

CONTACT POINTS

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Mercury-induced acute generalized exanthematous pustulosis misdiagnosed as a drug-related case

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Acute generalized exanthematous pustulosis (AGEP) is characterized by the acute onset of fever with a generalized erythematous pustular eruption (1, 2). It is drug induced in more than 90% of cases (1, 2). However, it can be caused in rare cases by other

agents such as mercury (2, 3). We report a case of mercury-induced AGEP that was misdiagnosed as a drug-related one.

Case Story

An 18-year-old girl was treated with fluconazole (Funzol®; SAIPH, Sfax, Tunisia) 150 mg once a week for onychomycosis. 17 days after starting fluconazole, she developed a generalized eruption with fever (38.5 celsius). Physical examination showed several non-follicular pustules occurring on a diffuse, oedematous erythema distributed all over the body with marked lesions on the trunk and folds. The patient denied any intake of other medications during the previous weeks and had no history of mercury exposure. Laboratory investigations showed a total white blood cell count at 11 000/ μ l with 70% neutrophils and 10% eosinophils. Blood and pustule cultures were negative. The mycological examination of a pustule was negative. A skin biopsy showed spongiform subcorneal pustules and perivascular infiltrates with neutrophils and eosinophils. The diagnosis of AGEP was made, and fluconazole was suspected to be the trigger agent. Fluconazole was discontinued, and erythema, pustules, and subsequent desquamation resolved within 5 days without any medications. On the sixth day, the patient's little brother showed that he had broken a mercurial thermometer in the room he shared with his sister 1 day before the onset of the eruption. Subsequently, serum and urine mercury levels were measured and were both found to be high: 39 nmol/l (normal <25 nmol/l) and 65 nmol/l (normal <3 nmol/l), respectively. 6 weeks after complete resolution, the patient was patch tested with European standard series, metals series, and fluconazole (30% in pet. and 30% in water) (4). Reactions were evaluated at D2 and D3 according to International Contact Dermatitis Research Group (ICDRG) guidelines. The results are summarized in Table 1 (Fig. 1). Oral provocation test with 150 mg of fluconazole was negative. The diagnosis of mercury-induced AGEP was confirmed. Thus, our patient restarted her treatment with fluconazole without any incidents.

Discussion

In our patient, the diagnosis of AGEP was definite according to the

Table 1. Results of patch tests

Allergen	D2	D3
Metallic mercury 0.5% pet.	++	+++
Phenylmercuric acetate 0.01% aq.	+	++
Mercury ammonium chloride 1% pet.	++	++
Thimerosal 0.1% pet.	++	++
Amalgam 1% pet.	—	—
Fluconazole 30% pet.	—	—
Fluconazole 30% aq.	—	—

aq., aqua.

EuroSCAR group criteria (1). Mercury exposure had been reported in the literature as a possible trigger of AGEP (2, 3) and baboon syndrome (or systemically induced allergic contact dermatitis) (3, 5, 6). The latter is characterized by the occurrence of diffuse and symmetric erythematous maculopapular eruption of the flexural areas, with a V-shaped pattern on the medial thighs and diffuse erythema of the buttocks within a few days after exposure to mercury (usually from a broken thermometer) (3, 5, 6). Patients with mercury-induced baboon syndrome usually do not present with systemic symptoms, as do those with mercury-induced AGEP (3). It had been suggested that AGEP and baboon syndrome may be variants of a continuous spectrum of possible clinical manifestations (3).

Several studies in patients with AGEP showed a high rate of strongly positive drug patch tests compared with patients with other drug-related eruptions (7–11). This leads to the question as to why a primarily neutrophilic reaction (AGEP) would cause a lymphocytic patch test response? Involvement of T cells in

drug-induced AGEP was suggested by positive patch tests and lymphocyte transformation tests (11). Drug-specific CD4+ and CD8+ T cells could be isolated and propagated *in vitro* from patch test sites and blood from AGEP patients (10, 11). Britschgi et al. (10) had showed the involvement of drug-specific T cells in the accumulation of polymorphonuclear neutrophils (PMN) at the site of the lesions of AGEP by the preferential release of PMN-attractive chemokines such as interleukin-8 (now called CXCL8). Thus, AGEP serves as a valuable model for characterizing T cells with a particular function – namely, production of CXCL8 – leading to neutrophilic inflammation (11). Sometimes, patch tests in AGEP patients showed pustular reactions (9). Demitsu et al. (9) described pustule formation on patch test reaction of AGEP patients after longer patch test application (4 days). According to Schmid et al. (12), patch test lesions might reflect an earlier stage of AGEP in which activated CD4+ and CD8+ T cells are infiltrating dermis and epidermis and subcorneal vesicles are formed and filled with

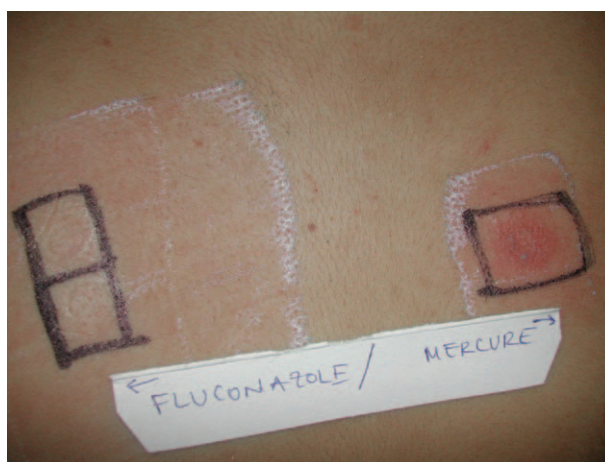


Fig. 1. Positive reactions (++) with metallic mercury 0.5% pet., while patch tests with fluconazole (30% in pet. and 30% in water) were negative.

T cells (mainly CD4+). At a later stage, vesicles are filled with neutrophils, transforming them into pustules (12). In our case, patch test readings were made at D2 and D3 and we had observed only vesicle formation but not pustular reactions. Later readings (not performed in our case) might be necessary to observe pustule formation on patch tests. Patch test with amalgam was negative in our patient, while metallic mercury was positive. This may be explained by the concentration of 1% used in our patch test, which is considered by Von Mayenburg et al. (13) as not suitable. Only 2 patients of their series of 13 with positive reactions to 20% amalgam reacted to 1% amalgam, while 10 of them reacted to 5% amalgam (13). According to Von Mayenburg et al. (13), 5% amalgam appears to be a suitable patch test concentration.

Initially, in our case, mercury exposure was not evident and fluconazole was suspected to be the trigger agent. Following a thermometer breakage, and especially in poorly ventilated premises, mercury vapour can remain even in adjacent rooms over long periods reaching 3 weeks (14). Although our patient did not break the thermometer herself, she was exposed to mercury vapour as shown by the high levels of serum and urine mercury. As mercurial thermometers are still widely used in several countries, questions about mercury exposure should be asked about in patients with AGEF, despite any history of drug intake.

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