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Drug Induced Psoriasis

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SUMMARY Psoriasis is a chronic inflammatory skin disorder clinically characterized by erythematous, sharply demarcated papules and rounded plaques covered by silvery micaceous scale. While the exact causes of psoriasis have yet to be discovered, the immune system and genetics are known to play major roles in its development. Many external factors including infections, stress and medications may exacerbate psoriasis. Some of the most common medications know to trigger or worsen existing psoriasis include lithium, gold salts, beta blockers and antimalarials. Exacerbation of psoriasis due to the following medications has also been observed: adrenergic antagonists, interferon, gemfibrozil, iodine, digoxin and chlonidine. Having reviewed a variety of cases, we observed a relationship between certain medications and documented their involvement in exacerbating or inducing psoriasis.

KEY WORDS: psoriasis, drug eruption, drug induced psoriasis

INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder clinically characterized by erythematous, sharply demarcated papules and rounded plaques covered by silvery micaceous scale (1). While the exact causes of psoriasis have yet to be discovered, the immune system and genetics are known to play major roles in its development. The immune system is somehow mistakenly triggered, which speeds up the growth cycle of skin cells among other immune reactions (2). Current research suggests that the inflammatory mechanisms are immune based and most likely initiated and maintained primarily by T cells in the dermis (3). Antigen-presenting cells in the skin, such as Langerhans cells, are believed to migrate from the skin to regional lymph nodes, where they interact with T cells. Presentation of an as yet unidentified antigen to the T cells, as well as a number of co-stimulatory signals, triggers an immune response, which leads to T cell activation and release of various cytokines. Co-stimulatory signals are initiated *via* interaction of adhesion molecules on the antigen-presenting cells, such as lymphocyte function-associated antigen (LFA)-3 and intercellular adhesion molecule-1, with their respective receptors CD2 and LFA-1 on T cells. Afterwards, these T cells are released into the circulation and return to the skin. T cell reactivation in the dermis and epidermis and the local effect of cytokines such as tumor necrosis factor lead to the inflammation, cell-mediated immune responses, and epidermal hyperproliferation observed in patients with psoriasis. Also, the interleukin (IL)-12-related cytokine, IL-23, was recognized to be involved in the establishment of chronic inflammation and in the development of a T helper (Th)-cell subset producing IL-17 (Th17). These cells are

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very distinct from Th1 and Th2 populations and Th17 cells are now recognized as a third T-effector cell subset. The IL-23/IL-17 pathway has recently been implicated in the induction and progression of a number of inflammatory diseases, including psoriasis. Genetic factors also seem to have a role in the development and course of psoriasis: HLA-B13, -B17, DR7 and -Cw6 are all associated with plaque psoriasis. Many families appear to exhibit autosomal dominant patterns of inheritance with decreased penetrance. Studies of twin siblings have shown concordant disease in 73% of monozygotic twins compared with 20% in dizygotic twins. Several genetic susceptibility loci have also been identified, including psoriasis susceptibility 1 (PSOR1) on chromosome 6, which is associated with up to 50% of cases. Eight other psoriasis susceptibility loci (PSOR2, PSOR3, PSOR4, PSOR5, PSOR6, PSOR7, PSOR8 and PSOR9) have been discovered, as well as the transcription factor RUNX1 (4).

Extrinsic factors are also important in the pathogenesis of psoriasis, perhaps as triggers in genetically susceptible patients. The role of streptococcal infections has been suspected as a triggering factor for psoriasis for many decades, especially in children and guttate forms. The role of streptococcal organisms in chronic plaque psoriasis is less certain compared to the guttate form (5). Viral infections may also play a role in the etiology of psoriasis, as the eruption appears, or the pre-existing disease is aggravated, by an influenza-type illness. External trauma can induce local lesions of psoriasis (the Koebner or isomorphic phenomenon) (6). Patients frequently complain that psychological stress causes flares of psoriasis activity. Review of the literature suggests that stress from major life events, and some personality traits such as difficulty in expressing emotion, may play a role in psoriasis (7). It is not known how stress induces or aggravates psoriasis. Stress has effects on hormones, and on the autonomic nervous and immune systems. There is some evidence that psoriasis is associated with a number of diseases strongly linked to alcohol consumption and smoking (8,9).

