Fixed Drug Eruption due to Atenolol : A Case Report

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Abstract

We report a case of (generalized) fixed drug eruption induced by atenolol, a beta adreno-receptor blocking agent. Atenolol has been shown to be effective treatment for hypertension, angina pectoris and cardiac arrhythmia. However, adverse skin reactions are very rare. We present a case of (generalized) fixed drug eruption due to atenolol and review the cutaneous reaction to the drug.

Key word : Fixed Drug Eruption, Atenolol, Case Report

Fixed drug eruption (FDE), first described by Brocq(1) is a specific type of cutaneous reaction characterized by recurrence of circumscribed lesions at the same site. The drugs that most commonly cause this type of reaction are antipyrine, phenolphthalein, barbiturates, sulfonamides, dapsone, guinine and its derivatives, tetracycline, oxyphenbutazone and chlordiazepoxide(2). Cutaneous drug eruptions due to nifedipine are extremely rare. In the literature, however, we did not find any report on the occurrence of fixed drug eruptions due to Atenolol.

CASE REPORT

A 50 year-old woman attended the general practictioner clinic of Ramathibodi Hospital in April 1996 with an exacerbation of her bronchitis. Her blood pressure (BP) was significantly raised at 240/120 mm Hg and therapy with nifedipine 10 mg twice a day was initiated. Hydrochlorothiazide 50 mg daily was added 2 weeks later with atenolol 50 mg daily after a further 8 days, as her BP remained high. Later in April her BP was 210/90 mm Hg and she gave a history of recurrent eruption on the skin of both forearms, both hands, trunk and both legs,

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which flared up intermittently, always in the same areas. There was a past history of hypertension during her pregnancy 20 years before, and of peripheral vascular disease with intermittent claudication of both calves on walking 100 meters. Her family history was noncontributory. She smoked 10 cigarettes daily. At the height of an exacerbation the affected skin was itchy, bright red and edematous. On examination there was an eruption of symmetrical well circumscribed brownish red macular lesions, nummular and annular on both hands, left shoulders, legs and thighs, the lesions being slightly pigmented and scaling (Fig. 1, 2). A provisional diagnosis of fixed drug eruption was made. Histologic examination showed hydropic degeneration of the epidermal basal cells resulting in pigmentary incontinence and a moderate perivascular mononuclear cells infitrate in the dermis, a characteristic feature of fixed drug eruption (Fig. 3) Atenolol was stopped, methyldopa 250 mg three times a day was substituted for atenolol and within 2 weeks her rash had completely settled. Her unstable BP came under control and all other antihypertensive drugs were subsequently discontinued.

Direct immunofluorescence test showed strong linear deposition of fibrinogen in the dermo-epidermal junction. She was treated symtomatically with systemic antihistamines and topical 0.1 per cent triamcinolone cream. After the lesions had subsided (about 2 weeks) provocation tests were done. The patient showed reactivation of the old lesions following administration of one tablet of atenolol (50 mg). Subsequent provocation tests with hydrochlorothiazide 50 mg/ day and Nifedipine 10 mg were negative.

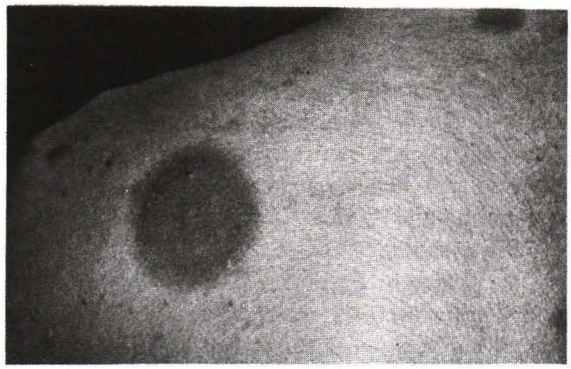

Fig. 1. The lesions of this patient show coin-shaped pigmented lesions on left shoulder.

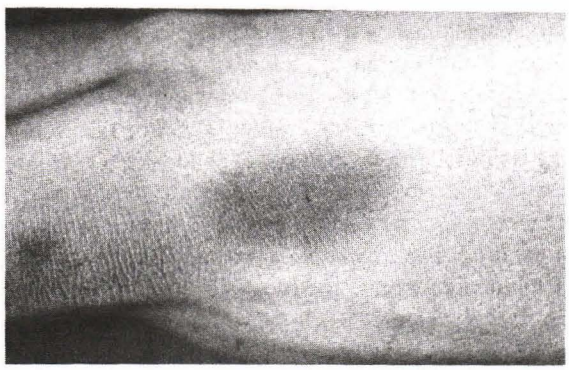

Fig. 2. The same lesions on both hands.

