eMedicine Specialties > Dermatology > Allergy & Immunology

Fixed Drug Eruptions

David F Butler, MD, Professor of Dermatology, Texas A&M University College of Medicine; Chair, Department of Dermatology, Director, Dermatology Residency Training Program, Scott and White Clinic, Northside Clinic
Jordan R Ilse, MD, Staff Physician, Scott and White Internal Medicine Residency Program, Temple, Texas

Updated: Aug 24, 2009

Introduction

Background

Adverse reactions to medications are common and often manifest as a cutaneous eruption.

Drug-induced cutaneous disorders frequently display a characteristic clinical morphology such as morbilliform exanthem, urticaria, hypersensitivity syndrome, pseudolymphoma, photosensitivity, pigmentary changes, acute generalized exanthematous pustulosis, lichenoid dermatitis, vasculitis, Stevens-Johnson syndrome, or fixed drug eruption (FDE). The term fixed drug eruption describes the development of one or more annular or oval erythematous patches as a result of systemic exposure to a drug; these reactions normally resolve with hyperpigmentation and may recur at the same site with reexposure to the drug. Repeated exposure to the offending drug may cause new lesions to develop in addition to "lighting up" the older hyperpigmented lesions.

Several variants of fixed drug eruption have been described, based on their clinical features and the distribution of the lesions.[1,2,3,4] These include the following:

- Pigmenting fixed drug eruption
- Generalized or multiple fixed drug eruption
- Linear fixed drug eruption
- Wandering fixed drug eruption
- Nonpigmenting fixed drug eruption
- Bullous fixed drug eruption
- Eczematous fixed drug eruption
- Urticarial fixed drug eruption
- Erythema dyschromicum perstans–like fixed drug eruption
- Vulvitis

Also see the following related eMedicine articles:

- Drug Eruptions
- Drug-Induced Bullous Disorders
- Drug-Induced Gingival Hyperplasia
- Drug-Induced Photosensitivity

- Drug-Induced Pigmentation
- Drug-Induced Pseudolymphoma Syndrome

Pathophysiology

Although the exact mechanism is unknown, recent research suggests a cell-mediated process that initiates both the active and quiescent lesions. The process may involve an antibody-dependent, cell-mediated cytotoxic response.[5] $CD8^+$ effector/memory T cells play an important role in reactivation of lesions with re-exposure to the offending drug.[6,7]

The offending drug is thought to function as a hapten that preferentially binds to basal keratinocytes, leading to an inflammatory response.[8] Through liberation of cytokines such as tumor necrosis factor-alpha, keratinocytes may locally up-regulate expression of the intercellular adhesion molecule-1 (ICAM1).[9] The up-regulated ICAM1 has been shown to help T cells (CD4 and CD8) migrate to the site of an insult.[10,11]

The newly arriving and residential CD8 cells likely perpetuate tissue damage by their production of the inflammatory cytokines interferon-gamma and tumor necrosis factor-alpha. CD8 cells isolated from active lesions have also been shown to express alpha E beta 7, a ligand for E-cadherin, which may further contribute to the lymphocyte's ability to localize to the epidermis. Other cell surface molecules, such as CLA/alpha4beta1/CD4a, that bind E-selectin/vascular cellular adhesion molecule-2/ICAM1 help to further attract CD8 cells to the area.[5]

Changes in cell surface markers allow vascular endothelium to select CD4 cells for migration into active lesions. These regulatory CD4 cells likely produce interleukin 10, which has been shown to help suppress immune function, resulting in a resting lesion.[5] As the inflammatory response dissipates, interleukin 15 expression from keratinocytes is thought to help ensure the survival of CD8 cells, helping them fulfill their effector memory phenotypes. Thus, when reexposure to the drug occurs, a more rapid response develops in the exact location of any pralvato da Windows Internet Explorer 8> Subject: Fixed Drug Eruptions: [Print] - eMedicine Dermatology Date: Fri, 4 Sep 2009 00:34:34 +0200 MIME-Version: 1.0 Content-Type: multipart/related; type="text/html"; boundary="----=_NextPart_000_0063_01CA2CF7.79A3E990" X-MimeOLE: Produced By Microsoft MimeOLE V6.00.2900.5579 This is a multi-part message in MIME format. ------=_NextPart_000_0063_01CA2CF7.79A3E990 Content-Type: text/html; charset="Windows-1252" Content-Transfer-Encoding: quoted-printable Content-Location: http://emedicine.medscape.com/article/1336702-print

eMedicine Specialties > Dermatology > Allergy & Immunology

Fixed Drug Eruptions

David F Butler, MD, Professor of Dermatology, Texas A&M University College of Medicine; Chair, Department of Dermatology, Director, Dermatology Residency Training Program, Scott and White Clinic, Northside Clinic
Jordan R Ilse, MD, Staff Physician, Scott and White Internal Medicine Residency Program, Temple, Texas

Updated: Aug 24, 2009

Introduction

Background

Adverse reactions to medications are common and often manifest as a cutaneous eruption.

Drug-induced cutaneous disorders frequently display a characteristic clinical morphology such as morbilliform exanthem, urticaria, hypersensitivity syndrome, pseudolymphoma, photosensitivity, pigmentary changes, acute generalized exanthematous pustulosis, lichenoid dermatitis, vasculitis, Stevens-Johnson syndrome, or fixed drug eruption (FDE). The term fixed drug eruption describes the development of one or more annular or oval erythematous patches as a result of systemic exposure to a drug; these reactions normally resolve with hyperpigmentation and may recur at the same site with reexposure to the drug. Repeated exposure to the offending drug may cause new lesions to develop in addition to "lighting up" the older hyperpigmented lesions.

Several variants of fixed drug eruption have been described, based on their clinical features and the distribution of the lesions.[1,2,3,4] These include the following:

- Pigmenting fixed drug eruption
- Generalized or multiple fixed drug eruption
- Linear fixed drug eruption
- Wandering fixed drug eruption
- Nonpigmenting fixed drug eruption
- Bullous fixed drug eruption
- Eczematous fixed drug eruption
- Urticarial fixed drug eruption
- Erythema dyschromicum perstans–like fixed drug eruption
- Vulvitis

Also see the following related eMedicine articles:

- Drug Eruptions
- Drug-Induced Bullous Disorders
- Drug-Induced Gingival Hyperplasia
- Drug-Induced Photosensitivity
- Drug-Induced Pigmentation
- Drug-Induced Pseudolymphoma Syndrome

Pathophysiology

Although the exact mechanism is unknown, recent research suggests a cell-mediated process that initiates both the active and quiescent lesions. The process may involve an antibody-dependent, cell-mediated cytotoxic response.[5] $CD8^+$ effector/memory T cells play an important role in reactivation of lesions with re-exposure to the offending drug.[6,7]

The offending drug is thought to function as a hapten that preferentially binds to basal keratinocytes, leading to an inflammatory response.[8] Through liberation of cytokines such as tumor necrosis factor-alpha, keratinocytes may locally up-regulate expression of the intercellular adhesion molecule-1 (ICAM1).[9] The up-regulated ICAM1 has been shown to help T cells (CD4 and CD8) migrate to the site of an insult.[10,11]

The newly arriving and residential CD8 cells likely perpetuate tissue damage by their production of the inflammatory cytokines interferon-gamma and tumor necrosis factor-alpha. CD8 cells isolated from active lesions have also been shown to express alpha E beta 7, a ligand for E-cadherin, which may further contribute to the lymphocyte's ability to localize to the epidermis. Other cell surface molecules, such as CLA/alpha4beta1/CD4a, that bind E-selectin/vascular cellular adhesion molecule-2/ICAM1 help to further attract CD8 cells to the area.[5]

Changes in cell surface markers allow vascular endothelium to select CD4 cells for migration into active lesions. These regulatory CD4 cells likely produce interleukin 10, which has been shown to help suppress immune function, resulting in a resting lesion.[5] As the inflammatory response dissipates, interleukin 15 expression from keratinocytes is thought to help ensure the survival of CD8 cells, helping them fulfill their effector memory phenotypes. Thus, when reexposure to the drug occurs, a more rapid response develops in the exact location of any prior lesions.[5]

Frequency

United States

The prevalence of drug eruptions has been reported to range from 2-5% for inpatients and greater than 1% for outpatients.[12] Fixed drug eruptions may account for as much as 16-21% of all cutaneous drug eruptions. The actual frequency may be higher than current estimates, owing to the availability of a variety of over-the-counter medications and nutritional supplements that are known to elicit fixed drug eruptions.

