

REFERENCES

- Shibagaki Y, Takaichi K. Significant reduction of the large-vessel blood volume by food intake during hemodialysis. *Clin Nephrol*. 1998;49:49–54.
- Kitai T, Tanaka A, Tokuka A, Tanaka K, Yamaoka Y, Ozawa K, et al. Quantitative detection of hemoglobin saturation in the liver with near-infrared spectroscopy. *Hepatology*. 1993;18:926–36, <http://dx.doi.org/10.1002/hep.1840180426>.
- Hughes S, Yang W, Juszczak M, Jones GL, Powis SH, Seifalian AM, et al. Effect of inspired oxygen on portal and hepatic oxygenation: effective arterialization of portal blood by hyperoxia. *Cell Transplant*. 2004;13:801–8, <http://dx.doi.org/10.3727/000000004783983413>.
- Ookawara S, Ito K, Ueda Y, Miyazawa H, Hayasaka H, Kofuji M, et al. Differences in tissue oxygenation and changes in total hemoglobin signal strength in the brain, liver, and lower-limb muscle during hemodialysis. *J Artif Organs*. 2018;21:86–93, <http://dx.doi.org/10.1007/s10047-017-0978-1>.
- Imai S, Ookawara S, Ito K, Kiryu S, Tabai K, Morishita Y. Deterioration of hepatic oxygenation precedes an onset of intradialytic hypotension with little changes in blood volume during hemodialysis. *Blood Purif*. 2018;45:345–6, <http://dx.doi.org/10.1159/000486232>.
- Hentz F, Kozloski GV, Zeni D, Brun MV, Stefanello S. Relationship between level of forage intake, blood flow and oxygen consumption by splanchnic tissues of sheep fed a tropical grass forage. *J Anim Physiol Anim Nutr (Berl)*. 2017;101:121–6, <http://dx.doi.org/10.1111/jpn.12519>.
- Berzigotti A, De Gottardi A, Vukotic R, Siramolpiwat S, Abraldes JG, Garcia-Pagan JC, et al. Effect of meal ingestion on liver stiffness in patients with cirrhosis and portal hypertension. *PLOS ONE*. 2013;8:e58742, <http://dx.doi.org/10.1371/journal.pone.0058742>.
- Lautt WW. Mechanism and role of intrinsic regulation of hepatic arterial blood flow: Hepatic arterial buffer response. *Am J Physiol*. 1985;249:G549–56, <http://dx.doi.org/10.1152/ajpgi.1985.249.5.G549>.
- Richter S, Mucke I, Menger MD, Vollmar B. Impact of intrinsic blood flow regulation in cirrhosis: maintenance of hepatic arterial buffer response. *Am J Physiol*. 2000;279:G454–62, <http://dx.doi.org/10.1152/ajpgi.2000.279.2.G454>.

Sojiro Imai^a, Kiyonori Ito^b, Susumu Ookawara^{b,*}, Satoshi Kiryu^a, Miho Iguchi^a, Hidenori Sanayama^c, Masafumi Kakei^d, Kaoru Tabai^d, Yoshiyuki Morishita^b

^a Department of Dialysis, Minami-Uonuma City Hospital, Niigata, Japan

^b Division of Nephrology, Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, Saitama, Japan

^c Division of Neurology, Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, Saitama, Japan

^d Department of Internal Medicine, Minami-Uonuma City Hospital, Niigata, Japan

* Corresponding author.

E-mail address: su-ooka@hb.tp1.jp (S. Ookawara).

2013-2514/© 2021 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

<https://doi.org/10.1016/j.nefro.2022.11.009>

Erythematous-violaceous and bullous skin lesions after administration of iodinated contrast in a patient on hemodialysis. A case of fixed drug eruption due to iodinated contrast

Lesiones cutáneas eritematovioláceas y ampollosas tras administración de contraste yodado en un paciente en hemodiálisis. Un caso de exantema fijo medicamentoso por contraste yodado

Dear Editor,

Non-immediate hypersensitivity adverse reactions secondary to the use of iodinated contrast generally occur between 6 and 72 h after exposure,¹ with the most common manifestation being maculopapular rash, urticaria with or without

angioedema and contact dermatitis. Most cases involve a mild to moderate acute rash. Severe late skin reactions are rare, but there have been reports of acute generalised exanthematous pustulosis, DRESS syndrome, vasculitis, Stevens–Johnson syndrome and toxic epidermal necrolysis.² Fixed drug eruption (FDE) is another non-immediate hypersensitivity reaction that



Fig. 1 – Lesions on the skin and mucous membranes after the administration of iodinated contrast.

can be caused by iodinated contrast, but which has rarely been described in the literature.³

FDE is characterised by the appearance of one or several skin lesions in a fixed location, predominantly on the limbs, with a predilection for the hands, feet, lips, glans penis and perianal area. The lesions are erythematous-violaceous macules, of variable size from a few millimetres to 10–20 cm. They appear a few hours after the administration of a drug, forming oedematous plaques, which can sometimes develop vesicles and bullae containing blood-stained serous fluid, that, when broken, cause erosions, which are particularly painful in the genital and oral mucosa. Once the drug is withdrawn, the lesions evolve until they disappear within a couple of weeks, with subsequent reappearance in the same location after re-exposure to the drug, if that is the case. This is the pathognomonic characteristic of the condition.

