Eur J Clin Pharmacol (2015) 71:767–768
DOI 10.1007/s00228-015-1840-0

LETTER TO THE EDITORS

Subacute cutaneous lupus erythematosus induced by lansoprazole

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Received: 12 November 2014 / Accepted: 24 March 2015 / Published online: 10 April 2015

A 48-year-old woman presented us with multiple annular erythematous-squamous plaques over trunk and limbs appeared 3 weeks before. There was no mucosal involvement. Her medical history included systemic lupus erythematosus (LES), diagnosed 3 years before and currently no longer treated, and gastroesophageal reflux for which she was in therapy with lansoprazole (30 mg/daily) from 2 months. Microscopy in 10 % potassium hydroxide and culture for mycoses was negative. Routine laboratory investigations were normal, antinuclear antibodies (ANA) negative, and anti-Ro/SSA antibodies positive (titer 1/80). Histology of an annular lesion showed atrophy of the epidermis, hydropic degeneration of the basal layer, edema in the upper dermis, and perivascular and periadnexial lymphohistiocytic infiltrate, consistent with subacute cutaneous lupus erythematosus (SCLE). A direct immunofluorescence test was negative. The patient received oral methylprednisolone (0.5 mg/kg/daily), topical steroids, and continued lansoprazole with improvement but without complete resolution of the lesions. Therefore, lansoprazole was suspected to be responsible of the eruption and replaced by alginate and bicarbonate sodium with complete remission in a few days. Hence, diagnosis of drug-induced SCLE (DI-SCLE) was made.

SCLE is a subtype of cutaneous lupus erythematosus that usually manifests as annular, psoriasiform lesions with limited systemic involvement and typically associated with positive ANA, anti-Ro/SSA, and anti-La/SSB antibodies. It may also be induced or exacerbated by drugs, including thiazide diuretics, calcium channel blockers, and also proton pump inhibitors (PPI) [1]. DI-SCLE does not differ clinically, histopathologically, or immunologically from idiopathic SCLE even though some authors have emphasized that DI-SCLE presented more disseminated cutaneous manifestations (as in our patient) and more frequent occurrence of malar rash and bullous, targetoid, and vasculitic lesions [1].

Patients with autoimmune diseases are more prone to drug-induced or exacerbated SCLE [1], but the pathogenesis of DI-SCLE is not completely understood. However, it may be correlated to antimicrobial peptides (AMPs), small effector molecules of the innate immune system with well-known antimicrobial activity [2, 3]. In fact, several AMPs are increased in CLE at both gene and protein levels. In particular, AMPs were found to be significantly more highly induced in subacute CLE as compared with discoid LE and LE tumidus [2]. This might also explain the low prevalence of skin infections in CLE [2]. The selectivity of AMPs to bacterial cells relies on their cationic structures that are crucial for the interaction with negatively charged bacterial membranes [3]. Cathelicidins are a family of evolutionarily conserved AMPs, and hCAP-18 is the only cathelicidin in humans. Proteolytic cleavage of this preprotein releases a 37-residue known as LL-37 that is secreted by bone marrow cells, circulating leukocytes, and numerous types of epithelial tissues, such as skin. LL-37 could mediate innate immunity through regulating chemotaxis of leukocytes and production of cytokines at sites of infection/inflammation as well as promoting re-epithelization during wound healing. LL-37 orients near the surface of phospholipid bilayers and forms oligomeric structures possessing the ability to disrupt cell membrane [3]. Depending on cellular context, autophagy may serve as a pro-death either pro-survival mechanism through p53 activation [3]. Human LL-37 and its derivatives may contribute to the control of immune-mediated inflammatory diseases through the regulation of pro- and anti-inflammatory cytokines [4].

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Alteration of membrane polarity induced by PPI's administration may induce some surface-exposed epitopes on negatively charged membrane to become visible to immune system recognition. In these circumstances, the activation of autophagic cathelicidin mechanism with pro-apoptotic characteristics could lead to clinical manifestations. In conclusion, DI-SCLE shows spontaneous resolution when the triggering drug is stopped and the clinical improvement could be promptly achieved. We hypothesized that in genetically susceptible hosts, PPI administration could enhance cathelicidin autophagic activity against local antigens such as cutaneous epitopes, inducing the occurrence of DI-SCLE.

Author statement All the authors contributed equally.

Compliance with ethical standards

Funding None.

Conflict of interest The authors declare that they have no conflict of interest.

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