International

The international prevalence is variable but is likely similar to that in the United States. Most studies report fixed drug eruptions to be the second or third most common skin manifestation of adverse drug events.[13]

Mortality/Morbidity

No deaths have been attributed to fixed drug eruptions. Widespread lesions may initially mimic toxic epidermal necrolysis, but they have a benign clinical course.[14] Localized hyperpigmentation is a common complication, but pain, infection, and, rarely, hypopigmentation, also may occur.[1]

Race

Fixed drug eruptions have no known racial predilection. A genetic susceptibility to developing a fixed drug eruption with an increased incidence of HLA-B22 is possible.[15,16]

Sex

One large study of 450 patients revealed a male-to-female ratio of 1:1.1 for fixed drug eruptions.[1]

Age

Fixed drug eruptions have been reported in patients as young as 1.5 years and as old as 87 years. The mean age at presentation is 30.4 years in males and 31.3 years in females.[1]

Clinical

History

The initial eruption is often solitary and frequently located on the lip or genitalia. Other common locations of the initial lesion are the hip, lower back/sacrum, or proximal extremity. With the initial fixed drug eruption attack, a delay of up to 2 weeks may occur from the initial exposure to the drug to the development of the skin lesion.[17] Skin lesions develop over a period of hours but require days to become necrotic. Lesions may persist from days to weeks and then fade slowly to residual oval hyperpigmented patches.

Subsequent reexposure to the medication results in a reactivation of the site, with inflammation occurring within 30 minutes to 16 hours.[18] The reactivation of old lesions also may be associated with the development of new lesions at other sites.

Patients may not be cognizant that a drug, nutritional supplement, over-the-counter medication, or, rarely, food (eg, fruits, nuts) triggered the skin problem. They may be convinced that an insect, particularly a spider, may be the culprit. A careful history is required to elicit the fact that a drug has been taken and is temporally related to the onset of the eruption. Medications taken episodically, such as pain relievers, antibiotics, or laxatives, are often to blame. When able to be identified, patients often report ingestion of one the following types of medications[19]:

- Analgesics
- Muscle relaxants
- Sedatives
- Anticonvulsants
- Antibiotics

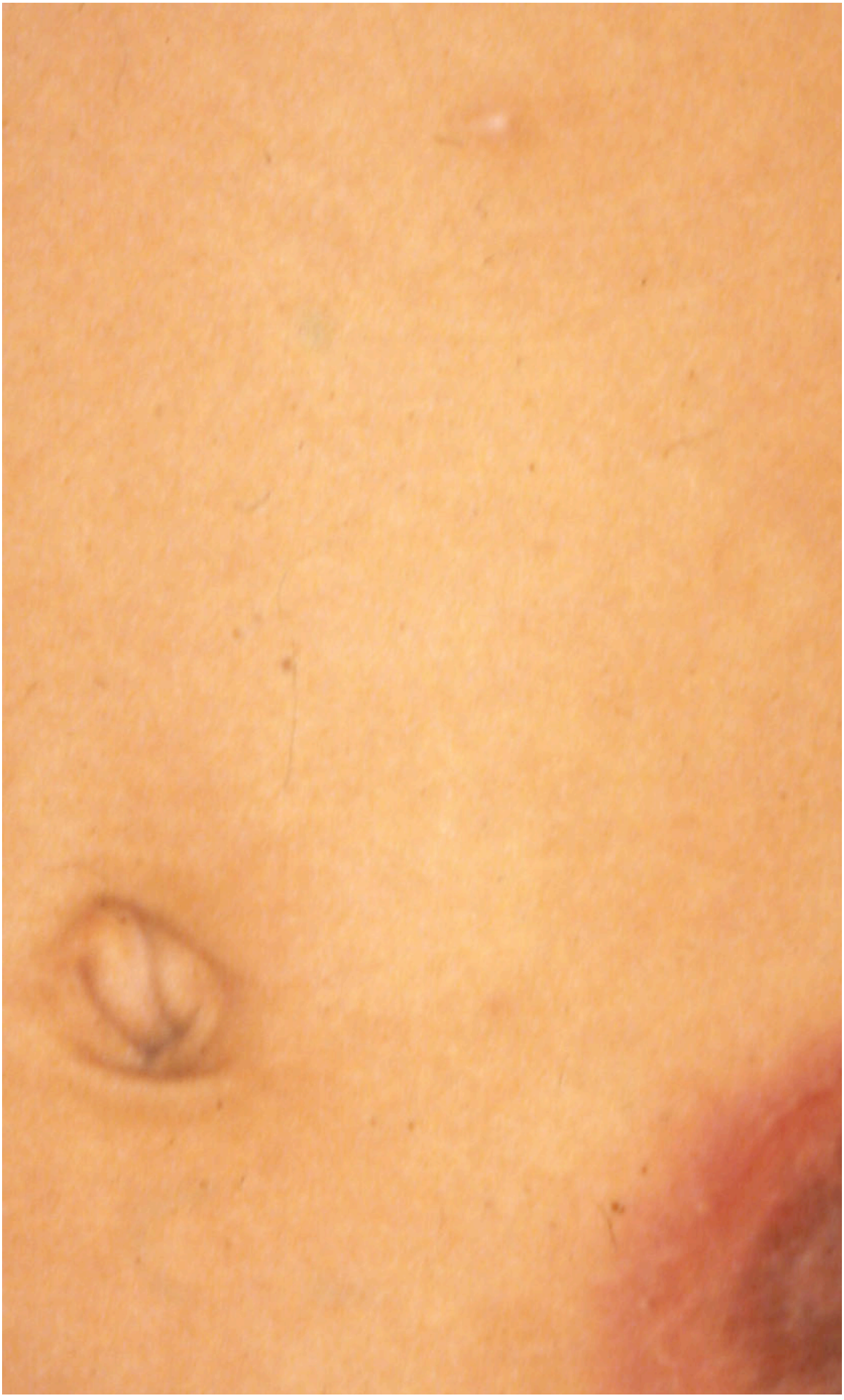
Local symptoms may include pruritus, burning, and pain.[1] Systemic symptoms are uncommon, but fever, malaise, nausea, diarrhea, abdominal cramps, anorexia, and dysuria have been reported.[18,19]

Further questioning may reveal prior episodes of fixed drug eruption, atopic disease, or other past drug reactions. Family history may render a history of atopy, drug reactions, or diabetes mellitus.[1]

Several cases of fixed drug eruption on the genitalia have been reported in patients who were not ingesting the drug but whose sexual partner was taking the offending drug and the patient was exposed to the drug through sexual contact.[20,21,22]