Diagnosis is essentially clinical, based on the type of skin lesions, the history of drug administration and their resolution after discontinuation. Treatment consists of withdrawing the offending drug and symptomatic treatment.⁴

We present the case of a 77-year-old man with diabetic nephropathy and micronodular goitre, receiving regular treatment with acetylsalicylic acid, folic acid, omeprazole, insulin and atorvastatin. He had no history of drug or food allergies, atopy or other diseases. He had been on haemodialysis since 2013 through a left radiocephalic fistula, with multiple angioplasties for stenosis since 2014.

In July 2020, the patient had a repeat angioplasty due to dysfunction of his left radiocephalic fistula. The following day, a non-pruritic violaceous macular lesion was observed in the palm of his left hand, which looked like a bruise. Three days later, he developed pruritic violaceous macular lesions on the palms of both his hands and on the back of his fingers; a topical corticosteroid was prescribed. A week later, the violaceous macular lesions persisted on the palms of his hands and some had blistered. In addition, there was painful involvement of the palate and nostrils, with no other lesions on the rest of the skin or mucous membranes (Fig. 1). He had not taken any other drugs.

After 12 days, the mucosal lesions had disappeared, but hyperpigmented areas persisted on the palms of his hands, which did eventually disappear at around 20 days (Fig. 2).

There is a description in the patient's medical records of him developing pruritic macular lesions and some localised blisters on his hands, as well as scabs in his nostrils, after the last two angioplasties in 2018 and 2019. The lesions improved spontaneously within a few days, both types being mild in nature, for which no tests were carried out.

The images of the latest lesions were assessed by the Dermatology and Allergy Departments, with the latter performing an allergy study to a battery of iodinated contrasts (including the one involved: iodixanol) using intradermal skin tests with immediate and delayed readings (48 and 72 h), with negative results to the five contrast media tested. Epicutaneous testing with iodinated contrast in areas where skin lesions appeared could not be carried out because the locations made them difficult to perform. FDE induced by iodinated contrast was diagnosed based on compatible clinical data and an alternative contrast medium was indicated for the patient: iobitridol (with less potential for late-onset hypersensitivity).

Three months later, he required angioplasty once again due to dysfunction of the left radiocephalic fistula; the recommended contrast medium was used, without premedication, and the patient had no adverse skin reactions.

Diagnostic tests that can help diagnose FDE are skin biopsy and testing the suspected drug using skin patches on the affected skin area. However, given the absence of pathognomonic histopathology and the low sensitivity of patch tests (they can be positive in up to 30% of cases and are usually negative on healthy skin), it should be remembered that the diagnosis of FDE has to be based on the patient's history and physical examination, assessing the morphology and fixed location of the skin lesions.⁴

In patients with suspected hypersensitivity reaction to iodinated contrast, allergic assessment with a complete medical history and an allergy study using a battery of iodinated contrast media are recommended. Based on these results, an alternative contrast can be indicated,^{5,6} as was the case with our patient.



Fig. 2 – Disappearance of lesions 20 days after administering contrast.

REFERENCES

1. Brockow K, Romano A, Aberer W, Bircher AJ, Barbaud A, Bonadonna P, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media — a European multicenter study. *Allergy*. 2009;64:234, <http://dx.doi.org/10.1111/j.1398-9995.2008.01832.x>.
2. Brockow K. Immediate and delayed cutaneous reactions to radiocontrast media. *Chem Immunol Allergy*. 2012;97:180–90, <http://dx.doi.org/10.1159/000335631>.
3. Frías M, Fernandez E, Audicana MT, Longo N, Muñoz D, Reyes SM. Fixed drug eruption caused by iodinated contrast media. *Contact Dermatitis*. 2011;65:43–4, <http://dx.doi.org/10.1111/j.1600-0536.2010.01816.x>.
4. Avilés Izquierdo J, Huerta Brogeras M, Suárez Fernández R, Lázaro Ochaíta P. Exantema fijo medicamentoso. *Med Integral*. 2002;40:251–5 <https://www.elsevier.es/es-revista-medicina-integral-63-articulo-exantema-fijo-medicamentoso-13038548>
5. Torres MJ, Gomez F, Doña I, Rosendo A, Mayorga C, Garcia I, et al. Diagnostic evaluation of patients with noninmediate cutaneous hypersensitivity reactions to iodinated contrast media. *Allergy*. 2012;67:929–35, <http://dx.doi.org/10.1111/j.1398-9995.2012.02840.x>.
6. Rosado Ingelmo A, Doña Díaz I, Cabañas Moreno R, Moya Quesada MC, García-Avilés C, García Nuñez I, et al. Clinical practice guidelines for diagnosis and management of hypersensitivity reactions to contrast media. *J Investig Allergol Clin Immunol*. 2016;26:144–55, <http://dx.doi.org/10.18176/jiaci.0058>.

Mara Lisbet Cabana Carcasi^{a,*},
Sara Rosalía Santana Romero^a, Laura Beato Coa^a,
Maria Carmen Marcos Bravo^b

^a Centro de Hemodiálisis Os Carballos II, Fundación Renal Iñigo Álvarez de Toledo, Porriño, Pontevedra, Spain

^b Servicio de Alergología, Complejo Hospitalario Universitario de Vigo, Vigo, Pontevedra, Spain

* Corresponding author.

E-mail address: mlcabana@friat.es (M.L. Cabana Carcasi).

2013-2514/© 2021 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).
<https://doi.org/10.1016/j.nefro.2021.05.009>