

Fixed Drug Eruption Due to Doxycycline and Metronidazole

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Fixed drug eruption (FDE) can be caused by an assortment of drugs. Although cross-sensitivity to 2 chemically related drugs has been frequently described, FDE to 2 unrelated agents rarely has been reported. To our knowledge, we report the first such case due to doxycycline and metronidazole.

The term *fixed drug eruption* (FDE) is used to characterize recurring circumscribed lesions at the same site or sites each time an offending drug is administered. Early in the course, the lesion is a well-defined round or oval plaque of erythema and edema that may be surmounted by a bulla. Several days later, the lesion subsides and becomes dusky brown. Repeated attacks result in an intense purple-brown-black hyperpigmentation that may persist for many months to years. At any time, the same or a related drug may precipitate an identical series of events in previously affected sites. Although numerous drugs have been implicated as the cause of FDE, polysensitivity rarely has occurred as a result of chemically unrelated drugs.

Case Report

A 22-year-old black woman with bacterial vaginitis presented to the emergency department of Mount Sinai Hospital complaining of an eruption on her extremities. The lesions appeared one hour after taking her first dose of metronidazole. One year earlier, an almost identical eruption appeared after taking doxycycline for a urinary tract infection.

The dermatology department was consulted to evaluate a hemorrhagic reaction to metronidazole. Physical examination revealed a striking pattern. Numerous annular patches of erythema, measuring 3 to 7 cm in diameter, surrounded central areas of



Fixed drug eruption to metronidazole. One year earlier, lesions at these identical sites appeared as a reaction to doxycycline.

hyperpigmentation on the proximal extremities (Figure). Biopsy results from the erythematous outer zone revealed lichenoid dermatitis with occasional necrotic keratinocytes, eosinophils, and rare dermal melanophages.

Comment

FDE can be caused by an assortment of drugs. The most common are oxyphenbutazone, tetracycline, sulfonamides, phenolphthalein, analgin, phenobarbital, and dapsone.^{1,2} Although a single drug is usually responsible for FDE, there are patients in whom FDE develops following the ingestion of multiple drugs at different times. This occurs more commonly when the offending drugs are chemically related. Such cross-sensitivity reactions occur with the tetracycline family of drugs. In rare instances,

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Previous Cases of Polysensitivity to 2 Chemically Unrelated Drugs

Oxyphenbutazone and phenobarbital³
Metamizole and saridon³
Metamizole and penicillin G³
Phenytoin, sodium valproate, and carbamazepine⁴
Oxyphenbutazone and tetracycline⁵

polysensitivity occurs to 2 or more chemically unrelated drugs (Table).

In our patient, the lesions of FDE developed at the same site after the ingestion of doxycycline and metronidazole. Although doxycycline and

metronidazole may cause FDE independently, the present case is one of polysensitivity to both of these agents. To our knowledge, this phenomenon is the first of its type involving these 2 drugs.

REFERENCES

1. Savin JA. Current causes of fixed drug eruption. *Br J Dermatol.* 1970;83:546-549.
2. Pasricha JS. Drugs causing fixed eruptions. *Br J Dermatol.* 1979;100:183-185.
3. Pasricha JS, Shukla SR. Independent lesions of fixed drug eruption due to two unrelated drugs in the patient. *Br J Dermatol.* 1979;101:361-362.
4. Chan HL, Tan KC. Fixed drug eruption to three anticonvulsant drugs: an unusual case of polysensitivity. *J Am Acad Dermatol.* 1997;36:259.
5. Bhargava NC, Singh G. Fixed eruption due to two unrelated drugs: oxyphenbutazone and tetracycline. *Int J Dermatol.* 1981;20:435.



Figure 1. Annular lesion on the head.



Figure 2. Keratotic follicular involvement and perifollicular inflammatory infiltrate of lymphocytes (H&E, original magnification $\times 100$).

Results of a histopathologic examination showed keratotic follicular involvement, thickening of the granular layer, vacuolization of the basal layer, perifollicular inflammatory infiltrate of the lymphocytes, and numerous colloid bodies (Figure 2).

Comment

This type of LP is characterized by follicular (histopathologic) and annular (clinical) features. Histopathologic findings were the same as that of typical LP but with follicular involvement; clinical findings were similar to annular LP papules. Two important features of these lesions are the long-standing course of therapy, as well as the lack of effi-

cacy of conventional LP treatments. This also is seen in another rare variant of LP called annular atrophic LP.^{3,4} To our knowledge, this is the first case of annular follicular LP reported in the literature.

REFERENCES

1. Little EG. Lichen planus. *J Cutan Dis.* 1919;37:639-670.
2. Toribio J, Tejerina JA, Pérez ON, et al. Liquen plano anular. *Actas Dermosifiliogr.* 1980;71:317-318.
3. Friedman DB, Hashimoto K. Annular atrophic lichen planus. *J Am Acad Dermatol.* 1991;25:392-394.
4. Requena L, Olivares M, Piqué E, et al. Annular atrophic lichen planus. *Dermatology.* 1994;189:95-98.