Many drugs have also been suspected to trigger psoriasis (10). There have been many medications documented to directly cause the eruption of psoriasis (Table 1), along with others that have been documented to induce psoriasis (Table 2). How these different drugs with different chemical structures can have the same effect is difficult to explain; they may affect the psoriatic process at different stages but with the same results.

It is evident by the large number of associated medications linked to psoriasis seen in Tables 1 and 2 that a great deal of thought and care must be invest-

Table 1. Drugs responsible for the eruption of psoriasis (11)

Acebutolol	Ketoprofen
Acitr patients etin	Labetalol
Aldesleukin (interleukin 2)	Letrozole
Alefacept	Levamizol
Amiodarone	Levobetaxolol
Amoxicillin	Lithium
Ampicillin	Metipranolol
Arpiprazole	Modafinil
Arsenic	Morphine
Aspirin	Meclofenamate
Atenolol	Mefloquine
Auranofin	Mesalamine
Aurotioglucosis	Methyltestosterone
Betaxolol	Metoprolol
Bisoprolol	Nadolol
Botulinum toxin (A & B)	Omeprazole
Captopril	Oral contraceptives
Carbamazepine	Peg interferon
Carteolol	Infliximab
Carvedilol	Penbutolol
Celecoxib	Penicillamine
Chlorambucil	Pentostatin
Chloroquine	Perindopril
Chlorthalidone	Pindolol
Cimetidine	Potassium iodide
Citalopram	Primaquine
Claritromycin	Propranolol
Clomipramine	Psoralens
Clonidine	Paroxetine
Co-trimoxazole	Peginterferon
Cyclosporin	Quinidine
Dexfenfluoramine	Quinine
Diclofenac	Rabeprazol
Digoxin	Ranitidine
Diltiazem	Risperidone
Dipyridamole	Ritonavir
Diphenylhydatonin	Rivastigmine
Doxycycline	Rofecoxib
Doxorubicin	Ropinirol
Efalizumab	Saquinavir
Eletriptan	Sotalol
Enalapril	Sodium chromoglycate
Esmolol	Sulfamethoxazole
Etanercept	Sulfasalazine
Flecainide	Sulfazolamine
Fluorouracil	Tacrine
Fluoxetine	Terbinafine
Fluoxymesterone	Terfenadine
Foscarnet	Testosterone
Gancyclovir	Tetracycline
Gemfibrozil	Thalidomide
Glimepride	Thiabendazole
Glatiramer	Thioguanine
Glipizide	Tiagabine
Glyburide	Timolol
Gold	Trazodone
Granulocyte colony-stimulating factor (GCSF)	Ursodiol
	Valdecoxib
Henna	Valproic acid
Hydroxyurea	Venlafaxine
Ibuprofen	Voriconazole
Interferon alfa-2	Zaleplon
Interferon beta-1b	

JZ Litt: Psoriasis. Drug eruption reference manual 2006:643.

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Table 2. Drugs responsible for the induction of psoriasis (11)

Acetazolamide	Diclofenac
Aminoglutethimide	Diltiazem
Amiodarone	Hydroxychloroquine
Amoxicillin	Indomethacin
Ampicillin	Lithium
Aspirin	Methicillin
Atenolol	Penicillins
Chloroquine	Potassium iodide
Cimetidine	Propranolol
Corticosteroids	Terbinafine
Cyclosporin	

Litt JZ: Psoriasis. Drug eruption reference manual 2006:645.

ed by the physician when choosing the appropriate therapy for patients. There is always a potential risk when prescribing any type of medication and physicians should be constantly reminded of the harmful effects of the therapy they are giving.

