Pharmacology and therapeutics

**Intertriginous lymphomatoid drug eruption**

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**Abstract**

A 76-year-old man developed a maculopapular purpuric eruption confined to the intertriginous areas (i.e. the inguinal, gluteal, and axillary folds). Two days before the eruption appeared, he had received a second course of chemotherapy consisting of cisplatinum 40 mg and gemcitabine (Gemzar) 1700 mg for the treatment of squamous cell carcinoma of the lung stage III B. The histologic picture was of either lymphomatoid drug eruption or lymphomatoid papulosis. The antineoplastic therapy was changed to once-weekly intravenous vinorelbine (Navelbine) 50 mg, a Vinca alkaloid, and the eruption resolved completely within two weeks without any further therapy. These circumstantial evidences support the diagnosis of intertriginous drug eruption. Our case is interesting and unusual in that it demonstrated a rare clinical presentation of drug eruption, namely, intertriginous drug eruption or baboon syndrome, with a histologic picture of a lymphomatoid drug eruption that can mimic lymphoma. We are unaware of any earlier reported case of baboon syndrome with a histologic picture of lymphomatoid drug eruption. The pathomechanisms of both types of drug eruption, i.e. baboon syndrome and lymphomatoid drug eruption, are not fully understood.

**Report of a case**

A 76-year-old man presented with a maculopapular purpuric eruption confined to the intertriginous areas (Fig. 1) (i.e. the inguinal, gluteal, and axillary folds). Two days before the eruption appeared, he had received a second course of chemotherapy consisting of cisplatinum 40 mg and gemcitabine (Gemzar) 1700 mg for the treatment of squamous cell carcinoma of the lung stage III B. He had also been administered dexamethasone and granisetron prior to the chemotherapy to avoid nausea and vomiting associated with the antineoplastic therapy. He denied using any other medication except for omeprazole, which he had been taking for years. The patient had no other systemic symptoms or any other areas of affected skin. He had no lymph node, liver, or spleen enlargement on palpation. A skin biopsy specimen was obtained from the eruption of the buttocks for histologic examination with hematoxylin-eosin. The histologic picture revealed superficial and deep perivascular lymphocytic infiltrate (Fig. 2) with sparse nuclear dust, interstitial eosinophils, and large atypical lymphocytes, some of them showing prominent nucleolus (Fig. 3). On immunohistochemical stainings, these cells were positive for CD30 with membranous staining and few also showed perinuclear dot.

The antineoplastic therapy was changed to once-weekly intravenous vinorelbine (Navelbine) 50 mg, a Vinca alkaloid, and the eruption resolved completely within 2 weeks without any further therapy.

**Discussion**

Although drug-associated eruptions can mimic a variety of skin diseases, intertrigo is generally easily distinguishable, and is, therefore, not listed in the differential diagnosis of these kinds of reactions. Our diagnosis was based mainly on circumstantial evidence: the appearance of the eruption 11 days after the first course of chemotherapy and 2 days after the second course, as well as the resolution of the eruption within 2 weeks following cessation of the offending drug, without any further therapy. The biopsy finding raised the possibility of either lymphomatoid drug eruption or lymphomatoid papulosis. The latter could be excluded when considering the clinical appearance, the course of the rash, and the fact that the culprit drugs have immune dysregulating properties.
which are often associated with this kind of drug eruption.¹

In 1984, Andersen et al. described an eruption with a very characteristic distribution pattern provoked by several allergens, such as ampicillin, nickel, and mercury.² They gave this reaction pattern the catch-name “the baboon syndrome” because of the characteristic, bright red, well-demarcated eruption, predominantly located on the buttocks and genital area – reminiscent of the red bottom of the baboon. They were convinced that this syndrome represented a special form of hematogenous or systemic contact-type dermatitis. Other authors who later described the syndrome accepted Andersen et al.’s hypothesis (reviewed in).³ Several important studies that appeared during the last 5 years.⁴⁻⁵ suggested what we had emphasized some 15 years ago⁶ – that the baboon syndrome should be distinguished from hematogenous or systemic contact-type dermatitis. In two articles which proposed criteria for diagnosing this syndrome, the first criterion was “Exposure to a systemically administered drug, first or repeated doses (contact allergen excluded)”⁴⁻⁵. In a review of 100 published cases of baboon syndrome, 50 were found to be drug-induced. Of these, only eight were considered representatives of systematically induced allergic contact dermatitis, and 42 were considered examples of drug eruptions of oral or intravenous drugs.⁵

In contrast to the homogeneity of baboon syndrome cases, in terms of clinical distribution, range of primary cutaneous lesions, latency period after drug intake and courses, the syndrome’s histologic picture is very variable. The main finding in drug-induced baboon syndrome is the superficial perivascular infiltrate composed of mononuclear cells, sometimes including neutrophils and eosinophils. Other rare findings include vacuolar and hydropic alteration of the basal cell layer with necrotic keratinocytes, and histologic pictures seen in bullous drug eruption, fixed drug eruption, and others.⁵

We are unaware of any earlier reported case of baboon syndrome with a histologic picture of lymphomatoid drug eruption. Lymphomatoid drug eruption is a form of cutaneous pseudolymphoma that most frequently mimics the patch and plaque lesions of mycosis fungoides and occasionally mimics lymphomatoid papulosis or B-cell lymphoma. The pathogenesis of lymphomatoid drug eruption is not clear. Unlike other forms of cutaneous drug eruption, the lymphomatoid type does not represent an allergic or hypersensitivity reaction to the drug. The skin eruption most likely is caused by a direct effect of the drug on the lymphocyte function, resulting in immune dysregulation.⁷ Most, if not all, of the cases of pseudolymphoma

**Figure 1** Erythematous purpuric plaques on the buttocks, reminiscent of the red buttocks of a baboon

**Figure 2** Superficial and deep perivascular lymphocytic infiltrate with interstitial eosinophils (H&E 100×)

**Figure 3** Higher magnification reveals atypical lymphocytes with prominent nucleoli (H&E 400×)
are associated with drugs known to alter lymphocyte function, particularly in the setting of systemic immune dysregulation or multidrug therapy, where agents may act synergistically or cumulatively to alter lymphoid function.¹

Unlike classical drug eruptions that usually clear up in several days to a few weeks after cessation of therapy, the skin lesions of lymphomatoid drug eruption may persist several weeks to a few months after discontinuation of the drug. In our case, the interval between cessation and resolution was closer to that of a classical drug eruption, and to that of other cases of the baboon syndrome.

Our case is interesting and unusual in that it demonstrated a rare clinical presentation of drug eruption, namely, intertriginous drug eruption or baboon syndrome, with a histologic picture of a lymphomatoid drug eruption that can mimic lymphoma. The pathomechanism of both types of drug eruption, i.e., baboon syndrome and lymphomatoid drug eruption, is not fully understood.

Cases of drug-related eruptions are easily overlooked and misdiagnosed. Heightened awareness during history taking and knowledge of their clinical and histologic presentations will hasten correct diagnosis and appropriate patient management.

References


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