Acute generalized exanthematous pustulosis during the puerperal period: a case report

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Summary

Background: Acute generalized exanthematous pustulosis (AGEP) is an uncommon adverse cutaneous reaction, most commonly associated with drugs. *Case:* A 38-year-old primigravida whose labor had been induced developed erythema over her chest and abdomen. She was transferred to our department after a failed vacuum extraction, and delivered a mature infant by forceps. On day three postpartum she developed a 40.4°C fever. Although ceftriaxone was administered, her fever persisted (> 38°C). On day six of the puerperium, diffuse non-follicular pustules appeared over her neck and trunk, and AGEP was suspected. Two days after ceftriaxone was withdrawn, the eruptions started to resolve without any medical intervention. *Conclusion:* Once the diagnosis of AGEP has been made, the antibiotics being administered must be discontinued. If continued treatment is required, pharmacologically distinct antibiotics must be used instead to aid the rapid self-limitation of the disease.

Key words: Acute generalized exanthematous pustulosis; Antibiotics; Puerperium.

Introduction

Although recent advances in the use of antibiotics during pregnancy have improved maternal and perinatal outcomes, inappropriate antibacterial treatment and overuse of antibiotics can sometimes cause harmful side effects to pregnant women and their fetuses. We report a case of acute generalized exanthematous pustulosis (AGEP) that manifested during the puerperal period.

Case Report

Labor was induced in a 38-year-old primigravid post-term woman at 41^{+1} weeks gestation by her practitioner using an intrauterine extra-amniotic Foley catheter. She started to take an empirical cephalosporin (cefditoren pivoxil, CDTR-PI) after the procedure. Her previous medical history did not include drug eruption or psoriasis, and her current pregnancy was otherwise uncomplicated. Two days later she developed erythema over her chest and abdomen. At 41^{+5} weeks gestation she was referred to us following a failed vacuum extraction. On admission, the patient appeared strained and was wet with perspiration. Her body temperature was 37.2°C, and her blood pressure was 139/74 mmHg. She had the following clinicopathological characteristics: white blood cell count, 20,400/mm^3 with 95.5% neutrophils; hemoglobin, 12.4 g/dl; platelet count, 32.6×10^4/mm^3; and C-reactive protein (CRP), 2.20 mg/dl. Her uterine cervix was fully dilated, and one hour after admission a mature infant was delivered by forceps following an episiotomy. The infant weighed 3,690 g and had Apgar scores of 7 and 8 at 1 and 5 min, respectively. After labor, the patient was treated prophylactically with two 1 gram doses of intravenous oxacephem (flomoxef sodium, FMOX) followed by an oral cephalosporin (cefteram pivoxil, CFTM-PI) for two days. On day two postpartum she developed a high fever (> 39°C). Her body temperature was 40.4°C the following day, her erythema was exacerbated and her serum CRP was elevated to 13.7 mg/dl. Although the antibiotic she was taking was changed to ceftriaxone (CTRX) and administered at a dosage of 2 g/day for three days, her body temperature remained elevated above 38°C. On day six postparturition, diffuse non-follicular pustules appeared over her neck and trunk on an erythematous base (Figures 1a, 1b). CTRX administration was discontinued, and intravenous fosfomycin (FOM) and oral clarithromycin (CAM) were administered instead. Two days later the eruptions began to resolve and desquamation occurred without any medical intervention (Figure 1c). These findings indicated that she had suffered from acute generalized exanthematous pustulosis (AGEP). Histopathological analysis of the skin biopsy revealed a spongiform subcorneal pustule with marked infiltration of neutrophils (Figure 1d), which is consistent with the typical features of AGEP. However, lymphocyte transformation tests (LTT) performed on day 10 and 26 of the puerperium failed to find possible associations between AGEP and CTRX, FMOX, CFTM-PI or CDTR-PI.

Discussion

AGEP is an uncommon (one to five cases per million/year) adverse cutaneous reaction that is characterized by: (1) numerous, small non-follicular, intraepidermal or subcorneal pustules (< 5 mm) on an erythematous background; (2) typical histopathological changes; (3) fever (> 38°C); (4) blood neutrophil count > 7,000/mm^3; and (5) acute evolution with spontaneous resolution of pustules in less than 15 days [1, 2]. The EuroSCAR study group developed a validation score system for diagnosis of AGEP based on three aspects: (1) morphology (pustules; erythema; distribution/pattern; postpustular desquamation); (2) course (mucosal involvement; acute onset (≤ 10 d); resolution ≤ 15 d; fever ≥38°C; polynuclear neutrophils ≥ 7,000/mm^3); and histology [3]. Our patient scored 10 points using this system, which was interpreted as "definite" AGEP.

AGEP is drug induced in more than 90% of cases, with β-lactam and macrolide antibiotics being the most common causative agents, followed by acute infections

