Immunopharmacology and Immunotoxicology

ISSN: 0892-3973 (Print) 1532-2513 (Online) Journal homepage: informahealthcare.com/journals/iipi20

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To cite this article: Gino A. Vena & Nicoletta Cassano (2012) Toxic drug-induced chronic pruritus, Immunopharmacology and Immunotoxicology, 34:6, 1075-1076, DOI: 10.3109/08923973.2012.690100

To link to this article: https://doi.org/10.3109/08923973.2012.690100

Published online: 18 May 2012.

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Immunopharmacology and Immunotoxicology, 2012; 34(6): 1075–1076
© 2012 Informa Healthcare USA, Inc.
ISSN 0892-3973 print/ISSN 1532-2513 online
DOI: 10.3109/08923973.2012.690100

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LETTER

Toxic drug-induced chronic pruritus

Gino A. Vena and Nicoletta Cassano

Department of Biomedical Sciences and Human Oncology, Unit of Dermatology and Venereology, University of Bari, Bari, Italy

Keywords: Chronic pruritus, itch, drugs, iatrogenic, antihypertensive medications, aspirin, adverse drug reactions

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Chronic pruritus, defined on the basis of a duration of 6 weeks or more, is a very distressing and challenging condition.[1] Chronic pruritus in the absence of any skin disease, previously called "pruritus sine materia," can present as pruritus on normal skin or associated with nonspecific skin lesions secondary to rubbing or scratching. It may be the epiphenomenon of several disorders, including endocrine and metabolic diseases, infections, and malignancies.[1,2] Numerous drugs can induce pruritus without specific skin changes.[2–4] Drug-induced pruritus is likely to be underestimated in the general population, particularly in elderly subjects.[2,5]

We retrospectively reviewed 15 patients, diagnosed with drug-induced pruritus and evaluated during a 3-year period. The series consisted of eight females and seven males with a mean age of 70.3 years; 11 patients were receiving three or more medications and six subjects had mild signs of renal dysfunction (Table 1). A modest increase of circulating eosinophils was detected in five patients. No other abnormal findings (i.e. liver dysfunction or cholestasis) were detected by routine laboratory investigations and physical examination. Dermatologic assessment ruled out the presence of specific skin lesions, including dermographism. Sparse excoriated papules and other nonspecific lesions due to scratching were evident in nine patients, and modest xerosis in eight subjects. The suspected culprit drugs were represented by angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers, in most cases combined with hydrochlorothiazide, and low-dose aspirin, alone or associated with the already mentioned antihypertensive drugs (Table 1). Pruritus developed after a mean latency period of 14 months (range, 8–39 months) from the start of the treatment, and was described as severe, disabling and associated with stinging and/or tingling sensations, or dysesthesia. Patients also reported that itch tended to be generalized, often migratory, particularly intense and persistent on the legs and the scalp, and refractory to conventional symptomatic therapies and emollients. On questioning, all patients admitted an insufficient water intake (in most cases less than 1 L per day) and many subjects complained of xerostomia.

Table 1. General characteristics of the patients.

N.	Sex	Age (years)	Suspected drugs	Polytherapy (with ≥3 drugs)	Renal function
1	F	77	ACE-inhibitor + HCTZ	No	Normal
2	F	61	ACE-inhibitor + HCTZ	No	Normal
3	M	59	ACE-inhibitor + HCTZ	Yes	MRI
4	F	72	ACE-inhibitor + HCTZ	No	Normal
5	F	73	ACE-inhibitor + HCTZ	Yes	Normal
6	M	76	ACE-inhibitor	Yes	Normal
7	F	57	ACE-inhibitor	Yes	MRI
8	M	64	ACE-inhibitor, aspirin	No	Normal
9	F	66	ACE-inhibitor, aspirin	Yes	MRI
10	M	71	Sartan + HCTZ	Yes	MRI
11	M	81	Sartan + HCTZ	Yes	Normal
12	F	76	Sartan + HCTZ, aspirin	Yes	MRI
13	M	68	Sartan, aspirin	Yes	Normal
14	F	69	Aspirin	Yes	Normal
15	M	85	Aspirin	Yes	MRI

ACE, angiotensin-converting enzyme; HCTZ, hydrochlorothiazide; F, female; M, male; MRI, mild renal insufficiency (creatinine clearance 50–80 mL/min and/or creatinine 1.2–1.9 mg/dL).

Address for Correspondence: Prof. Gino A. Vena, MD, Unit of Dermatology and Venereology, University of Bari, Policlinico, Piazza Giulio Cesare, 11, 70124 Bari, Italy. Tel/Fax: +39 080 5478920. E-mail: g.vena@dermatologia.uniba.it

(Received 25 March 2012; accepted 28 April 2012)

After consulting patients' primary care physicians and/or cardiologists, the following measures were undertaken for at least 2–3 months: (i) administration of the lowest possible number of medications, limited to the most important drugs (performed in six patients on polytherapy); (ii) discontinuation of the suspected drugs and substitution with alternative molecules if required. In particular, aspirin was replaced with ticlopidine in two cases, and antihypertensive agents with nifedipine in nine cases, doxazosin in one patient, and a β-blocker in another. No alternative drugs were necessary in the remaining cases. Moreover, all patients were instructed to drink at least 1.5–2 L of water per day. In all cases, pruritus improved after 4–6 weeks and disappeared within 12–16 weeks. Over a follow-up period of 12–18 months, the original therapy was gradually reintroduced in 11 patients, with the inclusion of the culprit molecules, which were given, however, in six patients at dosages lower than those used earlier. Pruritus reappeared in three patients 10–13 months after restarting the treatment, and in two cases it was followed by the development of an eczema-like eruption. Such cutaneous manifestations were again responsive to the measures previously described.

Several mechanisms have been proposed to explain the pathogenesis of drug-induced pruritus but often they remain unknown and elusive.[2–4] In the cases herein reported, a "toxic" nature might be hypothesized, with accumulation of drugs secondary to many factors: old age and/or possible impairment of liver metabolism and renal excretion, drug interactions due to long-term polytherapy, and reduced water intake. The approach used in our pilot experience might be helpful to assess the iatrogenic origin of chronic pruritus and may be considered throughout the step-by-step diagnostic work-up, at least in selected cases.

Declaration of interest

The authors declare no conflicts of interest.

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