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Baboon syndrome and toxic erythema of chemotherapy: Fold (intertriginous) dermatoses

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Abstract Three decades ago, researchers described an eruption with a very characteristic distribution pattern that was confined to the buttocks and the intertriginous and flexor areas. They gave this reaction pattern one of the most unforgettable names in dermatology, *baboon syndrome* (BS), due to the characteristic, bright-red, well-demarcated eruption predominantly on the buttocks and genital area, reminiscent of the red bottom of a baboon. The authors described three cases provoked by ampicillin, nickel, and mercury. They were convinced that BS represented a special form of hematogenous or systemic contact-type dermatitis, but several important papers that appeared during the past decade disagreed and suggested that BS should be distinguished from hematogenous or systemic contact-type dermatitis. A new acronym, SDRIFE (symmetrical drug-related intertriginous and flexoral exanthema), was proposed along with five diagnostic criteria: (1) exposure to a systemically administered drug at the time of first or repeated doses (contact allergens excluded), (2) sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area, (3) involvement of at least one other intertriginous/flexural fold, (4) symmetry of affected areas, and (5) absence of systemic symptoms and signs. Although there are merits to the arguments in favor of SDRIFE, many of us still prefer to use the wittier name *baboon syndrome*, and even more authors use both terms. We confess that we find it difficult to relinquish the term BS, which has served us so well for years; however, recognition, familiarity, and knowledge of the characteristics of this form of drug eruption must supersede sentimental attachment to a certain nomenclature and so, however reluctantly, we must embrace change.

Another intertriginous drug eruption is the one induced by chemotherapy. *Toxic erythema of chemotherapy* (TEC) is a useful clinical term that recently has been introduced to describe this group of chemotherapy-induced eruptions. This group of overlapping toxic reactions is characterized by areas of painful erythema often accompanied by edema usually involving the hands and feet, intertriginous zones (eg, axilla, groin), and, less often, the elbows, knees, and ears. Toxic erythema of chemotherapy is briefly discussed.

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Introduction of the term *baboon syndrome*

Drug-associated eruptions can mimic a variety of skin diseases, but intertrigo is generally easily distinguishable and is, therefore, not listed in the differential diagnosis of these kinds of reactions. We will concentrate on this type of drug eruption and present the main characteristics of intertriginous drug reactions.

In 1984, researchers described an eruption with a very characteristic distribution pattern that was confined to the buttocks and the intertriginous and flexor areas.[1] They gave this reaction pattern one of the most memorable names in dermatology, *baboon syndrome* (BS), due to the characteristic bright-red, well-demarcated eruption, predominantly located on the buttocks and genital area, reminiscent of the red bottom of the baboon. The authors described three cases provoked by ampicillin, nickel, and mercury. They were convinced that BS represented a special form of hematogenous or systehoimic contact-type dermatitis (title: "The BS: Systemically-induced allergic contact dermatitis"), because all of their patients had been previously sensitized by topical exposure to the allergen. Interestingly, the patient with an ampicillin allergy had been sensitized by a gelatin foam moistened with an ampicillin solution applied in the middle ear during a stapedectomy. The authors admitted that "a rationale for the distribution pattern is difficult to offer."

Other authors who later described the syndrome accepted the hypothesis.[2] In a textbook on contact dermatitis,[3] systemic contact dermatitis is divided into (1) "Dermatitis in areas of previous exposure" (flare-up of dermatitis at positive patch test sites), and (2) "Dermatitis on previously **un**affected skin." BS is mentioned in this group together with vesicular hand eczema, flexural dermatitis, maculopapular rash (toxicoderma), and vasculitis-like lesions.

Is BS a type of systemic contact dermatitis?

Several important papers that appeared during the last decade[4–6] suggested that BS should be distinguished from hematogenous or systemic contact-type dermatitis (SCD). In two papers that 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 BS, 50 were found to be drug induced. Of these, only eight were considered representatives of systemically induced allergic contact dermatitis, and the remaining 42 reported cases were considered examples of drug eruptions of oral or intravenous drugs with no history of previous cutaneous sensitization.[5]

Reported cases

In that excellent 2004 review of 50 cases of BS,[5] the main clinical findings included sharp demarcation of a V-shaped erythema in inguinal/genital and gluteal/perianal areas and, in most cases, additional involvement of at least one other flexural or intertriginous fold. In 14 of 42 cases of drug eruptions (excluding the eight cases of SCD), amoxicillin was the culpable drug. Thirty of the 42 patients were men, and the latency periods were between hours and few days. Other cases have been reported since then, some of them using the proposed name *symmetric drug-related intertriginous and flexural exanthema* (SDRIFE) and others using the terms SCD or BS.[7,8]

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

Terminology, classification, and criteria proposed for BS

The new acronym for this syndrome, SDRIFE, was proposed in a review[5] and five diagnostic criteria were suggested for it: (1) exposure to a systemically administered drug at the time of first or repeated doses (contact allergens excluded); (2) sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area; (3) involvement of at least one other intertriginous/flexural fold; (4) symmetry of affected areas; and (5) absence of systemic symptoms and signs.

After its introduction, the term BS was widely used for many conditions other than SDRIFE—for example, the historical definition of characteristic mercury-induced eruptions with previous sensitization to mercury, topical drug-induced syndrome, SCD-induced BS, and other gluteal erythemas, such as candida intertrigo, or diaper dermatitis, etc. A new proposal for a clinically oriented subclassification of BS was recently suggested by a Japanese group of dermatologists.[8] They divided BS into four groups. The first was classical BS, which is often historically equated with a mercury-induced exanthema resulting from SCD in patients with previous contact sensitization. Although there are many case reports on this type of BS, the number of causative agents are few and include mercury, nickel, balsam of Peru, and poison ivy. The second type was topical drug-induced BS and the third was systemic drug-induced BS, both types representing an SCD, meaning that the patients had been sensitized to the offending drug via skin contact. The formal difference between the two types is the method of exposure to the challenge dose—that is, topical (via absorption of the drug from the skin or mucosal surfaces) or systemic. The fourth type was non-contact allergenic drug-induced BS,