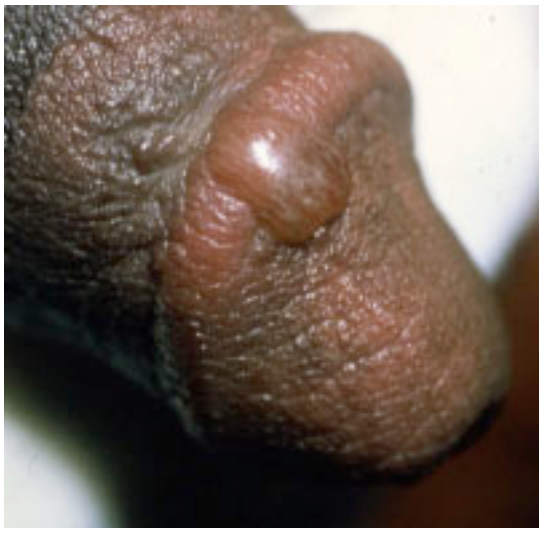
Physical

The most common clinical manifestation is the pigmenting fixed drug eruption, which usually manifests as round or oval, sharply demarcated erythematous/edematous plaques located on the lip, hip, sacrum, or genitalia.[2] These erythematous patches or plaques gradually fade with residual hyperpigmentation (see Media Files 1-5). The center of the patch may blister or become necrotic. Other less common variants may manifest as lesions resembling erythema multiforme, toxic epidermal necrolysis, eczema, urticaria, a linear pattern following Blaschko lines, bullous lesions, a migrating eruption, or a nonpigmenting form with no postinflammatory hyperpigmentation.[3]

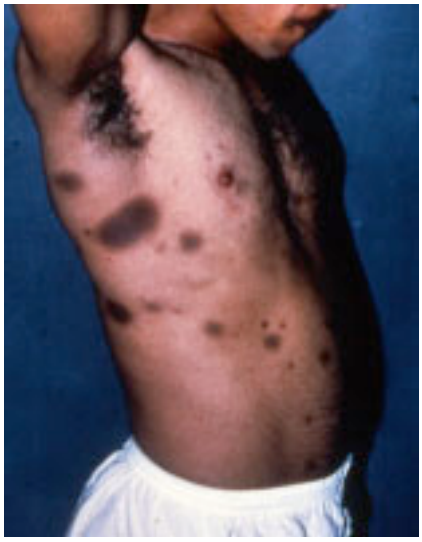


Targetoid fixed drug eruption on the abdomen of a child.

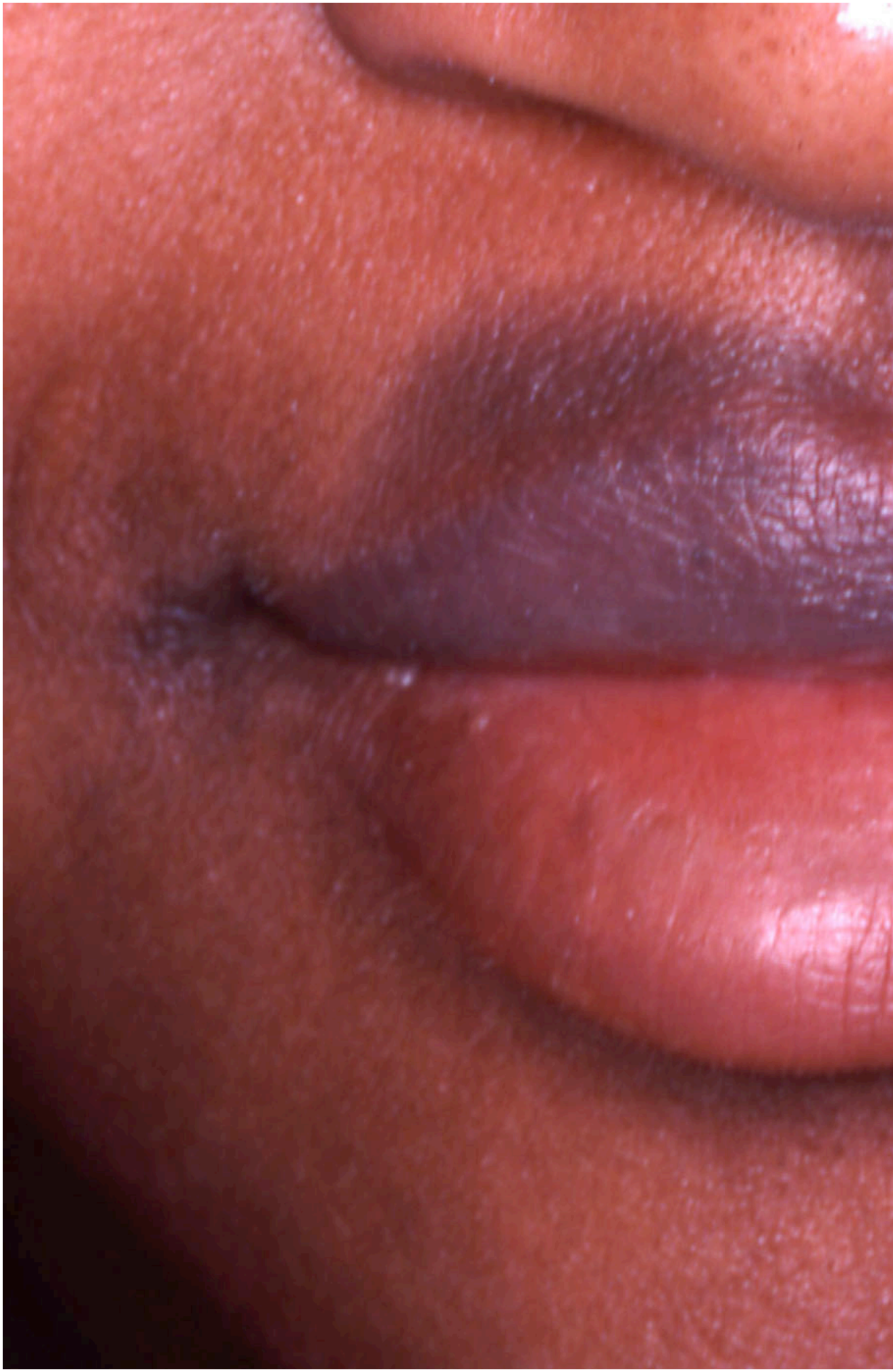
Hyperpigmented fixed drug eruption on the hip of an adult.



Vesicular fixed drug eruption on the glans penis.



Multiple hyperpigmented fixed drug eruptions on the trunk.



Hyperpigmented fixed drug eruption on the right side of the upper lip.

Initially, a single lesion or a few lesions develop, but, with reexposure, additional lesions occur. The vast majority of patients present with 1-30 lesions, ranging in size of 0.5-5 cm, but reports of lesions greater than 10 cm have been published. Lesions may be generalized. The most common reported site is the lips, and these may be seen in up to half of all cases.[1]

Medications may also follow a site-specific eruption pattern. For example, trimethoprim-sulfamethoxazole (Bactrim) has been shown to favor the genital region (especially in males) and naproxen and the oxicams involve the lips.[2]

Resting/inactive lesions tend to appear as round or oval, gray, hyperpigmented macules.

Upon reexposure, the resting hyperpigmented macules activate, developing a violaceous center encircled by concentric rings of erythema. Re-administration of the medication poses the risk of increased pigmentation, size, and number of lesions.

