Acute reversible renal failure in acute generalized exanthematous pustulosis

Sir,

Acute generalized exanthematous pustulosis (AGEP) is characterized by rapidly evolving, generalized, aseptic non-follicular pustular eruption arising on a widespread oedematous erythema [1,2]. AGEP was introduced to the international literature as distinct clinical entity only in 1980 [3] and it is in >80% of all cases considered to be a special subtype of cutaneous adverse drug reaction [1,2]. Reduced renal function has been described previously in about a third of all cases without further details [1]. In our report we document for the first time in literature acute, reversible glomerular damage in a patient with amoxicillin-induced AGEP.

Case. A 51-year-old, previously healthy Caucasian man was treated with amoxicillin p.o. for 5 days (day 1–5) for suspected sinusitis. On day 4 a diffuse oedematous erythema including trunk and extremities developed acutely and 1 day later multiple pinhead-sized pustules erupted predominantly on the man’s back accompanied by generalized pruritus. Amoxicillin was stopped and 50 mg/day prednisolon was administered orally between days 4 and 7 without improvement. Some purpuric lesions emerged on the lower extremities. Upon admission at day 8, blood pressure and heart rate were normal. Axillary temperature was 40.1°C and the patient suffered from severe malaise. Discrete ankle oedema was present. Dermatological examination revealed hundreds of pinhead-sized pustules especially on the trunk emerging from a generalized erythematous eruption. The clinical diagnosis of AGEP was established. Laboratory examination showed hyponatraemia (130 mmol/l) (normal range 135–144), hypocalcaemia (1.93 mmol/l) (2.10–2.60), hypoproteinaemia (49 g/l) (66–83), elevated C-reactive protein (CRP) (194 mg/l) (<5 mg/l) and significant leukocytosis (36.1 g/l) (4.3–10.0) with neutrophilia (94%) and no eosinophilia. Platelet count, liver enzymes, and blood coagulation tests were normal. Serum creatinine levels were elevated to 1.8 mg/dl (0.7–1.2) and BUN was 55 mg/dl (20–50). Mild glomerular proteinuria and microhematuria were present. Examination of urinary sediment showed red blood cell casts and >90% of erythrocytes were dysmorphic. The patient refused renal biopsy. Test for antinuclear antibodies, antineutrophil cytoplasmic antibodies, circulating immune complexes, and cryoglobulins were negative. The antistreptolysin O titer was not elevated. C3-complement level was 0.8 (0.9–1.8) at day 9 and 1.2 at day 11. Cultures obtained from blood samples and pustular swabs were sterile. Upon day 10 the itching sensation disappeared and a widespread cutaneous desquamation occurred. On day 15 the cutaneous eruption had resolved completely without specific therapy. In the interval between days 8 and 15, complete blood count was normalized but eosinophils were now elevated to 14% (<8). CRP levels fell continuously to 11 mg/l and body temperature was normalized since day 12. Hyponatraemia, hypocalcaemia, and hypoproteinaemia were also normalized at day 15. Creatinine levels fell to 1.4 mg/dl at day 9 and have continued to be normal since day 10. Urinary sediment has been free of erythrocytic casts or dysmorphic erythrocytes.
since day 11. Proteinuria was reduced to normal levels at
day 15. After 6 months of follow-up, renal function tests were
in normal ranges.

Comment. We present a patient with typical clinical findings
and laboratory tests for AGEP, for which amoxicillin is a
well-documented causative agent [1,2]. There is, however,
no satisfactory hypothesis established yet, why only a small
percentage of all patients with cutaneous adverse drug
reactions develop AGEP. In several previous studies of
patients with AGEP, the liver and kidney were reported to
be also affected [1,2,4]. These findings in combination with
malaise and severe inflammatory response suggest the
presence of multi-organ involvement beyond simple cuta-
neous drug reaction in AGEP [5]. Concerning kidney
function, 32% of patients with AGEP were found to have
disturbed renal function in a retrospective analysis [1]. There
is, however, no detailed information available in the liter-
ature about the nature of renal involvement. Acute inter-
stitial nephritis is a well-established mechanism of adverse
renal drug reaction [6]. However, in our patient there was
strong evidence for predominantly glomerular renal damage.

The exact renal pathology remains unclear, as no biopsy
specimen was obtained. In the present case, glomerulo-
nephritic urinary sediment was transient, completely reversible
and showed a parallel course to the cutaneous eruptions.

Some cases of renal failure in AGEP may find an explanation
in concomitant leukocytoclastic vaskulitis (20% of cases [1]),
as hypersensitivity vasculitis may affect renal function [7].

Recent data demonstrated an involvement of T cells in the
pathogenesis of AGEP, suggesting that renal involvement
may be due to a type III or type IV hypersensitivity reac-
tion [8]. A role of drug-specific antibodies has not been
demonstrated yet.

In conclusion, our case report is indicative of AGEP being
part of a multi-system disease with strong evidence for
glomerular involvement.

Vincent M. Brandenburg
Christian Kurts
Frank Eitner
Emma Hamilton-Williams
Bernhard Heintz

Department of Nephrology and Immunology
University Hospital Rheinisch-Westfälische Technische Hochschule
(RWTH) Aachen Germany
Email: vincent.brandenburg@post.rwth-aachen.de

1. Roujeau JC, Bioulac-Sage P, Bourseau C et al. Acute generalized exan-

2. Sidoroff A, Haley S, Bavinck JN, Vaillant L, Roujeau JC. Acute
generalized exanthematous pustulosis (AGEP) — a clinical re-

3. Beylot C, Bioulac P, Doutre MS. Acute generalized exan-
themtic pustuloses (four cases). Ann Dermatol Venereol 1980;
107: 37–48

4. Leger F, Machet L, Jan V, Machet C, Lorette G, Vaillant L. Acute
generalized exanthematous pustulosis associated with

5. De CA, Van SA, Pipeleers-Marichal MA, Huyghens LP, Suys ET,
Roseeuw DI. Acute generalized exanthematous pustulosis
induced by paracetamol. A case with severe hemodynamic

2001; 60: 804–817


8. Britschgi M, Steiner UC, Schmid S et al. T-cell involvement in
drug-induced acute generalized exanthematous pustulosis. J Clin
Invest 2001; 107: 1433–1441