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Case Report

ACE Inhibitors-Induced Skin Reaction: A Case Report

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Abstract:

Angiotensin-converting enzyme (ACE) inhibitors are widely used as antihypertensives, remodeling agents in heart failure, to stop the progression of diabetic nephropathy, as well as for a variety of other clinical purposes. Some side effects of ACE inhibitors are well recognized such as dry cough, hypotension, hyperkaliemia, proteinuria, renal failure. Also, these substances are known to have a wide range of dermatological side effects in addition to their adverse effects on other systems. (1,2)

We report the case of a 46-year-old man treated for dilated cardiomyopathy with severe left ventricle dysfunction, who developed a cutaneous reaction secondary to the introduction of an ACE inhibitor.

Keywords: ACE-inhibitors - cutaneous reaction - side effects

Introduction:

ACE inhibitors are commonly prescribed drugs. Their main indications include hypertension, heart failure, and diabetic nephropathy. They can be responsible of various side effects. In this case, we will focus on the dermatological side effects of ACE inhibitors that physicians should be aware of when prescribing these drugs.

Case report:

We report the case of a 46-year-old patient, chronic smoker, followed for ischemic cardiopathy with severe LV dysfunction. The patient has started a therapy including an ACE inhibitor (ramipril), a beta blocker, and anti-platelet drugs. After one week of the introduction of the ACE inhibitor, the patient developed a painful skin rash with purpuric eruption on the limbs and back.

The clinical examination showed a bullous purpura of the lower limbs and infiltrated purpura on the back, abdomen and upper limbs; The hemostasis test, platelet count, and blood count were normal. There were no abnormalities in the hepatic and renal tests. a skin biopsy revealed subsequent drug-induced neutrophilic vasculitis, which was confirmed by the pharmacovigilance center. After starting an antibiotic treatment based on amoxicillin and clavulanic acid, the patient's condition has improved without further recurrence of his skin lesions.

Discussion

The efficacy and toxicity of a given medicine may vary depending on the individual. The most frequent kind of adverse drug responses is drug-induced skin injury (DISI), which can range from maculopapular eruptions to severe adverse cutaneous drug reactions with mortality rates as high as 40%. Several kinds of DISI are susceptible to particular genetic variations. (3)

ACE inhibitors are widely prescribed for the treatment of hypertension and heart failure. Their side effects are diverse and can be general or mainly manifested by skin involvement of different forms (Table 1). The dermatological side effects are mainly due to hypersensitivity to this drug (4). Ramipril prescription has been associated with rare cases of pemphigus or stevens-Johnson syndrome (5).

Studies in vitro have shown that ACE inhibitors-induced adverse effects in the skin are mostly based on two distinct non-immunological mechanisms.

The first mechanism is described by the ability of medications having thiol groups (sulfhydryl), like captopril, to cause acantholysis through mechanisms that disrupt the balance between the disulfide and thiol group (6, 7). Enalapril and Ramipril, on the other hand, include an amide group and seem to be even more potent acantholytics than captopril or other thiol medications. Although the exact processes of how Ramipril causes acantholytic effects are still unknown, it appears that transglutaminase activity is inhibited (6).

As a result, ACE inhibitors may directly interfere with cell cohesion and result in bullous eruptions without the participation of immunologic processes (8).

Other cutaneous side effects caused by ACE inhibitors have only been documented in isolated case reports. They include psoriasiform (9), pityriasis rosea-like (10), lichenoid eruptions (11), maculo-papular (12), onycholysis (13), erythema multiforme (14), photosensitivity (15), and hair loss (16). Furthermore, pruritus has been noted and is particularly significant because it frequently comes before angioedema (17,18).

Although the function of the AT1 and AT2 receptor subtypes has not been determined, research has shown that the entire renin-angiotensin system, including the precursor of angiotensin II, angiotensinogen, renin, and angiotensin converting enzyme, is expressed in human skin (19). Additional frequent adverse effects of ACE inhibitor medication include proteinuria, agranulocytosis, dysgeusia (gustatory hallucinations), hypotension, hyperkalemia, renal failure, and dry cough (20% of patients). Additional rare side effects include hair loss, hepatitis, cholestatic jaundice, acute pancreatitis, lethargy, nausea, diarrhea, impotence, loss of libido, myalgia, muscle cramps, and the development of anti-nuclear antibodies (20).
Patients should be instructed to report pruritus as soon as possible since in that situation it may be necessary to stop taking ACE-inhibitor medication.

Conclusion

Skin involvement secondary to ACE inhibitors is uncommon and can manifest as a wide range of lesions; the underlying mechanism is unclear. The effects of stopping ACE medications are favorable and usually without complications.

General adverse effects	Cutaneous adverse effects
First-dose hypotension	Angioedema
Hyperkalaemia	Bullous eruptions
Renal failure	Pruritus
Dry cough	Urticaria
Discomfort of the throat	Pityriasis rosea
Voice changes	Erythema multiforme
Disturbances of taste	Psoriasiform, maculopapular and lichenoid eruptions
	Vasculitis
	Onycholysis
	Photosensitivity

Table 1: Summary of general and cutaneous adverse effects of ACE-inhibitors

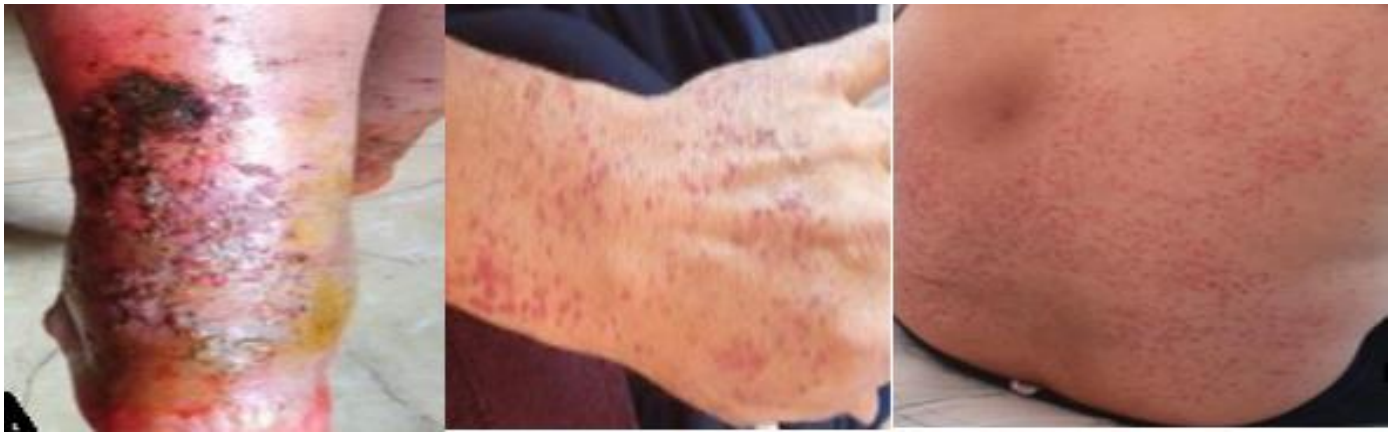

Figure 1: Ramipril induced skin eruptions in our patient

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