Individuals with darker pigmentation may develop postinflammatory hypopigmented macules once the lesions have resolved.[8]

Causes

The major categories of causative agents of fixed drug eruption include antibiotics, antiepileptics, nonsteroidal anti-inflammatory agents, and phenothiazines, although numerous other agents and certain foods have also been reported as causative agents. Ingestion of the causative agent may occur via any route, including oral, rectal, or intravenous.[19]

The most common cause is trimethoprim-sulfamethoxazole.[3] Other substances implicated to cause fixed drug eruptions are as follows[1,8,19,23,24,25,26,27,28,29,30,31]:

Acetaminophen	Acyclovir	Allopurinol	Allylisopropyl-acetylurea	Amide local anesthetics
Amlexanox	Amoxicillin	Anticonvulsants	Articaine	Aspirin
Atenolol	Barbiturates	Botulinum toxin	Carbamazepine	Cashew nut
Ceftriaxone	Celecoxib	Cetirizine	Chloral hydrate	Chlordiazepoxide
Chlorhexidine	Chlormezanone	Chlorphenesin carbonate	Citicoline	Clarithromycin
Clioquinol	Clopidogrel	Codeine	Colchicines	Cyclizine
Cyproterone acetate	Dextromethorphan	Dimenhydrinate	Diphenhydramine	Dipyrone
Docetaxel	Eperisone hydrochloride	Erythromycin	Ethenzamide	Feprazone
Finasteride	Flecainide	Fluconazole	Fluoroquinolones	Foscarnet
Gabapentin	Griseofulvin	Hydroxyzine	Ibuprofen	Interferon
Iodinated radiography contrast media	Iomeprol	Kakkon	Ketoconazole	Lactose
Lamotrigine	Lentils	Lomeprol	Lopamidoln	Loratadine
Lormetazepam	Magnesium trisilicate	Mefenamic acid	Melatonin	Methaqualone
Metramizole	Metronidazole	Metaform	Minocycline	Multivitamins

Naproxen	Nimesulide	Omeprazole	Ondansetron	Opium alkaloids
Oxyphenbutazone	Paclitaxel	Pamabrom	Papaverine	Para-aminosalicylic acid
Penicillins	Phenazone	Phenolphthalein	Phenylbutazone	Phenylephrine
Phenylpropanolamine	Phenytoin	Pipemidic acid	Piroxicam	Procarbazine
Prochlorperazine	Pseudoephedrine	Quinine	Rifampin	Scopolia
Sodium benzoate	Strawberries	Sulfamethoxazole	Tartrazine	Terbinafine
Tetracyclines	Theophylline	Thiacetazone	Ticlopidine	Tinidazole
Tolfenamic acid	Tosufloxacin	Tranexamic acid	Trimethoprim	Tropisetron

Differential Diagnoses

Bullous Pemphigoid
Cellulitis
Drug Eruptions
Drug-Induced Bullous Disorders
Eczema
Erythema Annulare Centrifugum
Erythema Dyschromicum Perstans
Erythema Multiforme
Herpes Simplex
Insect Bites
Lichen Planus
Lichen Planus Actinicus
Lupus Erythematosus, Discoid
Melasma
Pemphigus Vulgaris
Pemphigus, Drug-Induced
Pityriasis Rosea
Postinflammatory Hyperpigmentation
Psoriasis
Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
Urticaria, Acute

Workup

Laboratory Studies

Blood studies are not useful for the diagnosis of fixed drug eruption (FDE), although eosinophilia is common with drug eruptions.

Other Tests

Rechallenging the patient to the suspected offending drug is the only known test to possibly discern the causative agent. Patch testing of the suspected drug to lesional and non-lesional skin has been helpful in a few instances. The exact protocol of patch testing has varied.

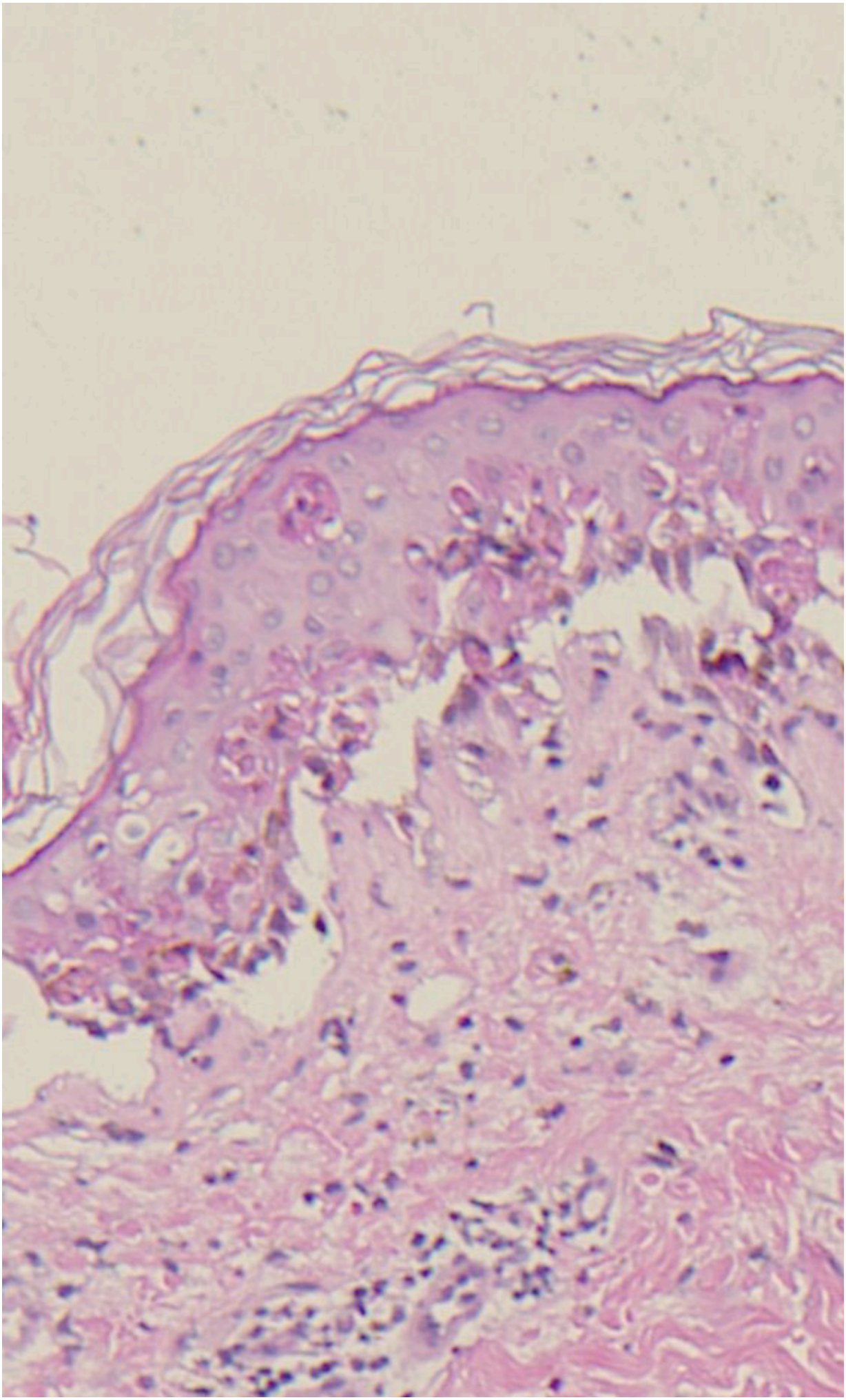
Patch testing and oral provocation have been used to identify the suspected agent and check for cross-sensitivities to medications.[32,33] A refractory period has been reported in fixed drug eruption; therefore, a delay before and between patch testing and oral provocation is recommended. One study used an 8-week time window after lesion resolution and between tests, which yielded positive results.[34] Patch testing must be performed on a previously involved site; otherwise, a false-negative result is likely.[33] Some locations may be inappropriate for patch testing; thus, clinical discretion is advised. Once patch testing is complete, oral provocation should follow, with the least likely culprits and the negative patch test agents first, followed by more likely causes. Oral provocation is thought to be the only reliable way to diagnose fixed drug eruption.

