Ankle edema after administration of selective serotonin reuptake inhibitors

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Abstract
Clinical manifestations of drug-induced skin reactions include a wide range of symptoms, from mild drug-induced exanthemas to dangerous and life-threatening generalized systemic reactions. Drug-induced skin reactions to psychotropic medication are usually associated with antiepileptic drugs. However, a significant role can be assigned to selective serotonin reuptake inhibitors. We report a case of a female patient, who after approximately one month therapy with escitalopram developed a bilateral ankle edema, which resolved completely within the first week following its discontinuation.

Case Report
This is a case of a 52-year-old female, with a recent history of panic attack and depression, according to DSM-IV-TR criteria, triggered by a recent retirement. Laboratory and clinical evaluations during the last years had never revealed any pathological findings. At her referral to our department (community mental health service), the patient was suffering from depressed mood most of the day, fatigue, diminished ability to think or concentrate, insomnia, feelings of worthlessness and periods of sweating, chest pain, dizziness and fear of losing control. ESC was administered with an initial dose of 10 mg once a day for a week, and thereafter to 20 mg per day. Three weeks later the patient’s depressive symptoms improved significantly; however she complained about a swelling in both of her feet and she could hardly wear her shoes. The clinical examination revealed a bilateral ankle edema.

Clinical and laboratory evaluations (electrocardiogram, ultrasonography, blood tests, albumins, renal and thyroid function tests, serum electrolytes) did not reveal any pathological findings. There was also no history of arterial hypertension, and after repeated measurements her arterial pressure was within normal range. The patient’s edema resolved completely within ten days after escitalopram discontinuation without any reappearing.

Discussion
In the literature there are several references concerning SSR1 administration and skin pathology. Welsh et al. described first an incidence of paroxetine induced urticarial vasculitis, which is chronic disorder marked by recurrent episodes of erythematous, indurated wheals that histologically manifest the features of leukocytoclastic vasculitis. Vermeer et al. described two case reports in two patients with mycosis fungoides who had an exacerbation of their disease shortly after starting fluoxetine. Fluoxetine is not a carcinogenic agent but it may have tumor growth promoting and immune-modulating properties. Kraskowa et al. has substantiated an increased risk of bleeding events probably caused by blockade of serotonin reuptake in platelets and subsequent platelet dysfunction. Other cutaneous effects of the most commonly used antidepressant medication with SSR1 are also petechiae, ecchymoses, spontaneous bruising, acneiform eruption, leukocytoclastic vasculitis, urticaria, angioedema, erythema nodosum, erythema multiforme, alopecia, phototoxic reactions, photoallergic reactions, acute generalized exanthematous pustulosis. Angioedema has been specifically associated with the use of paroxetine, bupropion and trazodone and it is believed to be type I hypersensitivity reactions. Angioedema affects the face, tongue and extremities and involves a larger edematous area including the dermis and...
subcutaneous tissue. As a possible pathophysiological mechanism lipid-soluble psychotropics are often used to treat skin diseases with psychosomatic indications and several lipid-soluble psychotropic drugs have been examined for their ability to inhibit protein kinase C (PKC)-catalyzed phosphorylation of exogenous substrates and endogenous skin proteins. Phosphorylation of three discrete skin protein substrates at 64, 42 and 28 kDa and a group crowded together at 15-18 kDa was prevented by the antidepressants/antipsychotics. Inhibition was more pronounced in a phospholipid (PL) dependent system, but both drug-PL and drug-PKC interactions seem to be important in the mechanism of action of these drugs. In addition to the tricyclic nucleus, the propanamine side chain or its N-methyl form may influence the interaction of these drugs with PKC and its substrate(s). Chlorpromazine, imipramine, fluoxetine, doxepin, amitriptyline and hydroxyzine used in the practice of deratology may exert their therapeutic effects by modulating skin PKC activity. The relation between cutaneous pseudolymphomas and antidepressant therapy in eight patients treated with fluoxetine hydrochloride revealed that cutaneous pseudolymphomas are associated with antidepressant (AD) therapy, possibly reflecting perturbation of lymphoid function. Concomitant therapy with agents that have additive or synergistic immunomodulatory effects or an immune-dysregulating systemic disease may increase patient’s susceptibility to developing atypical cutaneous lymphoid hyperplasia while the patient is receiving AD therapy.

Conclusions

Bilateral ankle edema constitutes a rare side effect during therapy with ESC. There is further need for close therapeutic monitoring in everyday clinical practice and before the prescription of any antidepressant agent, one should be aware of the specific guidelines, side-effect profile, drug-drug interactions and most current indications.

References