Revised manuscript accepted for publication January 16, 2012

Fig. 1a

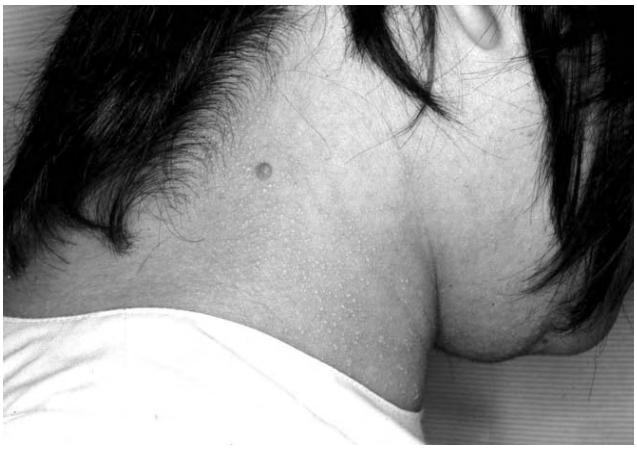

Fig. 1b

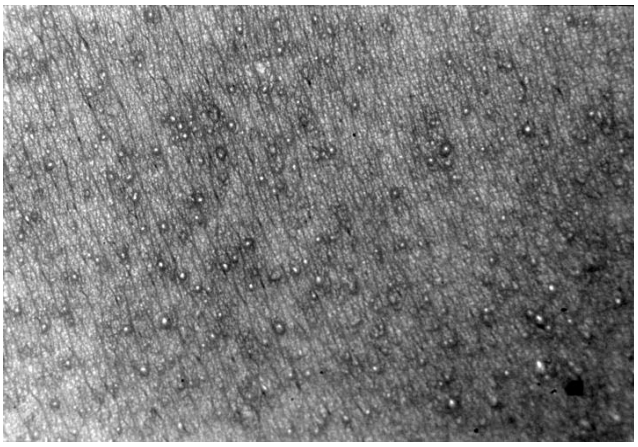

Fig. 1c

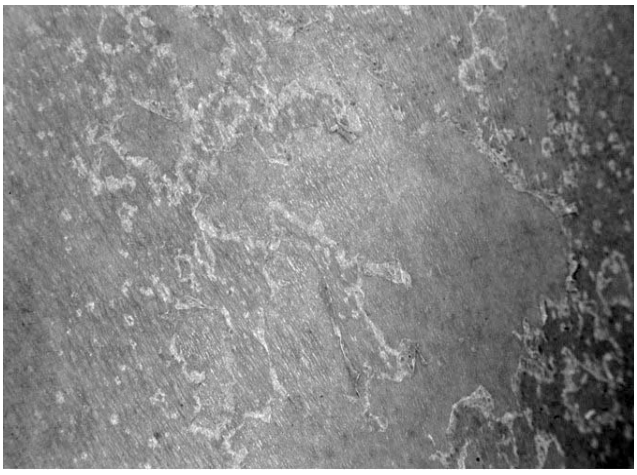

Fig. 1d

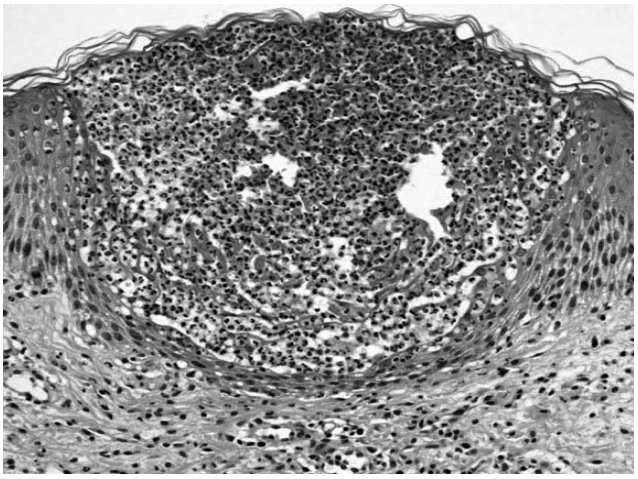

Figure 1. a) A fine pustular eruption located at the neck, consisting of numerous non-follicular pustules on an erythematous base, postpartum day 6; b) Close-up view of the same region, postpartum day 6; c) Close-up view of the same region showing desquamation, postpartum day 10; d) The histopathological findings of the skin biopsy showed spongiform subcorneal pustules of the epidermis (H&E staining, × 200).

[2, 3]. Once the diagnosis of AGEP is made, the causative drug must be discontinued and other antibiotics must not be administered unless there is a clear and well documented associated infection [3]. In the present case we hesitated to cease administration of antibiotics even though repeated blood cultures failed to detect microorganisms, because the patient had devastating vaginal injuries caused by the forceps delivery. Instead, we substituted CTRX, a β-lactam, with two pharmacologically distinct antibiotics, FOM and CAM, which resulted in a rapid self-limitation of the disease. We performed lymphocyte transformation tests (LTT) on day 10 and 26 of the puerperium to investigate possible associations between AGEP and CTRX, FMOX, CFTM-PI and CDTR-PI. However, we were unable to definitively determine the causative agent of AGEP in this patient. LTT measures the proliferation of T-cells in response to a drug *in vitro,* indicating sensitization, but has a limited sensitivity (60-70% for β-lactams) [4].

Pregnancy associated with AGEP is rare, and only five cases have been reported to date [5-9]. Although the pathogenesis of AGEP remains unknown, possible involvement of drug-specific T-cells has been raised. Drug-specific T-cell clones from lesional skin and the circulation have been found that are positive for the neutrophil-attracting cytokine interleukin (IL)-8 [2]. It is of note that these pregnancy-related AGEP cases developed following procedures that exposed patients to possible intrauterine infection, such as amniocentesis [5], cesarean section [8] and labor induction [9]. The present case of AGEP was also preceded by induction of labor using an intrauterine extra-amniotic Foley catheter. Reich et al. [6] reported a case of AGEP following premature labor that was likely caused by chorioamnionitis. The human placenta constitutively produces IL-8 during pregnancy and enhances its production in chorioamnionitis [10]. Further investigations are required to determine if there is an association between the specific immunological environment during pregnancy and the pathogenesis of AGEP.

In summary, once the diagnosis of AGEP has been

made, the antibiotics being administered must be discontinued. If continued treatment is required, pharmacologically distinct antibiotics must be used instead to aid the rapid self-limitation of the disease.

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