Procedures

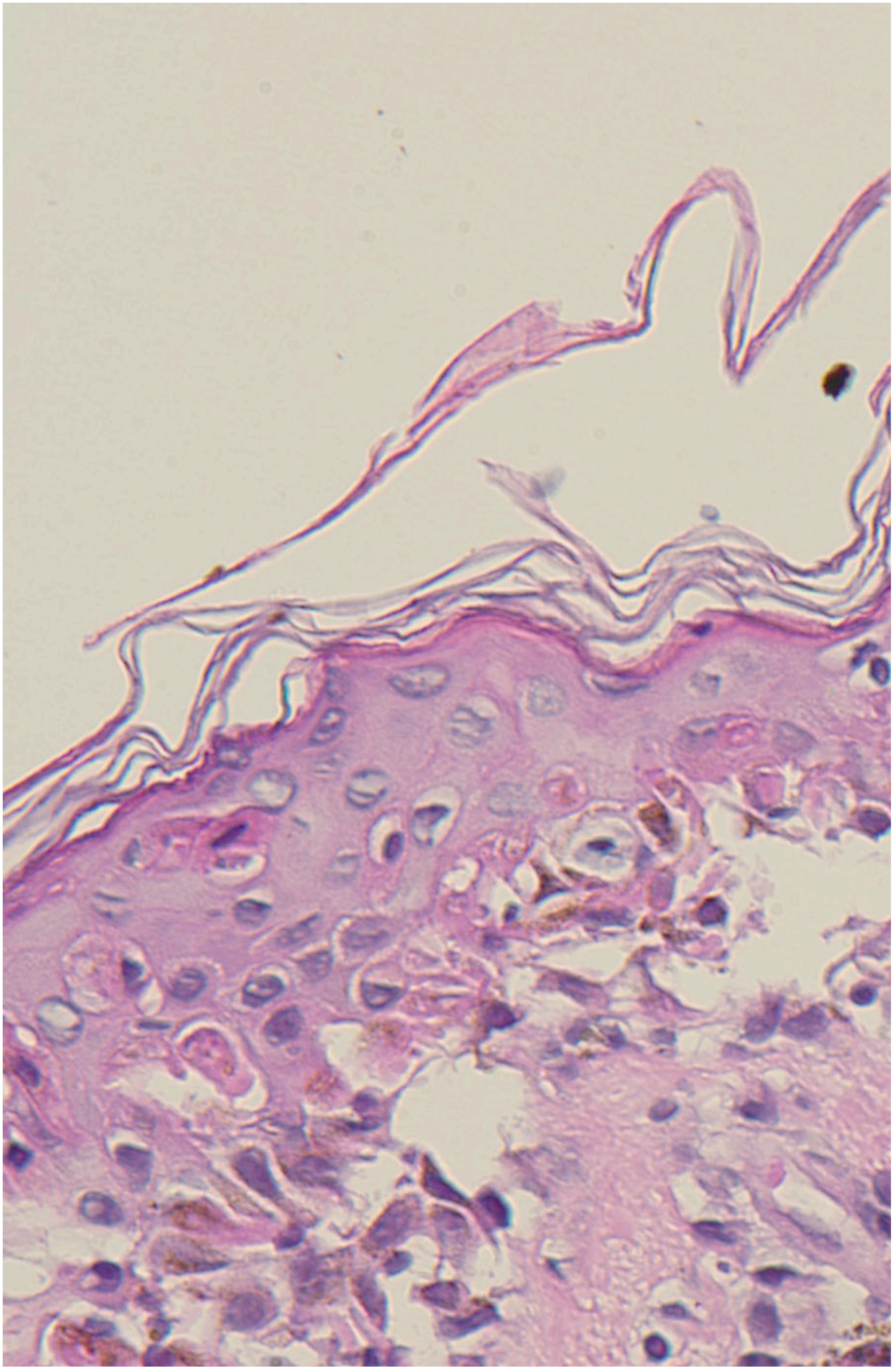
Skin biopsy is the diagnostic procedure of choice.

Histologic Findings

Histological examination of inflammatory/acute lesions shows an interface dermatitis with vacuolar change and Civatte bodies[8] (see Media File 6). The overall pattern may mimic that seen in erythema multiforme. Dyskeratosis and individual necrotic keratinocytes within the epidermis may be a prominent feature (see Media File 7). On occasion, the lymphocytic infiltrate can be prominent enough to obscure the dermoepidermal junction. Spongiosis, dermal edema, eosinophils, and occasional neutrophils may be present. Pigmentary incontinence within the papillary dermis is a characteristic feature and may be the only feature seen in older, noninflamed lesions. Chronic or inactive lesions may also show mild acanthosis, hyperkeratosis, and relatively few inflammatory cells.



Acute interface dermatitis with prominent vacuolar change and individual necrotic keratinocytes within the epidermis (X10).



Interface dermatitis, vacuolar change, necrotic keratinocytes, and incontinent pigment in the dermis (X40).

Treatment

Medical Care

The main goal of treatment is to identify the causative agent and avoid it. Treatment for fixed drug eruptions (FDEs) otherwise is symptomatic. Systemic antihistamines and topical corticosteroids may be all that are required. In cases in which infection is suspected, antibiotics and proper wound care are advised. Desensitization to medications has been reported in the literature, but this should be avoided unless no substitutes exist.[35]

Consultations

Consultation with a dermatologist is warranted if the diagnosis is in doubt. If patch testing is needed to determine which drug may be involved, a dermatologist with such experience may be required. If Stevens-Johnson syndrome or toxic epidermal necrolysis is suspected, hospitalization and possible referral to the intensive care unit or burn unit may be appropriate.

Diet

A regular diet is usually acceptable. However, food may be an exacerbating factor; reactivation has been reported with lentils and strawberries.[8]

Activity

Generally, no limits on activities are imposed. Multiple studies have sited male genital lesions occurring following intercourse with female partners taking trimethoprim-sulfamethoxazole.[36] Therefore, patients may consider avoiding sexual activity while a partner is taking a medication that has resulted in a prior fixed drug eruption. If open lesions are present, general wound care precautions are recommended.

Medication

Lesions of fixed drug eruption resolve spontaneously with avoidance of the inciting drug. Additional medications should be used to relieve symptoms associated with the condition. Generally, an oral antihistamine (eg, hydroxyzine) and a topical corticosteroid may be sufficient. The use of corticosteroids may interfere with later diagnostic provocation testing. Hyperpigmentation may take many months to resolve. Incontinent pigment in the dermis responds poorly to topical bleaching agents such as hydroquinones.

Follow-up

Deterrence/Prevention

Avoid the offending drug. Patch testing may be used to help identify agents that pose a risk of cross-sensitivity.[37]

Complications

Hyperpigmentation is the most likely complication of a fixed drug eruption (FDE). The potential for infection exists in the setting of multiple, eroded lesions. Generalized eruptions have been reported following topical and oral provocation testing.[19,38]

Prognosis

The prognosis is very good, and an uneventful recovery should be expected. No deaths due to fixed drug eruption have been reported. Residual hyperpigmentation is very common, but this is less likely with the nonpigmenting variant.

