overall concerning the decision of prescribing allergen-specific immunotherapy. Therefore, SPT could be considered a first line testing: useful for selecting patients with possible allergy. On the contrary, serum-IgE measurement may be a reliable tool for identifying true allergic patients and choosing the allergen extract for immunotherapy.

Ethical disclosures

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Conflict of interest

The authors have no conflict of interest to declare.

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Symmetrical drug-related intertriginous and flexural exanthema induced by two different antibiotics

To the Editor,

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is a benign drug reaction.[1] SDRIFE diagnostic criteria are exposure to a systemically administrated drug (at the first or subsequent doses, excluding contact allergens), sharply demarcated erythema of the gluteal area and/or V-shaped erythema of the inguinal/perigenital area, involvement of at least one other intertriginous/flexural localisation, symmetry of affected areas and absence of systemic symptoms and signs.[2] The difference between SDRIFE and baboon syndrome or stage 3B allergic contact dermatitis syndrome is that in SDRIFE there is no previous contact sensitisation.[3] The exact mechanism of SDRIFE is not known. A T-cell mediated delayed type of hypersensitivity reaction type IV may play a role in the pathogenesis.[1,2,4]

A twenty-two-month-old male patient presented with bilateral axillary rash and pruritus on the third day of a course of cefixime treatment for acute otitis media. Physical examination revealed a demarcated pruritic erythematous papulovesicular rash with slight desquamation in the bilateral axillary region (Fig. 1). The patient had been treated with prophylactic ampicillin since birth due to hydronephrosis and recurrent urinary tract infections. He did not use any antibiotics except for amoxicillin clavulanate and amikacin. No adverse drug reaction was reported. Other personal and family history was unremarkable.

Upon a presumptive diagnosis of SDRIFE, the patient's antibiotic therapy (cefixime) was ended. His complete blood count, liver, and renal function tests were normal, and viral serology was negative for CMV, EBV, rubella, hepatitis A, and hepatitis B. When sent for consultation with the dermatology

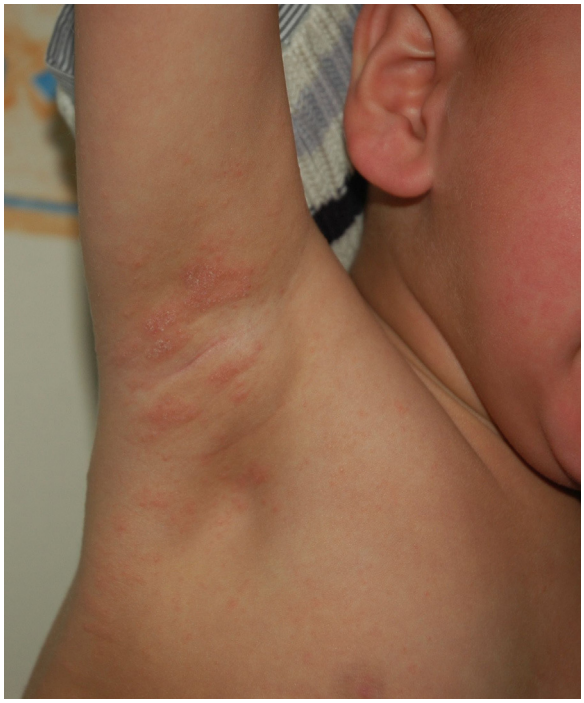

Figure 1 Demarcated pruritic erythematous papulovesicular rash with slight desquamation in right axillary region.

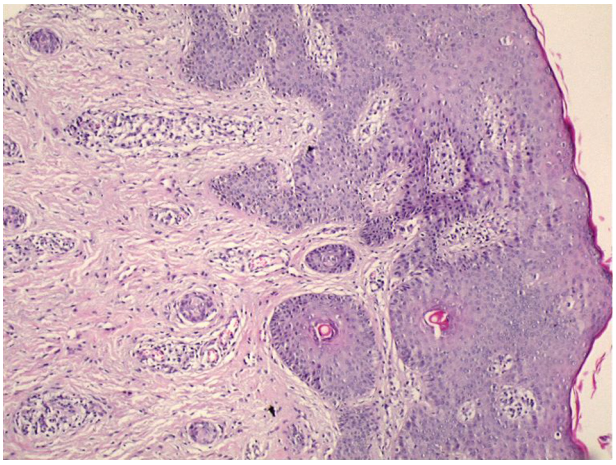

Figure 2 Significant focal spongiotic foci, a few apoptotic keratinocytes, and rare lymphocytes in epithelium; oedema, inflammation rich from lymphocytes and plasma cells in papillary dermis (H&E100×).

