An Acute Generalized Exanthematous Pustulosis Induced by Intravenous Iopromide: A Case Report

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Abstract

Acute Generalized Exanthematous Pustulosis (AGEP) is a relatively rare exfoliative dermatosis consisting of a generalized eruption of sterile, nonfollicular pustules arising on widespread erythematous and edematous skin. It is generally attributed to drugs, particularly β -lactam antibiotics, sulfonamide and macrolides. To date, only thirteen cases of contrast media induced AGEP (involving iohexol, iopamidol, iodixanol, and ioversol) have been reported. We describe a patient with AGEP induced by iopromide. He was aged of 49 years. He developed pustular eruption on the back and folds three days after coronarography using radio contrast dye: Iopromide. The culture from pustules was sterile. Laboratory examination revealed an elevated white blood cell count of 22,500/ L with an increased neutrophils count (19,700/ L). A skin biopsy showed the features of an AGEP. The cutaneous eruption resolved with topical corticosteroid within five days. We found only 1 previous reports of iopromide-induced AGEP.

Key-words: Drug eruptions; Acute Generalized Exanthematous Pustulosis(AGEP); Contrast Medias; Iopromide

Introduction

Acute Generalized Exanthematous Pustulosis (AGEP) is an uncommon disease. It is characterized by an erythematous pustular eruption and is usually caused by systemic medication especially β -lactam antibiotics, sulfonamide and macrolides [1]. We report a case of AGEP induced by iopromide. Iopromide-induced AGEP has been reported previously in only one case through the English literature.

Case report

A 49-year-old man was admitted to cardiology department for an acute coronary syndrome. The patient had a history of coronary heart disease for which an angioplasty was made a year ago. He reported that he was developed a cutaneous rash few days later with spontaneous resolution. He had also a psoriasis vulgaris which was in remission for years. Three days after receiving intravenous iopromide (Ultravist®) for

coronary angiography, the patient had developed a pruritic rash predominant in the folds. On physical examination, we noted multiple erythematous patches surmounted by numerous non follicular pustules scattered diffusely over his back and folds (Figure 1). There was no mucosa involvement. Nikolsky sign was absent. The patient had neither fever nor adenopathy. The culture from pustules was sterile. Laboratory examination revealed an elevated white blood cell count of 22,500/ L with an increased neutrophils count (19,700/ L) and eosinophilia (700/ L). C reactive protein was also elevated (62 mg/ L). Other laboratory values were unremarkable. A biopsy specimen was done. The histological findings showed spongiform subcorneal pustules and focal necrosis of keratinocytes. The papillary dermis was the seat of a marked oedema and a perivascular infiltrates with neutrophils and exocytosis of some eosinophils and lymphocytes (Figure 2). These findings were compatible with AGEP. The patient was treated with topical betamethasone leading to desquamation within 5 days with symptom resolution. Patch tests with iopromide (Ultravist), as well as with alternative contrast medias were planned, but the patient died before doing them due to a heart attack.

Discussion

The diagnosis of AGEP was definite in our patient with a score of 10 referring to the criteria of the Euro SCAR-study [2]. In fact, AGEP was first described in 1980 by Beylot, et al. [3]. AGEP has been described after the administration of several drugs, including amoxicillin, macrolides, paracetamol and nifedipine [4]. Our patient developed AGEP following iopromide which contains iodide. It is a non ionic monomeric contrast medium [5]. Iodinated contrast media cause both immediate and non immediate hypersensitivity reactions [5]. Non immediate cutaneous hypersensitivity reactions associated with the administration of iodinated contrast media have been described with different clinical presentation [5]. These were bullous exanthema, flexural exanthema, purpura/maculopapular eruption combined

Figure 1: Erythematous patches surmounted by numerous non follicular pustules in (a): neckline, (b) (c) and (d): trunk, (e): axillary fold, (f): buttocks and (g): leg.

with eosinophilia, psoriasis-like exanthema and AGEP [5]. Nevertheless, only thirteen cases of contrast media induced AGEP have been described [6, 7]. Cases reported incriminate iopamidol, ioversol, iohexol and iodixanol [1,5-14]. Patch tests have confirmed the diagnosis in 3 publications [8,9,11]. All cases of contrast media AGEP, including our, are summarized in table 1. Moreover, AGEP induced by iopromide has been previously

Figure 2: (a): Neutrophilic spongiosis, papillary dermal edema and a perivascular infiltrate containing eosinophils (HE: Original x40). Insert: eosinophils (HE: Original x400). (b): Foci of neutrophilic spongiosis with subcorneal pustules (HE: Original x200).

described in only one case [8]. It was about a 52-year-old woman who developed AGEP three hours after coronary angiography using iopromide (Ultravist®). The rapid onset delay of the AGEP in this woman was explained by advance sensitization as well as our patient [8]. In fact, the pathophysiological mechanism of AGEP is not yet clear. Some authors incriminate a type IV allergic reaction [7]. So, after drug administration, it may take 1–3 weeks before skin lesions appear [6]. However, in previously sensitized patients, the skin symptoms may occur within 24–48 hours [6]. On the other hand, the main differential diagnosis in our case was pustular psoriasis. Indeed, the predominance of the eruption in the folds, the rapid resolution of the eruption, the presence of eosinophils in the inflammatory infiltrate and the absence of histological features of conventional psoriasis suggest that our patient had an AGEP.