DISCUSSION

The importance of recognizing that medications may be the cause of either the eruption (Table 1) or induction (Table 2) of psoriasis must be acknowledged. Many authors also document the relationship between certain medications and the presence of psoriasis. Roujeau *et al*. report that within a small population of 63 patients, medications could be responsible for psoriasis in as many as 83% of cases (12). According to Braun Falco *et al*., some of the most common medications known to trigger or worsen existing psoriasis include lithium, gold salts, beta blockers and antimalarials (6). The exacerbation of psoriasis due to the following medications was observed by Abel *et al*.: lithium, antimalarials, beta blockers, adrenergic antagonists, interferon, gemfibrozil, iodine, digoxin and clonidine (10). Many other authors also observed the relationship between certain medications and documented their involvement in exacerbating or inducing psoriasis. They include lithium, chloroquine and beta blockers observed by Carr (13), antimalarials, lithium, beta adrenergic antagonists, corticosteroids and indomethacin observed by Van de Kerkhof (14), ACE inhibitors observed by Gilleaudeau *et al*. and Oskay (15,16), antimalarials observed by Beus (17), and angiotensin II inhibitors observed by Lamba *et al*. (18). Similarly, a variety of skin eruptions have been described in patients with rheumatic disease during treatment with TNF-α antagonists (19); chronic inflammatory skin diseases, such as psoriasis and eczema-like manifestations, represent the majority of cases (20). In patients taking antipsychotic medications, Brauchli *et al*. found that between the identified 36,702 incident cases of psoriasis and the same number of matched controls the use of 5 or more prescriptions for lithium and atypical antipsychotics yielded adjusted odds ratios (OR) of 1.68 (95% CI, 1.18-2.39; $P<0.01$) and 0.76 (95% CI, 0.55-1.06; $P=0.11$), respectively. They also found that the OR for olanzapine was 0.50 (95% CI, 0.28-0.89, $P=0.02$), suggesting that long-term use of lithium was associated with a small increase in the risk of incident psoriasis, while there is a suggestion of a possible reduced psoriasis risk associated with the use of atypical antipsychotics, mainly olanzapine (21). Bisoprolol, a commonly used beta blocker, was found by Waqar and Sarkar to cause acute worsening of psoriasis within 72 hours of being prescribed in one of their patients (22). Thakor *et al*. documented the first reported case of ramipril-induced psoriasis, which reminds us of the importance of recognizing new medications as the possible causes (23). Rongioletti *et al*. stress that therapeutic agents may be classified as follows: drugs with strong evidence for causal relationship to psoriasis, including lithium, beta blockers and synthetic antimalarial drugs; drugs with a considerable number of studies but insufficient data to support induction or aggravation of the disease; drugs occasionally reported to be associated with aggravation or induction of the disease (24). Physicians must be reminded that psoriasis is not only a dermatologic condition, but a systemic disease with increased inflammatory markers. Life expectancy is reduced by about four years in patients with severe psoriasis, primarily due to their increased cardiovascular risk and therefore merits special attention by any physician faced with this condition (25). The fact that the medications prescribed by physicians may cause morbidity and disease is often overlooked (26). It is important that this problem be acknowledged in order to provide patients with the best healthcare possible and to prevent any serious complications or discomfort. According to the Drug Eruption Reference Manual 2006 by Litt, there is a wide array of documented medications (124 medications) responsible for either the eruption or induction of psoriasis (11). The number of prescribed medications *per* patient *per* year is increasing (26). As a result, this trend is important to recognize because the number of cases of psoriasis will also increase. Antibiotics, antihypertensives, non-steroidal anti-inflammatory drugs and antipsychotics are among the few medications that are responsible for causing psoriasis and require special mention as they are so frequently prescribed. The complexity and wide spectrum of drug induced psoriasis emphasize the importance of proper communication between the physician and

the patient in order to avoid confusion, noncompliance and harm. It is the duty of every physician to be aware of the many medications (Tables 1 and 2) known to induce or cause psoriasis.

CONCLUSION

Psoriasis is a chronic inflammatory skin disorder, which causes a great deal of morbidity and discomfort to the patient. Increasing the awareness of the potential drug side effects is important and physicians must recognize that the medications they prescribe to their patients may be responsible for the eruption, exacerbation or induction of psoriasis.

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