Permanent Renal Impairment after Treatment with Cyclosporin

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The effectiveness of cyclosporin (CsA) in severe plaque psoriasis is established [1, 2]. However, CsA may not be randomly used in clinical practice because of its side effects, which include hepatotoxicity, acute and chronic nephrotoxicity, hirsutism, hypertension and toxic effects on the central nervous system [3]. We here present a case of permanent renal impairment after treatment with CsA in a patient with pustular psoriasis and acrodermatitis continua (Hallopeau). The effectiveness of CsA treatment in this patient has been published previously [4].

Case Report. A 61-year-old healthy man, without a medical history, had therapy-resistant generalized pustular psoriasis and acrodermatitis continua (Hallopeau) since 1985. In 1988 oral therapy with CsA 8.0 mg/kg/day (CsA trough level 600 ng/ml) was started in combination with prednisone 10 mg/day. Within 3 weeks the skin was completely clear except for persistent severe nail lesions. Tapering off CsA or prednisone resulted in an exacerbation of acrodermatitis continua and pustular psoriasis. Therefore CsA and prednisone therapy was continued with unchanged dose. No concomitant medication was used.

Within a month serum creatinine started to rise to 157 $\mu\text{mol/l}$. In cooperation with the department of internal medicine, therapy was continued. After 3 months hypertension developed which could be controlled by atenolol 100 mg/day and furosemide 40 mg/day. Other side effects did not occur except for a slight increase in gammaGT, ALAT and LDH.

Within 12 months of CsA treatment, serum creatinine rose from 84 to 344 $\mu\text{mol/l}$. After CsA was lowered to 5.0 mg/kg/day (CsA trough level 290 ng/ml), gammaGT, ALAT and LDH normalized while serum creatinine decreased slowly in the following months. Hypertension however was persistent. Unfortunately the patient's pustular psoriasis and acrodermatitis continua could not be controlled with this dose. Even a combination therapy of CsA with etretinate and local therapy was not effective. Therefore CsA was discontinued and the patient was subsequently treated with methotrexate. He received CsA treatment during 18 months. When CsA treatment was discontinued, serum creatinine was 196 $\mu\text{mol/l}$. In the following 6 months blood pressure normalized and serum creatinine decreased to 138 $\mu\text{mol/l}$. Six months later serum creatinine was unchanged with a glomerular filtration rate of 53 ml/min and an extra renal plasma flow of 200 ml/min.

Discussion. Monotherapy CsA for generalized pustular psoriasis and acrodermatitis continua requires a high CsA dose [4, 5]. This can cause side effects as renal impairment within a short time. Long-term CsA treatment for pustular psoriasis or acrodermatitis continua is therefore not possible.

Serum creatinine improved until 6 months after stopping CsA therapy. Serum creatinine did not change in the following 6 months. Therefore it is likely the patient has irreversible renal impairment due to chronic nephrotoxicity in CsA treatment.

After CsA treatment permanent renal impairment may occur, especially when CsA is administered for a long time [6, 7]. Morphological changes in kidneys associated with CsA treatment suggest the probability of chronic and irreversible renal injury [7, 8]. This case report clearly shows that CsA should be used with restraint and caution until ways are found to mitigate its nephrotoxicity.

CsA has been demonstrated to be nephrotoxic if the concentration is maintained at more than 300 ng/ml for extended periods [7]. Some correlation exists between a rise in serum creatinine and morphological

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changes [8]. Therefore CsA trough level should not exceed 300 ng/ml and any rise in serum creatinine during CsA treatment should be avoided.