Table 1: Characteristic of radio contrast media acute generalized Exanthematous pustulosis.

Author	Year of publication	Age of the patient (Year)	Sex	Medical history	Time to onset (Hours)	Histopathology	EuroSCAR	Iodinated Contrast Media	Patch tests
Atasoy M, et al. [1]	2003	52	F	Abdominal pain	72	Subcorneal blisters including neutrophils and eosinophils, mildspongiosis, and a sparse infiltrate of neutrophils and eosinophils in the papillary dermis	11	Iohexol	Not done
Belgodere X, et al. [6]	2004	40	M	Subarachnoid hemorrhage Testicular tumor	20	Subcorneal blisters including neutrophils and a sparse infiltrate of neutrophils in the papillary dermis	10	Iopamidol	Not done
Peterson A, et al. [13]	2006	Case 1 : 44	F	Gastric bypass surgery	3 Episodes : 60 ; 14 ; 6	Subcorneal pustules, rare single apoptotic keratinocytes, and perivascular and interstitial lymphocytes with scattered eosinophils and neutrophils. Not done	9	Iodixanol	Not done
	2006	Case2 : 30	F	Hodgkin disease Chest pressures Paresthesias	48		6	Iodixanol	Not done

Hammerbeck AA, et al. [7]	2009	84	M	Bladder cancer Hypertension Parkinson disease Diabetes mellitus Hyperlipidemia Coronary artery disease Benign prostatic hyper trophy Right-sided hydronephrosis Chronic renal insufficiency	2 Episodes: 24, 24	Subcorneal pustules, epidermal edema and superficial neutrophilic infiltrate with eosinophils	8 For the two episodes	Ioversol for the 2 episodes	Not done
Paquet P, et al. [12]	2009	80	M	B-cell chronic lymphocytic leukemia	Few hours	Subcorneal pustules and perivascular and interstitial lymphocytes with scattered eosinophils and neutrophils in the papillary dermis	11	Iobitridol	Not done
Kim SJ, et al. [10]	2010	27	M	Chronic renal failure due to IgA nephropathy 2 Kidney transplant operations *Chronic allograft nephropathy Hemodialysis 3 times a week through a left arterio-venous fistula.	6	Not done	8	Ioversol	Not done
Poliak N, et al. [11]	2010	4	M	Tetralogy of Fallot	3 Episodes: 48H, 42H, 6H30min	Subcorneal intraepidermal pustules, spongiosis, rare Apoptotic keratinocytes, papillary dermis edema, inflammatory infiltrates, and few eosinophils,	11	Ioversol	Ioversol + Iohexol + Iothalamate -
Grandvuillemin A, et al. [9]	2014	Case1 : 45	F	allergic rhinitis, Migraine, cerebral arterial embolization	72	Subcorneal pustulosis with neutrophils infiltration	Not evaluated	Iodixanol	Iodixanol+ ioxaglate-iomeprol-Iopamidol-iohexol- iobitridol-
		Case 2 : 26	F	Asthma, migraine	24	Idem	Idem	Iomeprol	Iodixanol-ioxaglate-iomeprol+ Iopamidol-iohexol- iobitridol-
		Case3 ; 79	F	Osteoarthritis, primary amyloidosis, tramadol-induced urticaria	48	Idem	Idem	Iobitridol	Iodixanol-ioxaglate-iomeprol-Iopamidol-iohexol- iobitridol+/-
		Case4 : 24	M	Aneurysm rupture	24	Idem	Idem	Iodixanol	Iodixanol+ ioxaglate-iomeprol-Iopamidol-iohexol- iobitridol-

Bavbek S, et al. [8]	2014	52	F	Non-ST elevation Myocardial infarction	3-4	Epidermal acanthosis with multifocal pustule formation in the upper part of the epidermis, with inflammation and mild edema in the papillary dermis	10	Iopro-mide	Iodixanol+ iomeprol+ diatrizoate+ iopamidol+ iopromide +
Our case	2015	49	M	Coronary heart disease Psoriasis	72	Spongiform subcorneal pustules and focal necrosis of keratinocytes. An oedema and a perivascular infiltrates with neutrophils and exocytosis of some eosinophils and lymphocytes in the papillary dermis	10	Iopro-mide	Not done
F: female; M: Male; results of patch tests were assessed by the International Contact Dermatitis Research Group (ICDRG) scoring system: (-) negative reaction; (+/-) doubtful reaction; (+) positive reaction									

Finally, we report the second case of AGEF induced by iopromide. Our aim is to remain both radiologists and dermatologist aware of this side effect of contrast media.

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