Patient Education

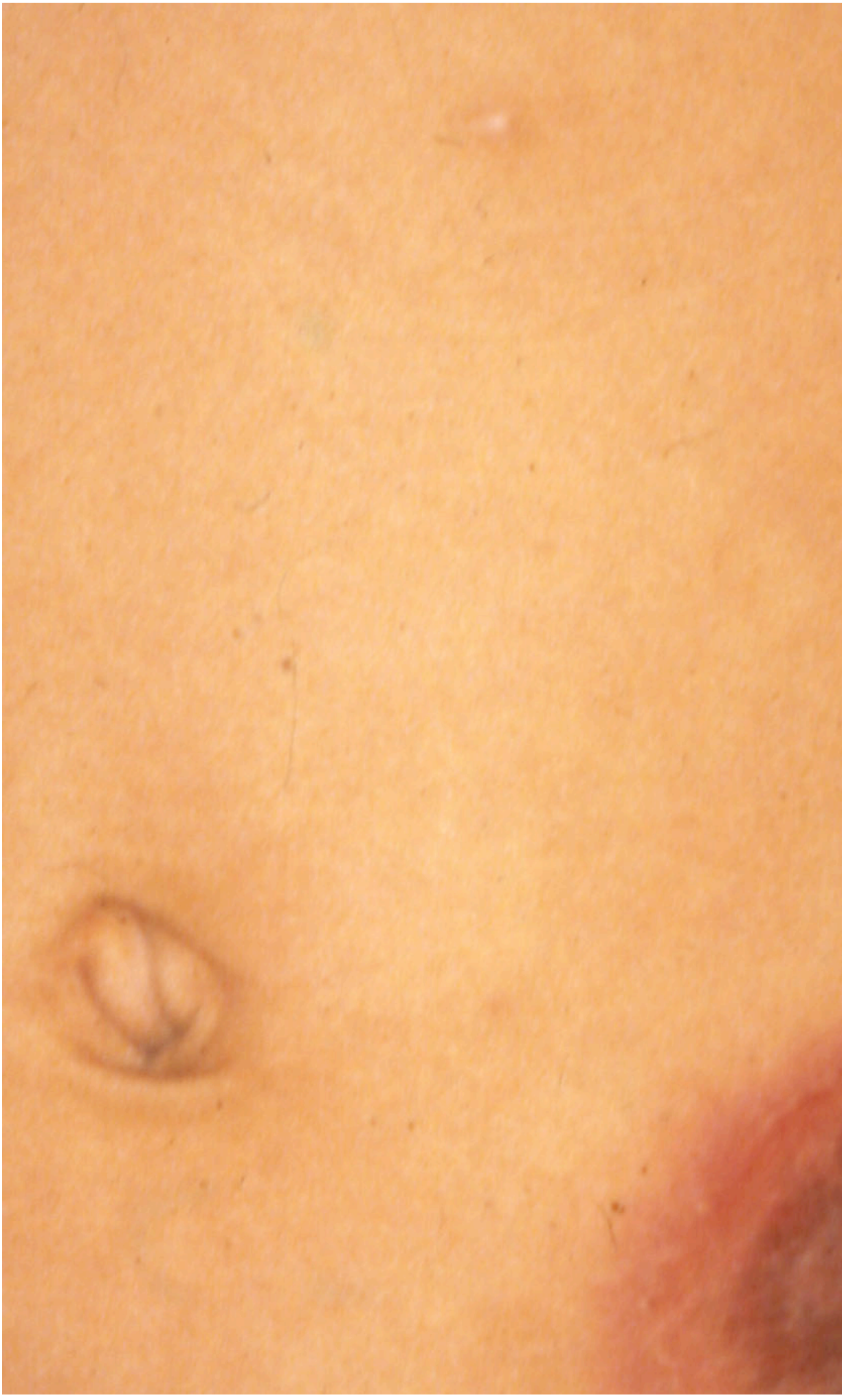
Patients should be counseled on medication avoidance and possible cross-reactions of similar medications. Patients should notify their physicians of all drug allergies they have experienced.

Miscellaneous

Medicolegal Pitfalls

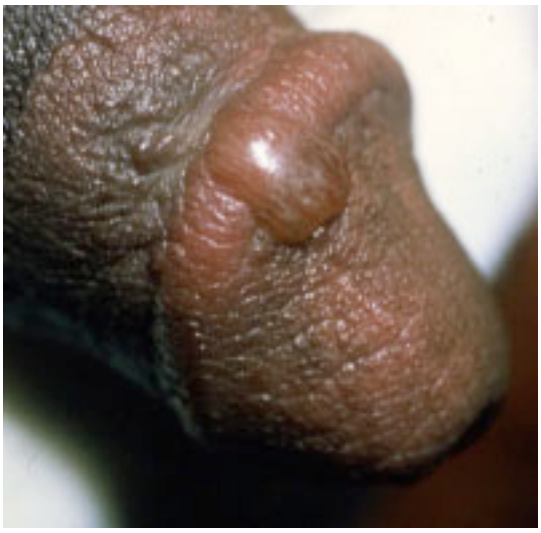
Drug reactions account for a large proportion of medical malpractice claims. Inadequate disclosure of potential adverse effects and failure to identify a drug as the cause of the patient's problem could be sources of legal action.

Multimedia

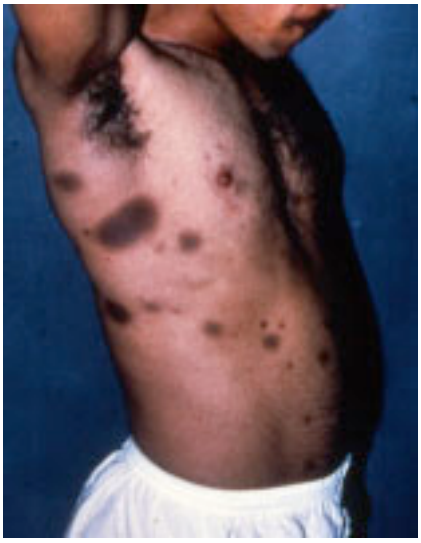


Media file 1: Targetoid fixed drug eruption on the abdomen of a child.

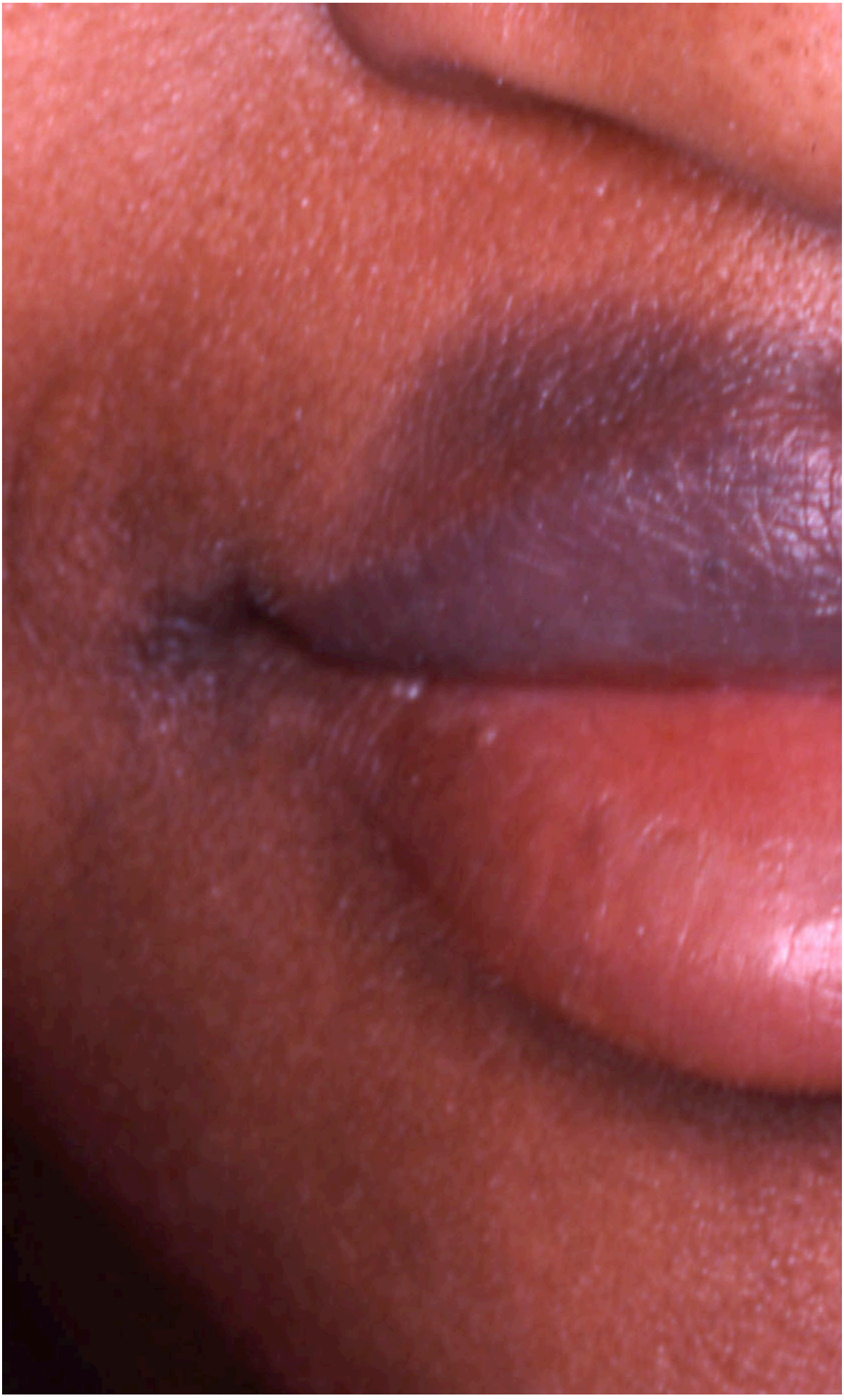
Media file 2: Hyperpigmented fixed drug eruption on the hip of an adult.



