Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), formally known as Baboon syndrome, is a rare drug eruption characterized by well demarcated, symmetric erythema of the anogenital and intertriginous areas. Traditionally, Baboon syndrome was diagnosed in patients with a systemic contact dermatitis, and the term SDRIFE was reserved for Baboon syndrome without a prior known sensitizing agent. β-lactam antibiotics (ie. amoxicillin, ampicillin) are most commonly implicated in SDRIFE. Other causative agents include metronidazole, clindamycin, valacyclovir, terbinafine, radiocontrast media, H2 blockers, IVIG, hydrochlorothiazide, cetuximab, everolimus, golimumab, risperidone, zoledronic acid, and allopurinol, none of which our patient had ever received. Based on review of the current literature, this represents the first case of SDRIFE attributed to liposomal daunorubicin and cytarabine, a recently FDA-approved medication for acute myeloid leukemia (AML).

CASE REPORT
An 80-year-old Caucasian male with a past medical history of myelodysplastic syndrome progressing to AML was referred to our clinic for a dusky patch in the gluteal cleft with peripheral erythema and acute scrotal and penile swelling. After failing previous treatments for AML, he was initiated on a new chemotherapeutic agent, a liposomal combination of daunorubicin and cytarabine. Approximately four or five hours after administration of the drugs, he began to develop a painful progressive dark rash in the gluteal cleft.

He presented to our office three days after initial onset. On clinical exam a large annular dusky patch of the gluteal cleft was noted with involvement of the inguinal folds, and peripheral erythema extended from the base of the scrotum to the superior gluteal cleft (Figure 1). Prominent penile and scrotal swelling was noted of the entire shaft and glans penis (Figure 2). He was afebrile, and no lymphadenopathy was palpated. Biopsy of the lesions was recommended, however the patient and family declined. Topical combination therapy with iodoquinol and 1% hydrocortisone was initiated. The patient’s oncologist discontinued the liposomal combination of daunorubicin, and cytarabine. The lesions slowly faded, and the patient experienced desquamation during a two-week period.

DISCUSSION
Liposomal daunorubicin and cytarabine was FDA-approved in 2017 for therapy-related AML and associated myelodysplasia-related changes. Daunorubicin is an intercalating agent that inhibits RNA and DNA synthesis by steric obstruction. Cytarabine is an antimetabolite, specific for the S phase of cell division and acts to inhibit DNA synthesis once converted intracellularly into its active metabolite, cytarabine-5'-triphosphate (ara-CTP). Liposomal preparation of these agents allows for smaller particle delivery size, gradual release, and longer circulation, resulting in prolonged exposure.

The diagnosis of SDRIFE was made after ruling out other possible causes. The clinical differential diagnosis includes other major drug-induced eruptions including, but not limited to, exanthematous eruption, urticaria, anaphylaxis, fixed drug eruption (FDE), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/drug induced hypersensitivity syndrome.
The patient had no previous exposure to liposomal daunorubicin or cytarabine, thus making FDE unlikely due to the abrupt onset. Due to the lack of systemic symptoms, AGEP, DRESS/DIHS, SJS, and TEN were also excluded. TEC was considered, as it has been previously described with use of cytarabine,

However, many of the diagnostic clinical manifestations including acral erythema, palmoplantar erythrodysesthesia, or “Ara-C ears” (erythema and edema of the ears after chemotherapy), were not present.

The patient also met the clinical criteria established for the diagnosis of SDRIFE:

- Eruption occurring with either initial or repeated dose of a systemically administered drug
- Sharply demarcated gluteal/perianal erythema and/or V-shaped erythema of the inguinal area
- Involvement of one or more other flexural folds and/or intertriginous sites
- Symmetric distribution of areas affected
- Lack of systemic signs and symptoms

The risk of rash with liposomal daunorubicin and cytarabine is reported to be 56 percent according to the manufacturer, not intravenous infusion.

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The authors have no relevant financial disclosures.

The first reported case of SDRIFE induced by liposomal daunorubicin and cytarabine. Clinicians should be vigilant to this rare but possible side effect when treating patients with AML.

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TABLE 1: ONSET OF DRUG-INDUCED ERUPTIONS AND COMMON IMPLEMENTED MEDICATIONS

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lesion Onset</th>
<th>Common Implemented Drugs</th>
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<tbody>
<tr>
<td>AGEP</td>
<td>Less than 4 days</td>
<td>β-lactam antibiotics, Calcium channel blockers, Macrolides</td>
</tr>
<tr>
<td>DRESS/DIHS</td>
<td>15-40 days</td>
<td>Minocycline, Sulfonamides, Dapsone, Allopurinol, Abacavir, Nevirapine, Anticonvulsants</td>
</tr>
<tr>
<td>Fixed Drug Eruption</td>
<td>After 1st exposure: 1-2 weeks; Re-exposure within 24-48 hours</td>
<td>Pigmented: Sulfonamides, Phenothiazine, Tetracyclines, NSAIDS. Non-pigmented: Barbiturates, Pseudoephedrine</td>
</tr>
<tr>
<td>SJS/TEN</td>
<td>7-21 days</td>
<td>Allopurinol, Anticonvulsants, Sulfonamides, NSAIDS, Nevirapine, Abacavir</td>
</tr>
<tr>
<td>TEC</td>
<td>2-3 weeks</td>
<td>Cytarabine, taxanes, methotrexate, anthracyclines, fluorouracil</td>
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