

## Anaphylactic reaction to rifamycin SV: Presence of specific IgE antibodies

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Allergic reactions during surgery are mostly related to anesthetic drugs, antibiotics, latex, or plasma expanders.<sup>1</sup> Rifamycin SV was shown to be responsible for severe anaphylaxis<sup>2</sup> occurring at the end of the surgical procedure. In fact, this semisynthetic antibiotic derived from

natural rifamycin B is topically used at the end of surgery to prevent local infections. An IgE-dependent mechanism was suggested by skin and in vitro indirect tests,<sup>3</sup> but the presence of rifamycin SV-specific IgE in such patients has not been demonstrated.

We report a case of severe anaphylactic reaction to rifamycin SV, in which specific IgE antibodies were found.

### CASE REPORT

A 57-year-old woman was referred to the allergy clinic for the etiological diagnosis of an anaphylactic reaction that occurred during abdominal surgery for traumatic lesions. Ninety minutes after anesthetic induction, as soon as a large amount of rifamycin SV was

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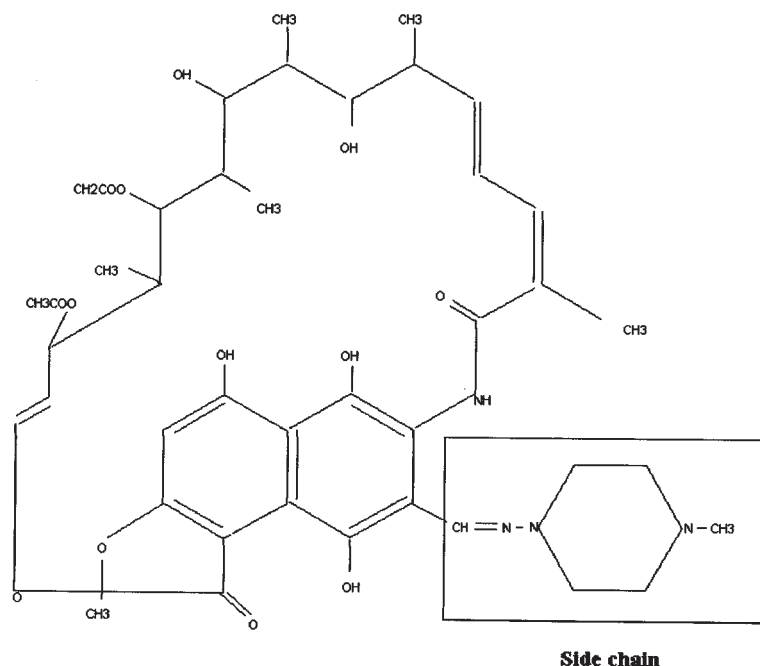


**FIG 1.** Structure of rifampicin and rifamycin. The side chain is present in rifampicin but not in rifamycin.

locally applied, the pulse rate increased to 150 beats/min, and the patient underwent vascular collapse. The episode was rapidly resolved by the intravenous administration of 0.5 mg of adrenaline, vollemic expansion, and administration of steroids. Six months previously, the patient had a local urticarial reaction after topical treatment of a wound with rifamycin SV.

Prick and intradermal skin tests with anesthetic agents (Propofol, Vecuronium bromide, Phenoperidine) used for anesthesia and with latex (standardized extract, 100 IR/mL; Stallergènes, France) were performed, and the responses were negative.

Scratch tests with rifamycin SV, rifampicin, and rifabutin induced a large wheal-and-flare reaction. We used the pure solution of rifamycin SV (50 mg/mL). Rifampicin and rifabutin were tested at concentrations of 60 mg/mL and 15 mg/mL, respectively. No positive skin test responses were found in 5 control subjects with the same drugs used in the same way.

### Determination of IgE antibodies to rifamycin SV

The rifamycin SV ImmunoCAP was an experimental prototype prepared by the following method. An excess of 3-formylrifamycin SV was conjugated to poly-L-lysine in carbonate buffer (pH 9.0) in the presence of ascorbic acid to prevent oxidation to the quinonic form. Subsequently, sodium cyanoborohydride was added to reduce the Schiff bases. This method, called "reductive amination," is a standard method for the conjugation of aldehyde-containing molecules to amine-containing molecules. The conjugate solution was gel filtrated by using a PD-10 column (Pharmacia Biotech) and then covalently coupled to the activated cellulose solid phase (ImmunoCAP). Rifamycin SV-specific IgE antibodies in serum were measured with UniCAP-specific IgE according to the directions for use (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden). A positive result (detectable specific IgE antibodies) was defined as a value greater than 0.35 kU<sub>A</sub>/L.

Rifamycin SV-specific IgE were determined in the patient's serum. A negative pool serum was used as control. This pool consists of sera from 20 different donors who had negative responses to

a large number (>100) of allergens. The level found in the patient's serum was 0.82 kU<sub>A</sub>/L, which corresponded to RAST class 2.

### DISCUSSION

This is the first reported case of the direct proof of the presence of specific IgE against rifamycin SV. A previous study was published by Bassi et al,<sup>4</sup> suggesting the presence of specific IgE directed against rifampicin in patients treated for pulmonary tuberculosis who displayed clinical manifestations ascribed to rifampicin sensitization. However, the evidence of the presence of specific IgE antibodies was indirect and derived from the release of histamine in the presence of rifampicin from rat peritoneal mast cells sensitized with patient sera. Significant histamine release was also induced by rifamycin SV, suggesting a cross-reactivity between both drugs. The structural difference between rifamycin SV and rifampicin resides in the presence of a side chain in the latter (Fig 1). Therefore the induction of antibodies directed to the common moiety of the molecules could explain the cross-reactivity. In our patient such a cross-reactivity was also found because skin test responses were positive for rifamycin SV and also for rifampicin and rifabutin. Cardot et al<sup>3</sup> recently reported 4 cases in which the presence of specific IgE against rifamycin SV could be suspected through the determination of histamine release from peripheral basophils and platelet cytotoxicity tests. However, no direct proof of the presence of specific IgE antibodies was shown.

Locally used rifamycin SV is well known to induce contact dermatitis<sup>5</sup> and local urticaria.<sup>6</sup> Anaphylactic shock to rifamycin SV was first described by Piazza in 1989,<sup>2</sup> and several cases were reported.<sup>3</sup> In all cases

rifamycin SV was used during surgery for its broad spectrum of activity to prevent wound infections.

We suggest that rifamycin SV must be considered in the etiological diagnosis of perioperative collapse caused by an IgE mechanism together with intravenous drugs (such as muscle relaxants) and latex. A diagnostic method based on skin tests and specific IgE determination could then be proposed.

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