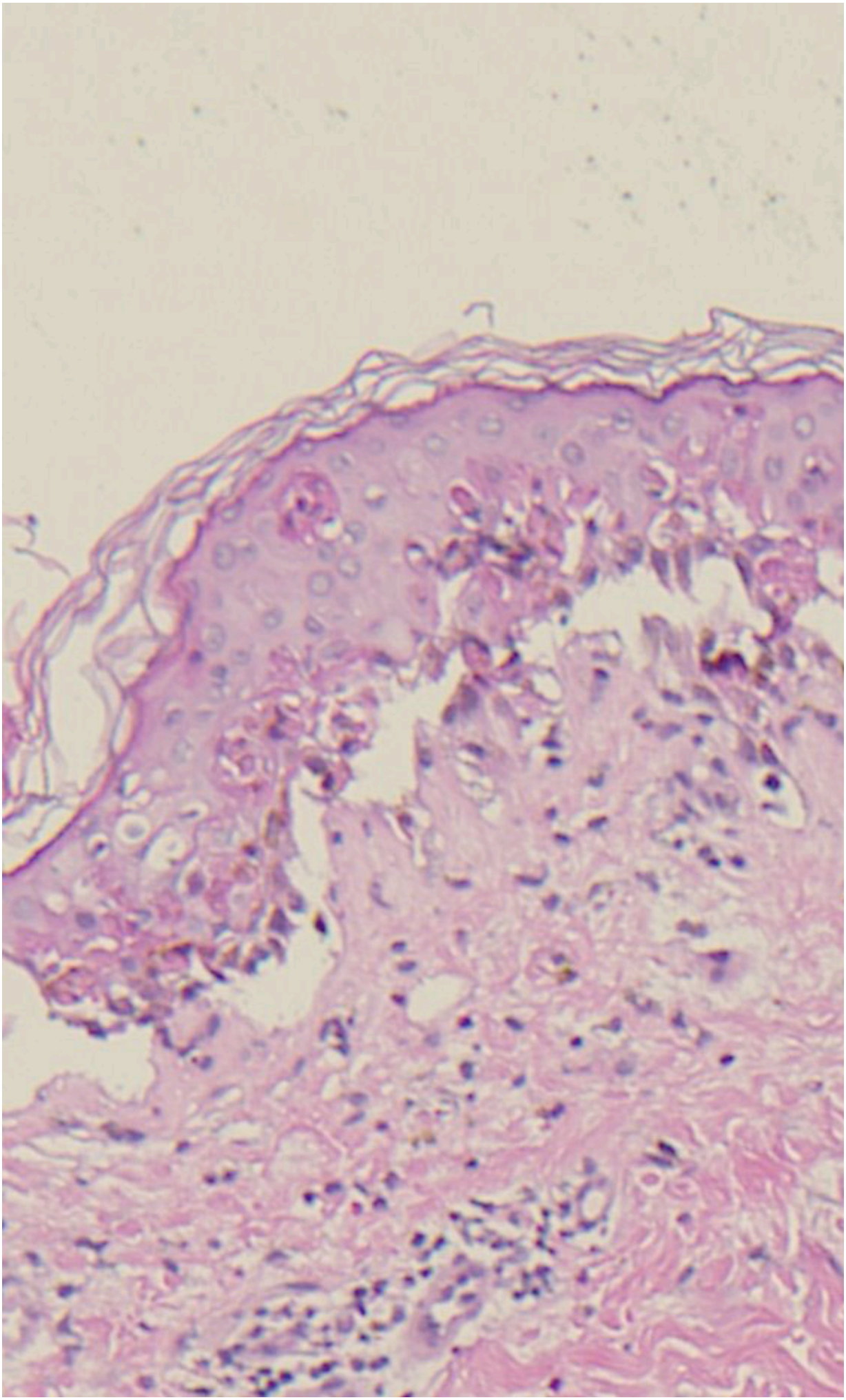
Media file 3: Vesicular fixed drug eruption on the glans penis.