References

- Van Joost T. Bos JD. Heule F. et al: Low-dose cyclosporin A in severe psoriasis. A double-blind study. *Br J Dermatol* 1988;118:183-190.
- Ellis CN. Gorsulowsky DC. Hamilton TD. et al: Cyclosporine improves psoriasis in a double blind study. *JAMA* 1986;256: 3110-3116.
- Von Graffenried B. Krupp P: Side effects of cyclosporine (Sandim-mune®) in renal transplant recipients and in patients with autoimmune disease. *Transplant Proc* 1986;116:885-888.
- Korstanje MJ. Bessems PJMJ. Hulsman RFHJ, et al: Pustular psoriasis and acrodermatitis continua (Hallopeau) need high doses of systemic cyclosporin. *Dermatologica* 1989; 178:60.
- Coulson IH. Evans CD. Holden CA: Generalized pustular psoriasis after renal transplantation – failure to suppress with cyclosporin A. *Clin Exp Dermatol* 1988;13:416-417.
- Dieperink H. Leyssac PP. Kemp E, et al: Nephrotoxicity of cyclosporin A in humans: Effects on glomerular filtration and tubular re-absorption rates. *Eur J Clin Invest* 1987; 17:493-496.
- Myers BD. Ross J. Newton L, et al: Cyclosporine-associated chronic nephropathy. *N Engl J Med* 1984;311:699-705.
- Mihatsch MJ. Thiel G, Basler V. et al: Morphological patterns in cyclosporine-treated renal transplant recipients. *Transplant Proc* 1985;17(suppl 1): 101-116.

In Reply

Sir.

We have read with great interest the letter by Beer et al. about the concomitance of psoriasis and atopic dermatitis (AD). We agree with the authors' opinion, that there are some interesting immunological comparisons. In Europe as well as in the US psoriasis is seen in approximately 1-2% of the population [1].

Incidence data for AD range from 0.7 to 2.4 depending upon the age as well as the ethnic group studied [2]. In a national screening survey performed in the US the prevalence of AD was estimated to be from 7 (adults) to 19 (children) per 1.000 [3]. In England a survey revealed a 3.1 % prevalence among children under the age of 5 [4]. As in psoriasis AD tends to become even more frequent in the northern countries of Europe [5].

Since both diseases occur at comparatively high frequencies especially in the younger age group, it would be reasonable to suspect that

in a considerable number of patients both skin diseases are simultaneously present. The calculated rates of simultaneous occurrence of both diseases should amount from 0.05 to 0.30% among the Caucasian population. However, the rate of concomitance which should be statistically expected in both diseases has not yet been proven.

Within a patient sample of 1,065 psoriatics attending an inpatient psoriasis clinic within half a year we found 18 (1.7%) cases with an additional diagnosis of AD confirmed by histological investigation. This finding was within the expected range. A positive history of the disease among family members could be found within 44% of all cases with psoriasis. 39% with AD and 33% with rhinitis allergica or asthma bronchiale. Besides typical psoriatic lesions and atopic eczemas (which were also examined histologically) the following marked symptoms were found in addition: pruritus within 100%; white dermographism within 89% (16 patients); a positive sign of the so-called Auspitz phenomena within 83% (15 patients); rhinitis allergica or asthma bronchiale within 72% (13 patients). In 89% of all patients (16 patients) the IgE level was increased with a geometrical mean of 888 U/ml. The HLA-Cw6 was positive within 50% (9 patients). Since we focused on patients with typical and fully developed symptoms and did not include patients with minimal or mixed symptoms the frequency of concomitant forms could be supposed to be much higher. A possible explanation of the low concomitance of both diseases found until now might be that in an acute state of disease psoriatic lesions might dominate AD and makes an exact diagnosis more difficult. Itching and seborrhea as the symptoms of a therapy thought to be too 'aggressive' might represent the first signs of an additional AD. With regard to the incidence of both diseases it should be expected that a lack of concomitance should rarely be found.

Therefore, in a more thorough documentation this combination should be found more frequently.

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References

Christophers E, Krueger G: Psoriasis; in Fitzpatrick et al (eds): Dermatology in General Medicine. New York, McGraw Hill, 1987, pp 461-491.

Christophers E: Anlagebedingte Hauterkrankungen. Hautarzt 1984(supplVII):3-6.

Hanifin JM: Atopic dermatitis. J Clin Immunol 1984;73:211-222.

Walker RB, Warin RP: Incidence of eczema in early childhood. Br J Dermatol 1956;68:182-187.

Christophers E: Leukocytes and skin diseases: The conflicting patterns of inflammation in atopic dermatitis and psoriasis. 85th Annu Meet Jap Dermatol Ass, Kyoto Kaikan, 1986.