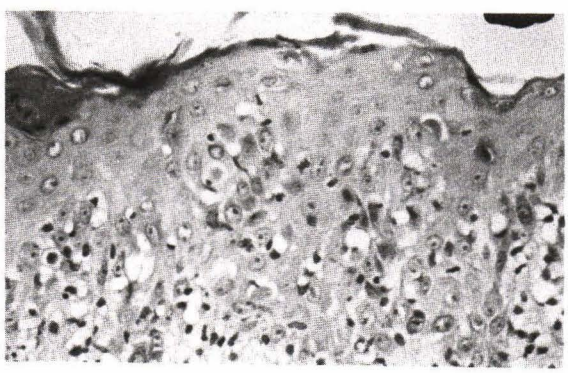

Fig. 3. Specimen from skin lesion of the fixed drug eruption showing exocytosis, spongiosis, basal cell degeneration, incontinence of pigment and perivascular inflammatory cells infiltrate in cutis. (Hematoxylin-eosin stain) (x 100).

DISCUSSION

Atenolol is a beta-adrenoreceptor blocking agent with uses similar to those of propanalol classified as cardioselective action and may therefore be less likely than propanalol to cause bronchospasm and is commonly used in the treatment of hypertension[3], angina pectoris and cardiac arrhythmia. This drug is normally well tolerated, overall side effects include cold extremities, fatique, sinus bradycardia, dry skin, dry eyes and heartburn. Skin reactions are extremely rare, multiple areas of skin necrosis are reported but[4] fixed drug eruption are not mentioned in the data sheet. Our patient produced clinically circumscribed lesions that recurred at the same site with each challenge of the offend-

ing agent. Erythematous and occasionally even bullous eruptions were produced that resolved, leaving pigmented areas. Histopathologic study revealed the presence of vacuolar alteration of the basal layer with subsequent pigmentary incontinence. To our knowledge such a severe reaction to atenolol has not previously documented. Generalized fixed drug eruptions caused by atenolol is not well documented in the literature.

Almagro P, et al[5] described multiple areas of skin necrosis on the feet of a 57-year-old man taking atenolol occuring several months after starting atenolol. Histology showed eosinophilic necrosis in the epidermis and a moderate perivascular infiltration in the dermis. Our additional case was reported where the time course of events suggested an association between the introduction of atenolol and the development of fixed drug eruptions and also rechallenge was undertaken. Our patient presented with the clinical picture of generalized fixed drug eruptions with the histological features of fixed drug eruption. We would suggest, therefore, that atenolol should be added to the list of drugs known to provoke fixed drug eruption. In our cases, cutaneous lesions disappeared after discontinuation of the drug. Since atenolol is a widely used drug it is of major importance to recognize these dermatologic complications.

The possible pathogenetic mechanisms involved in fixed drug eruptions indicate that the immune system plays a major role in the pathogenesis of fixed drug eruption (FDE). Antibodies, serum factors, tissue factors, and cell - mediated immunity have all been implicated in FDE. The drug in the circulation may act as hapten and bind to protein components or receptors in the cells of the lower epidermis. These cells may be either melanocytes[6] or basal layer keratinocytes. This drug protein complex is then detected, processed, and presented to lymphocytes in the dermis or regional lymph nodes by Langerhans cells in a fashion similar to that occurring in allergic contact dermatitis[7-11]. Both T and B lymphocytes are subsequently stimulated, producing lymphokines and antibodies that could eventually cause inflammation and damage cells in the basal cell layer. The mechanism of early dyskeratotic cell formation remains unclear. We suggest that antibody-dependent cellular cytotoxicity (ADCC) may play a role in inducing damage to the keratinocytes, resulting in dyskeratotic cells[12-14]. Such antibodies may bind to keratinocytes at a particular phase of the cell cycle or development. The attached antibodies may then be bound *via* the Fc receptor of K cells (a non-T, non-B subpopulation of lymphocytes) or other cells able to mediate ADCC. This inturn may result in the destruction of keratinocytes. The exact location for preferential localization of FDE lesions to certain skin sites remains unclear.

(Received for publication on January 12, 1998)

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ผื่นแพ้ยาชนิดเกิดซ้ำจากยาอะเทโนลอล : รายงานผู้ป่วย

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รายงานผู้ป่วยหนึ่งรายที่เกิดผื่นฟิกซ์ดรัก จากยาซึ่งเป็นสารปิดกั้นการทำงานของบีตา – อะดรีโนรีเซฟเตอร์ คือ ยาอะเทโนลอล ยานี้เป็นยาที่ใช้ได้ผลดีในการรักษาภาวะความดันโลหิตสูง อาการเจ็บหน้าอกจากโรคกล้ามเนื้อหัวใจขาดเลือด และภาวะการเต้นผิดปกติของหัวใจ ผลข้างเคียงทางผิวหนังจากยาตัวนี้พบได้น้อยมาก และผื่นแพ้ยาชนิดเกิดซ้ำจากยาตัวนี้ยังไม่เคยมีรายงานมาก่อน ในรายงานนี้ได้ทบทวนถึงผลข้างเคียงทางผิวหนังของยาและพยาธิสภาพของผิวหนัง ที่พบได้จากขนานตัวนี้

คำสำคัญ : ผื่นแพ้ยาชนิดเกิดซ้ำ, อะเทโนลอล, รายงานผู้ป่วย

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