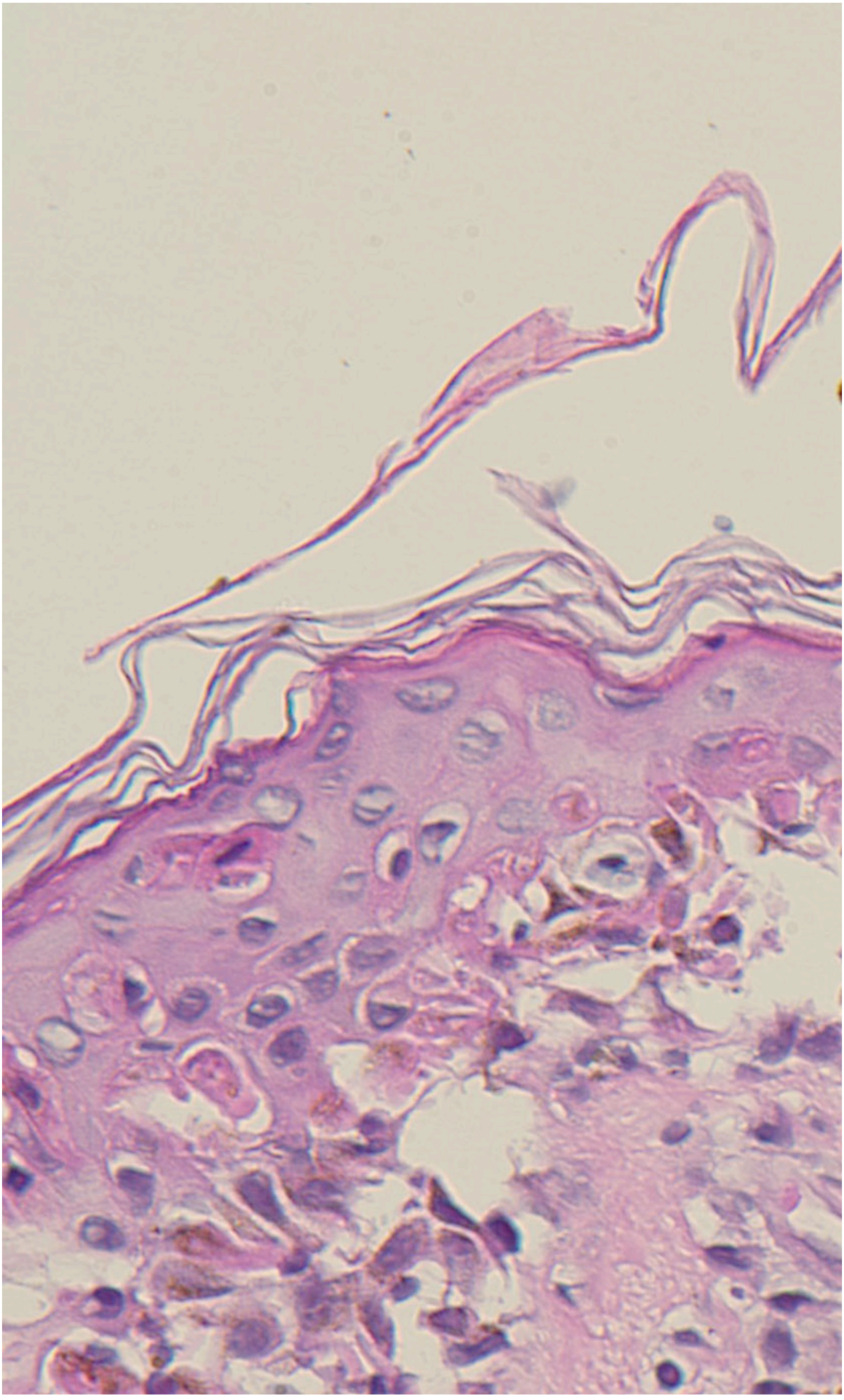
Media file 4: Multiple hyperpigmented fixed drug eruptions on the trunk.



Media file 5: Hyperpigmented fixed drug eruption on the right side of the upper lip.



Media file 6: Acute interface dermatitis with prominent vacuolar change and individual necrotic keratinocytes within the epidermis (X10).



Media file 7: Interface dermatitis, vacuolar change, necrotic keratinocytes, and incontinent pigment in the dermis (X40).

References

1. Mahboob A, Haroon TS. Drugs causing fixed eruptions: a study of 450 cases. *Int J Dermatol*. Nov 1998;37(11):833-8. [Medline].
2. Ozkaya-Bayazit E. Specific site involvement in fixed drug eruption. *J Am Acad Dermatol*. Dec 2003;49(6):1003-7. [Medline].
3. Ozkaya-Bayazit E, Bayazit H, Ozarmagan G. Drug related clinical pattern in fixed drug eruption. *Eur J Dermatol*. Jun 2000;10(4):288-91. [Medline].
4. Fischer G. Vulvar fixed drug eruption. A report of 13 cases. *J Reprod Med*. Feb 2007;52(2):81-6. [Medline].
5. Teraki Y, Shiohara T. IFN-gamma-producing effector CD8+ T cells and IL-10-producing regulatory CD4+ T cells in fixed drug eruption. *J Allergy Clin Immunol*. Sep 2003;112(3):609-15. [Medline].
6. Mizukawa Y, Shiohara T. Fixed drug eruption: a prototypic disorder mediated by effector memory T cells. *Curr Allergy Asthma Rep*. Jan 2009;9(1):71-7. [Medline].
7. Shiohara T. Fixed drug eruption: pathogenesis and diagnostic tests. *Curr Opin Allergy Clin Immunol*. Aug 2009;9(4):316-21. [Medline].
8. Weedon D. The lichenoid reaction pattern ('interface dermatitis'). In: *Skin Pathology*. 2nd ed. London, England: Churchill Livingstone; 2002:42-43.
9. Smoller BR, Luster AD, Krane JF, et al. Fixed drug eruptions: evidence for a cytokine-mediated process. *J Cutan Pathol*. Feb 1991;18(1):13-9. [Medline].
10. Hindsen M, Christensen OB, Gruic V, Lofberg H. Fixed drug eruption: an immunohistochemical investigation of the acute and healing phase. *Br J Dermatol*. Mar 1987;116(3):351-60. [Medline].
11. Shiohara T, Nickoloff BJ, Sagawa Y, Gomi T, Nagashima M. Fixed drug eruption. Expression of epidermal keratinocyte intercellular adhesion molecule-1 (ICAM-1). *Arch Dermatol*. Oct 1989;125(10):1371-6. [Medline].
12. Krahenbuhl-Melcher A, Schlienger R, Lampert M, Haschke M, Drewe J, Krahenbuhl S. Drug-related problems in hospitals: a review of the recent literature. *Drug Saf*. 2007;30(5):379-407. [Medline].
13. Lee AY. Fixed drug eruptions. Incidence, recognition, and avoidance. *Am J Clin Dermatol*. Sep-Oct 2000;1(5):277-85. [Medline].
14. Baird BJ, De Villez RL. Widespread bullous fixed drug eruption mimicking toxic epidermal necrolysis. *Int J Dermatol*. Apr 1988;27(3):170-4. [Medline].
15. Pellicano R, Ciavarella G, Lomuto M, Di Giorgio G. Genetic susceptibility to fixed drug eruption: evidence for a link with HLA-B22. *J Am Acad Dermatol*. Jan 1994;30(1):52-4. [Medline].
16. Pellicano R, Lomuto M, Ciavarella G, Di Giorgio G, Gasparini P. Fixed drug eruptions with feprazone are linked to HLA-B22. *J Am Acad Dermatol*. May 1997;36(5 Pt 1):782-4. [Medline].
17. Bolognia JL, Jorizzo JL, Rapini RP. Fixed drug eruptions. In: *Dermatology*. London, England: Mosby; 2003:344-5.
18. Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI. Fixed drug eruptions. In: *Fitzpatrick's Dermatology in General Medicine*. 6th ed. New York, NY: McGraw-Hill; 2003:1333.
19. Sehgal VN, Srivastava G. Fixed drug eruption (FDE): changing scenario of incriminating drugs. *Int J Dermatol*. Aug 2006;45(8):897-908. [Medline].
20. Zawar V, Chuh A. Fixed drug reaction may be sexually induced. *Int J Dermatol*. Aug 2006;45(8):1003-4; author reply 1004. [Medline].
21. Berger RE. Fixed drug eruption--a sexually inducible reaction?. *J Urol*. Jun 2005;173(6):1990. [Medline].
22. Zawar V, Kirloskar M, Chuh A. Fixed drug eruption - a sexually inducible reaction?. *Int J STD AIDS*. Aug 2004;15(8):560-3. [Medline].
23. Lopez Abad R, Iriarte Sotes P, Castro Murga M, Gracia Bara MT, Sesma Sanchez P. Fixed drug eruption induced by phenylephrine: a case of polysensitivity. *J Investig Allergol Clin Immunol*. 2009;19(4):322-3. [Medline].
24. Gupta S, Gupta S, Mittal A, David S. Oral fixed drug eruption caused by gabapentin. *J Eur Acad Dermatol Venereol*. Feb 19 2009;[Medline].
25. Ghosh SK, Bandyopadhyay D. Clopidogrel-induced fixed drug eruption. *J Eur Acad Dermatol Venereol*. Jan 20 2009;[Medline].
26. Oyama N, Kaneko F. Solitary fixed drug eruption caused b