Bullous FDE induced by an iodinated contrast media

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Abstract

Iopromide is one of the latest generations of non-ionic monomers (NIM) iodinated contrast media (CM). Its use is generally considered to be safe but can occasionally results in adverse events. The frequency of late adverse reactions to non-ionic monomers is between 0.52 and 23%. Delayed adverse reactions mainly manifest as skin reactions such as erythema, maculopapular exanthema and exceptionally as fixed drug eruption (FDE). To the best of our knowledge this is an exceptional case of bullous FDE diagnosed after administration of iopromide. This case was notified to the Tunisian Center of Pharmacovigilance on December 2020 and registered under the number 1925/2020. A 75-year-old woman, with a history of breast carcinoma underwent a chest CT scan with injection of contrast product (ultravist® iopromide) in November 2020. The same day, she developed four, 2 cm in diameter, well limited and oval shaped slightly erythematous itchy plaques on the trunk and right lower limb with a burning sensation. The next day, some of these lesions developed to bullae and erosions. There was not any pathological finding in the physical examination. Biopsy findings were in line with the clinical diagnosis of FDE. The skin lesions were treated with topical corticoids and showed complete resolution one month later with residual hyperpigmentation. Although very uncommon, bullous FDE induced by CM does exist and should be known by radiologists. In this case, we emphasize the importance of a thorough pharmacovigilance investigation with a detailed history and a careful examination of physical and histopathological findings, since patch tests expose the patient to the risk of reactivation and more severe reactions.

Introduction:

There are four types of iodinated contrast media (CM) (ionic monomers, ionic dimers, non-ionic monomers (NIM), and non-ionic dimers) whose side chain ensures high solubility and low toxicity. Iopromide is one of the latest generations of NIM. Although the use of this contrast media is generally considered to be safe and beneficial in medical imaging, it occasionally results in adverse events. The frequency of late adverse reactions to non-ionic monomers is between 0.52 and 23%(1). Delayed adverse reactions mainly manifest as skin reactions such as erythema, maculopapular exanthema and exceptionally as fixed drug eruption (FDE).

FDE can develop from 30 minutes to several days after ingestion of the drug. On re-challenge, the skin lesions occur on the same location. To the best of our knowledge this is an exceptional case of bullous FDE diagnosed after administration of iopromide.

This case was notified to the Tunisian Center of Pharmacovigilance on December 2020 and registered under the number 1925/2020. It was analyzed according to the French updated method for the causality assessment of adverse drug reactions (2).

Case report:

A 75-year-old hypertensive woman, with a history of breast carcinoma, was addressed to our pharmacovigilance center for investigation in December 2020. The patient underwent a chest CT scan with injection

of contrast product (ultravist® iopromide) in November 2020. The same day, she developed four, 2 cm in diameter, well limited and oval shaped slightly erythematous itchy plaques on the trunk and right lower limb with a burning sensation. The next day, some of these lesions developed to bullae and erosions.

The mucous membranes, the palms, the soles, and the face were not involved. There was not any pathological finding in the physical examination. Her temperature was 37°C, and her other vital signs were within the normal range. On histological examination, the acanthotic epidermis includes zones of parakeratosis without apoptotic keratinocytes. The dermis had a moderate lymphocytic inflammatory infiltrate with eosinophils. Biopsy findings were in line with the clinical diagnosis of FDE. The patient reported that she had undergone a chest CT scan using iopromide (ultravist® iopromide) previously on June 2020 and showed no cutaneous adverse event. Therefore, a FDE due to iopromide was suspected clinically and confirmed after histological findings. The skin lesions were treated with topical corticoids and showed complete resolution one month later with residual hyperpigmentation. She was advised to avoid taking iopromide in the future. But, the patient refused to test other commercially available CM.

Discussion:

In our case, the responsibility of iopromide in inducing the bullous FDE was evaluated as I6 (C3S3) according to the updated French method of imputability (2,3) in front of the evocative delay (few hours after receiving the drug), mainly the favorable outcome after drug withdrawal and the data of skin biopsy. In literature, iopromide-induced FDE has been reported for the first time in 2007(4) in a 61-year old male patient. The patient had forgotten to report a similar reaction after iopromide injection, 12 months before this episode. He developed a macula of 2 cm in the right inguinal region which disappeared 5 weeks after the CT examination.

A second case of iopromide-induced FDE was published in 2011(5). In the first episode, the patient developed several painful, annular, erythematous patches on both palms and trunk several days after receiving iopromide. Three years later, he was mistakenly re-administered iopromide and developed on the following morning, painful and reddish papules with vesicles on the same sites.

Patch tests were carried out for these two patients, with a panel of the commercially available iodinated non-ionic and ionic CM since no bullous lesions were noted. The patch-tests remained completely negative for iopromide after 48, 72 and 96 hours.

As a delayed drug-hypersensitivity, both topical and systemic provocation tests could be used to identify the causative agents in patients with FDE. Patch tests are still the diagnostic tool of choice. In our case patch tests were not carried for iopromide considering the major risk of reactivation of bullous lesions and above all the occurrence of a generalized eruption.

The typical presentation of FDE is a solitary, well-demarcated erythematous, round to oval lesion with the possibility of new area involvement, each time the offending drug is taken. The lesions may present as blisters, vesicles, and/or bullae. In some cases, there is an extensive eruption of bullae in addition to the characteristic lesions of FDE, a condition that can be confused with Stevens-Johnson syndrome or toxic epidermal necrolysis(6). The frequency of serious bullous toxidermia due to CM is estimated to 0.3%. Two cases, induced by iopromide, have been reported in 2013 and 2017(7,8).

The first patient developed mild rash, a few bullae in <10% of total body surface area (TBSA), 4 days after the first exposure to iopromide. The second reactive exposure occurred in 24 hours with approximately 80% TBSA involvement. The third reactive exposure occurred within minutes with 100% TBSA involvement and was fatal after 13 days of admission at the burn unit. In the second case, the patient developed cutaneous-mucosal eruption after 5 days of a coronarography using iopromide. The skin biopsy was consistent with Stevens-Johnson syndrome. After an accidental re-exposure, 6 weeks later, he developed an epidermolysis of 30% TBSA with endo-buccal bullae. Histological findings confirmed a toxic epidermal necrolysis (TEN).

Fortunately, our patient did not go through a severe clinical presentation. The delay was relatively short

compared to the two cases described above and there was neither mucosal nor systemic involvement.

Conclusion:

Although very uncommon, bullous FDE induced by CM does exist and should be known by radiologists. In this case, we emphasize the importance of a thorough pharmacovigilance investigation with a detailed history and a careful examination of physical and histopathological findings, since patch tests expose the patient to the risk of reactivation and more severe reactions.

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