Acute generalized exanthematic pustulosis induced by icodextrin

A 61-year-old woman with a 20-year history of diabetes mellitus and bipolar disorder developed progressive renal insufficiency that was attributed to long-term lithium toxicity. She began peritoneal dialysis 10 months before consultation with the dermatology service.

She had been switched to icodextrin as a peritoneal dialysis solution 15 days before consultation, and it had been discontinued 9 days later because of poor flow of the solution. The day after discontinuation she noted an asymptomatic inflammatory erythematosus eruption which, over 24 h, became pruritic and extended to involve the rest of her torso, as well as to her scalp, ears and extremities, steadily worsening until the time of consultation.

Her medications included lithium, amitriptyline, trifluoperazine, clonazepam, thyroxine, diltiazem, ramipril, lovastatin, insulin, omeprazole, erythropoietin, vitamins, minerals and quinine as required. These had been unchanged for many weeks. She had no previous history of medication reaction, except for possible renal toxicity due to lithium.

Examination revealed an apparently well, moderately obese, febrile, middle-aged woman with a roughly symmetrical eruption of erythematous plaques and papules surmounted by minute, non-follicular pustules. These were confluent in her inframammary and inguinal regions, and more discrete over her extremities, but her central back and chest were extensively involved. Both hands were moderately swollen, with diffuse palmar erythema studded by minute pustulovesicles. Her full white blood cell, neutrophil and platelet counts were within normal limits.

A skin biopsy from lesional skin on her back showed features of AGEP: intraepidermal pustules filled with neutrophils. The adjacent epidermis was normal in histological appearance. A periodic acid–Schiff stain performed on the biopsy was negative for fungi. Swabs for bacterial and fungal culture were not taken.

Besides discontinuing icodextrin, supportive therapy was initiated including hydroxyzine 25–50 mg as required four times daily and betamethasone valerate 0.1% cream and scalp lotion twice daily.

On follow up 7 days after consultation, she showed 70% improvement overall in the intensity of erythema and the extent of the eruption, with complete resolution of the pustulation, which had been replaced by rings of superficial desquamative scale. The most significant area of persistent involvement was on the hands, which continued to show some degree of diffuse erythema, oedema, scale and superficial fissuring. By 60 days after consultation, the eruption had resolved completely without discontinuation of any medications other than the icodextrin solution.

In 1968, Baker and Ryan detected a clinically distinct subgroup of patients among their review of 104 cases of pustular psoriasis. Subsequently, many cases with similar clinical features have been described under various names. The term AGEP was introduced in 1980. Drugs have been implicated in more than 90% of reported cases, with antibiotics being the most frequent triggers; however, a wide range of offending drugs is reported in the literature, with comprehensive lists published in recent reviews. Two groups of patients have been identified with respect to the timing of onset after administration of the drug. In one group symptoms arise after 1–3 weeks while in the other group the delay is as short as a few hours to 3 days.

Although a precise pathophysiological mechanism has not been identified for AGEP, an immunological recall phenomenon has been suggested in which specific memory T lymphocytes produce neutrophil-promoting cytokines with interleukin (IL)-3 and IL-8 playing an important role.

References

In the present case, icodextrin, a new peritoneal dialysis solution, is incriminated as a cause of AGEP. A few reports have documented a variety of cutaneous reactions due to icodextrin, but AGEP has not been described. The first case of severe exfoliative dermatitis, 10 days after starting icodextrin, was reported in 1997. In a more recent review, two types of skin reactions to icodextrin were demonstrated: exfoliative and blistering dermatoses. The latter were noted to take a longer time to develop and to clear. Blisters were observed on sun-exposed areas. The patients’ skin biopsies showed non-specific findings and porphyrin studies were negative.

We believe that dermatologists should be aware of the various cutaneous reactions reported to be instigated by icodextrin. AGEP has not been observed previously with this solution, is incriminated as a cause of AGEP. A few reports showed non-specific findings and porphyrin studies were negative.

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References


The effect of treatment on serum levels of soluble intercellular adhesion molecules and tumour necrosis factor-receptor 1 in psoriasis

Str. The psoriatic process is mediated, at least in part, by immunological events including the trafficking of activated T lymphocytes and other inflammatory cells into the skin and the production of cytokines and growth factors by these cells and epidermal keratinocytes. Cellular expression of intercellular adhesion molecules (ICAM), ligands for lymphocyte function-associated antigen (LFA)-1, is a prerequisite for cutaneous leucocyte trafficking. ICAM-1 expression is up-regulated on endothelial cells and induced on keratinocytes by interferon-γ and tumour necrosis factor (TNF)-α, whereas ICAM-3 is constitutively expressed on lymphocytes and Langerhans’ cells but not on keratinocytes. The actions of TNF-α, a cytokine important in psoriasis, are mediated by two receptors of molecular weight 55 kDa (TNF-R1) and 75 kDa (TNF-R2).

Circulating levels of soluble ICAM-1 (sICAM-1), soluble ICAM-3 (sICAM-3) and soluble TNF-R1 (sTNF-R1) are increased in the sera of patients with psoriasis and correlate with clinical severity in untreated patients. We investigated whether the raised serum levels of sICAM-1, sICAM-3 and sTNF-R1 in patients with psoriasis, are influenced by treatment and if so whether a reduction in these levels precedes or predicts clinical improvement?

A total of 14 patients (eight male and six female), mean age 32.3 ± 4.4 years, with chronic plaque psoriasis, were enrolled. All patients had untreated, active psoriasis and gave written, informed consent. Four patients were started on cyclosporin at a dose of 5 mg kg⁻¹ day⁻¹; four patients received inpatient therapy with crude coal tar and broadband ultraviolet B phototherapy up to a maximum of 4 weeks; four were treated with twice weekly psoralen photochemotherapy (PUVA) for 12 weeks using a standard regimen; and two patients received treatment with methotrexate 5–10 mg weekly for 12 weeks. Patients were assessed prior to treatment and at 1, 2, 4, 8 and 12 weeks. At each assessment clinical severity using the Psoriasis Area Severity Index (PASI) was measured and serum samples taken for analysis.

Two different monoclonal antibodies (ICR-4 and ICR-8; ICOS Corporation, Bothell, WA, U.S.A.), directed to the extracellular domains of ICAM-3 and truncated, recombinant cICAM-3 expressed in SF9 cells, were used to develop a sandwich ELISA assay. This was used as previously described. Analyses of serum levels of cICAM-1 and cTNF-R1 were performed using a commercial sandwich ELISA assay (Bender Medsystems, Vienna, Austria). All serum assays were analysed in a blinded, coded fashion.

Relationships between pretreatment PASI and serum levels of cICAM-1, cICAM-3 or cTNF-R1 were assessed with the Pearson product-moment correlation analysis. As the