non-polyposis colorectal cancer. Microsatellites are repetitive DNA sequences less than 6 bases in length found throughout the human genome. Tumors with variations in the number of repeats at these loci as compared to DNA from normal tissue are said to possess “microsatellite instability.” These repeated sequences are unique for a given individual and are usually present in non-coding regions of DNA. Tumors are segregated into 3 groups: those with a low frequency of MSI (MSI-L), those with a high frequency of MSI (MSI-H) and those with stable microsatellites (MS). In tumor tissue where both alleles of an mismatch repair gene have been inactivated, uncorrected somatic replication errors occur in microsatellite repeats sequences both within noncoding and insignificant locations throughout the genome as well as in coding regions of genes involved in cell growth, DNA repair, and signaling.

The presence of MSI has been reported in a number of cutaneous neoplasms, including basal cell carcinomas and melanomas. Interestingly, neither sporadically arising actinic keratoses nor squamous cell carcinomas have demonstrated MSI. The negative MSI analysis in our patient was prescient in two respects. First, although other studies have employed MSI analysis in the evaluation of benign vascular proliferations, this is the seminal report of its use in a malignant or borderline malignant neoplasm of the skin. Second, internal malignancies with MSI have demonstrated an unfavorable prognosis. Evaluation of vascular tumors for MSI might provide clinicians with additional prognostic information.

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Fixed drug eruption caused by itraconazole: Reactivity and cross reactivity

To the Editor: Fixed drug eruption (FDE) characteristically occurs at the same site every time an offending drug is administered. Cross-reactions may occur with structurally similar drugs. Different immunologic mechanisms incriminated in the pathogenesis of FDE are based on the concept of the circulating drug acting as a hapten and its consequent binding to cellular proteins or receptors, thereby releasing lymphokines and antibodies damaging basal cell layer. Although a single drug is usually responsible in most patients, in rare instances multiple drugs may lead to a FDE. When drugs of totally different chemical structures precipitate exacerbations, it is termed polysensitivity.

A 52-year-old female was administered a single 400 mg dose of fluconazole for extensive pityriasis versicolor. Within 12 hours, she noticed 3 oval, painful, eroded, pigmented patches over her trunk with diameters of 3 cm to 4 cm and erythematous halos. A clinical diagnosis of FDE caused by fluconazole was made. An oral graded challenge with fluconazole, itraconazole, and ketoconazole was performed at 4 weeks. Initially, the dose used was one fourth of the minimum therapeutic dose. If no reactivation of the lesions was observed in next
24 hours, the dose was doubled every 24 hours until the therapeutic dose was achieved. In case of reactivation, the next drug was tested after 2 weeks of complete resolution of the previous eruption. Reactivation was observed with fluconazole (25 mg) and itraconazole (25 mg) orally within 12 hours, but ketoconazole (in 50, 100, and 200 mg doses) failed to reactivate the lesions. This confirmed a FDE to fluconazole with cross sensitivity to itraconazole but not to ketoconazole. Please see Table I for trade names and manufacturers of drugs used.

FDE caused by systemic azole antifungals is extremely rare. Only 5 cases caused by fluconazole and 1 case caused by ketoconazole have been reported. FDE caused by itraconazole has not been reported thus far. Fluconazole, itraconazole, and ketoconazole have a marked structural resemblance because they all belong to the azole group of antifungals. The variations are caused by different subgroups (ie, fluconazole and itraconazole are triazoles, with 3 nitrogen atoms, whereas ketoconazole is an imidazole containing 2 nitrogen atoms in a 5-membered azole ring; Fig 1). The present patient had a FDE to fluconazole with cross sensitivity to itraconazole but not to ketoconazole. Similar cross sensitivity patterns with tetracyclines and nitro-imidazoles suggest that the cross reactivity of drugs within a pharmacological group is not necessarily an all or none phenomenon. This information may be quite useful for selecting alternative drugs. Patch testing and other in vivo (scratch and intradermal) tests give variable results in FDE and because of their limited sensitivity, the most prudent way of establishing a diagnosis in a non-life threatening drug reaction would be a graded oral challenge.

We suggest that with a FDE to potentially useful drugs like fluconazole, a cross sensitivity may be ascertained with other analogues in order to use a possible non-reacting alternative. To the best of our knowledge, this is the first case of a FDE to itraconazole confirmed through graded oral challenge.

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Longitudinal melanonychia as the first sign of Addison’s disease
To the Editor: Addison’s disease frequently presents with cutaneous hyperpigmentation. It commonly appears diffuse, brown, and darkening and is most pronounced on light-exposed areas. A lentigo-like pigmentation may be present on the palms, soles, and mucous membranes. Nail pigmentation is less frequently observed, with few cases reported. A 65-year-old female presented with a 4-year history of nail pigmentation. She received oral anti-diabetic for diabetes mellitus type II. She had grey-