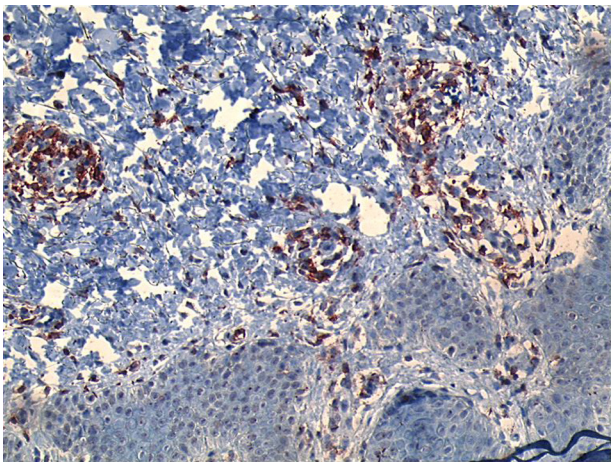

Figure 3 Immunohistochemically dermal lymphocytic infiltration showed a strongly positive reaction to anti-CD4 antibody (50×).

department, the patient was diagnosed with tinea corporis, and topical antifungal (ciclopirox olamine and isoconazole nitrate) treatment was initiated. On the second day of the topical antifungal treatment, he presented with spread of pruritic rash to the trunk and bilateral inguinal regions. Contact urticaria due to topical antifungal treatment was diagnosed and the antifungal treatment was stopped. The rash regressed in three days and was resolved in ten days.

Next, fifteen days later, on the fifth day of clarithromycin treatment for acute otitis media, the patient presented with rash and pruritus of his bilateral axillary regions. Physical examination revealed pruritic lesions in both axillary regions, similar to the previous lesions and pruritic erythema in both popliteal and inguinal regions. Routine laboratory tests were again normal. The clarithromycin treatment was ended and hydroxyzine therapy begun. An otoscopic examination was normal, and the prophylactic ampicillin treatment was continued. The child had punch biopsy of skin. There were significant focal spongiotic foci and a few apoptotic keratinocytes and rare lymphocytes in the epithelium, along with oedema, inflammation rich from lymphocytes and plasma cells in the papillary dermis (Fig. 2). Immunohistochemically, dermal lymphocytes showed diffuse, strongly positive labelling with anti-CD3 and anti-CD4 (Fig. 3), and less positive labelling with anti-CD8. They were rare positive for anti-CD20 and negative for anti-CD56.

The rash regressed in three days and was resolved in seven days. A patch test with cefixime and clarithromycin was performed five weeks later, according to the current guideline. Cefixime diluted 30% in water and in petrolatum, a drop of clarithromycin (50 mg/ml), and normal saline and petrolatum (as negative controls) were applied to normal skin on the child's upper back using Finn Chambers on 12 mm adhesive tape. The occlusion time was 48 h; results were read 15 min after removing the cups, and then again at 48 and 72 h.[5] A use test with ciclopirox olamine and isoconazole nitrate was performed three months later.[6] First, ciclopirox olamine was applied to the flexor forearm once a day for seven days, and isoconazole nitrate was similarly applied in the following week. No reaction was observed. An oral provocation test was not performed in view of the risk of a more severe generalised reaction.

SDRIFE is a rare drug eruption with benign prognosis. Häusermann et al. reviewed 42 cases of SDRIFE, including their own cases.[2] The most common offending drugs reported were beta-lactam antibiotics especially amoxicillin. Additionally, two cases of SDRIFE induced by penicillin, and amoxicillin-clavulanate have been reported.[7,8]

We diagnosed our patient as exhibiting SDRIFE. He had involvement of both axillary regions, the eruptions were symmetrical, and he had no systemic symptoms or signs. He had been taking prophylactic ampicillin treatment since birth without any reaction. In his first admission, the rash had started on the third day of cefixime treatment and was resolved in ten days after stopping cefixime (with topical antifungal treatment). In the second admission, pruritic rash which had started on the fifth day of clarithromycin treatment was resolved in seven days after stopping clarithromycin. On both occasions, the favourable response to discontinuation of newly introduced antibiotics without the cessation of ampicillin prophylaxis suggested that these drugs were responsible for the development of SDRIFE. The latency period between drug administration and eruption is from a few hours to days, and eruptions generally resolve spontaneously within three weeks of discontinuing the offending drug.[1,2] In our case, the eruptions did not involve gluteal or inguinal region in the initial admission. We thought that his eruptions could be a SDRIFE variant. During the second admission, his lesions in inguinal and axillary region were compatible with SDRIFE.

It has been reported that the pathomechanism of SDRIFE involves type IVa and IVc reactions.[4] Our data rather support the role of type IVa hypersensitivity reaction as disease mechanism. Similar findings have also been reported in a case of SDRIFE due to radiocontrast media.[9] $CD8^+$ T-cells may function as suppressor cells that dampen down the reaction, as suggested by Werfel et al. in allergic contact dermatitis.[10]

Patch tests are useful in defining the culprit drug in SDRIFE.[1] In our case, a patch test with cefixime and clarithromycin was negative. In Häusermann et al., patch tests were performed in 23 of 42 SDRIFE cases, with only half

(12) being positive.[2] For antifungal drugs, we performed a use test, which also resulted negative. The gold standard for diagnosis is the controlled drug provocation tests, but caution must be taken.[1]

To our knowledge, this is the first case report of SDRIFE with two different classes of antibiotics at two different times. While administering treatment with a different group of antibiotics to a patient having a history of SDRIFE, the risk of recurrence should be considered.

Ethical disclosures

Patients' data protection. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

Conflict of interest

The authors have no conflict of interest to declare.

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