-induced AGEP.¹² The use of different classes of contrast agents lacks consensus,¹ but monomeric agents with low osmolality should probably be preferred.⁴ Moreover, the intensity of the patch test reaction cannot predict the severity of a new episode of AGEP. Therefore, we anticipated a new occurrence of AGEP after coronarography with iopromide, so we administered a 5-day course of oral prednisone. This treatment allowed for a safe cardiological procedure with a moderate skin rash and no fever and no pustules. Because of the rarity of the reported cases, the use of corticosteroid premedication is not validated, and there is no evidence that systemic corticosteroids are superior to topical corticosteroids for treatment of the disease once it has occurred.¹³

In conclusion, patch testing in AGEP patients enables identification of the culprit ICM among several suspects and also alternative ICM agents. In our case, we had to choose iopromide because the patient was positive for all ICM agents available for coronarography. However, because of the corticosteroid treatment, the patient had only a mild reaction.

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REFERENCES

1. Egbert RE, De Cecco CN, Schoepf UJ, McQuistion AD, Meinel FG, Katzberg RW. Delayed adverse reactions to the parenteral administration of iodinated contrast media. *AJR Am J Roentgenol*. 2014;203:1163-1170.
2. Corbaux C, Seneschal J, Taïeb A, Cornelis F, Martinet J, Milpied B. Delayed cutaneous hypersensitivity reactions to iodinated contrast media. *Eur J Dermatol*. 2017;27:190-191.
3. Grandvuillemin A, Ripert C, Sgro C, Collet E. Iodinated contrast media-induced acute generalized exanthematous pustulosis confirmed by delayed skin tests. *J Allergy Clin Immunol Pract*. 2014;2:805-806.
4. Velter C, Schissler C, Moulinas C, et al. Acute generalized exanthematous pustulosis caused by an iodinated contrast radiocontrast medium for computed tomography arthrography of the knee. *Contact Dermatitis*. 2017;76:371-373.
5. Barbaud A, Collet E, Milpied B, et al. A multicentre study to determine the value and safety of drug patch tests for the three main classes of severe cutaneous adverse drug reactions. *Br J Dermatol*. 2013;168:555-562.
6. Brockow K, Romano A, Aberer W, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media—a European multicenter study. *Allergy*. 2009;64:234-241.
7. Sidoroff A, Halevy S, Bavinck JN, Vaillant L, Roujeau JC. Acute generalized exanthematous pustulosis (AGEP)—a clinical reaction pattern. *J Cutan Pathol*. 2001;28:113-119.
8. Vernassiere C, Trechot P, Commun N, Schmutz JL, Barbaud A. Low negative predictive value of skin tests in investigating delayed reactions to radio-contrast media. *Contact Dermatitis*. 2004;50:359-366.



FIGURE 1 (A), Diffuse acute exanthematous rash in an 88-year-old man undergoing radiological preoperative assessment of a tight aortic stenosis and ischaemic heart disease. (B), Numerous pustules on the cheek

9. Hasdenteufel F, Waton J, Cordebar V, et al. Delayed hypersensitivity reactions caused by iodixanol: an assessment of cross-reactivity in 22 patients. *J Allergy Clin Immunol*. 2011;128:1356-1357.
10. Torres MJ, Gomez F, Doña I, et al. Diagnostic evaluation of patients with nonimmediate cutaneous hypersensitivity reactions to iodinated contrast media. *Allergy*. 2012;67:929-935.
11. Lerondeau B, Trechot P, Waton J, et al. Analysis of cross-reactivity among radiocontrast media in 97 hypersensitivity reactions. *J Allergy Clin Immunol*. 2016;137:633-635.
12. Bavbek S, Sözen ZC, Aydın O, Özdemir SK, Gül U, Heper AO. First case report of acute generalized exanthematous pustulosis due to intravenous iopromide. *J Investig Allergol Clin Immunol*. 2014;24:66-67.
13. Ingen-Housz-Oro S, Hotz C, Valeyrie-Allanore L, et al. Acute generalized exanthematous pustulosis: a retrospective audit of practice

between 1994 and 2011 in a single center. *Br J Dermatol*. 2015;172:1455-1457.

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