

CORRESPONDENCE

Successful rapid desensitization in a glioma patient with procabazine-mediated anaphylaxis

Adjuvant treatment with radiotherapy followed by chemotherapy including procabazine increases survival in low-grade glioma.¹ Procabazine-related drug hypersensitivity reactions (DHR) may limit its use.² We recently described six patients with nonimmediate DHR on procabazine.³ Successful reintroduction of procabazine was possible in three patients, for one of them, a prolonged desensitization schedule was developed. At that time, we had not encountered patients with immediate DHR to procabazine. We now describe a case of severe immediate procabazine-mediated anaphylaxis and show that procabazine reintroduction via a 12-step desensitization schedule is feasible in this setting as well.

A 41-year-old man suffered from IDH-1-mutated diffuse astrocytoma WHO 2 since 12 years, and it was due to disease progression scheduled for 6 cycles of PCV chemotherapy, which includes orally administered lomustine (day 1) and procabazine (day 9–22), and intravenous vincristine (day 8 and 29). He underwent the first 3 cycles uneventfully. On day 18 of the fourth cycle (9th day of procabazine), he presented with generalized pruritic exanthema, which developed an hour after procabazine ingestion. The patient did not use any other medication that day, nor did he have a history of urticaria or documented allergies. At the emergency department, a generalized urticarial rash and initially normal vital parameters were observed. Despite treatment with intravenous dexamethasone and clemastine,

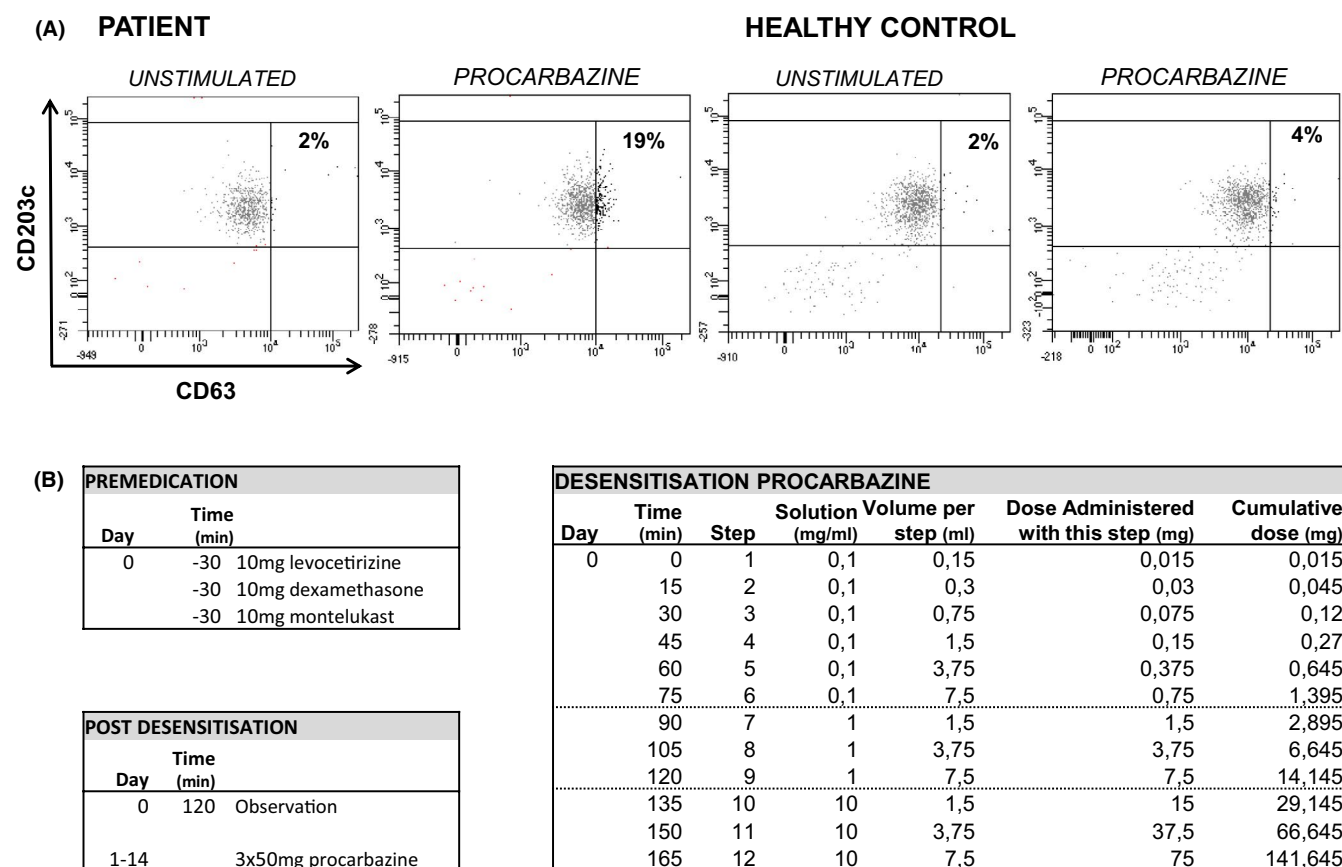


FIGURE 1 Basophil activation testing and desensitization in procabazine-mediated anaphylaxis. A, Results of the basophil activation test. Basophils are CD203c-positive (y-axis) and shown in the upper left quadrant; activated basophils express CD63 (x-axis) and move to the upper right quadrant. Basophils of the patient and a healthy control were stimulated with 250 µg/ml procabazine; B, twelve-step desensitization schedule for immediate drug hypersensitivity reactions to procabazine

he developed hypotension up to 70/40 mmHg despite fluid resuscitation, upon which 0.5 mg epinephrine i.m. was administered. Based on these clinical symptoms and the rapid recovery on epinephrine, a presumptive diagnosis of procabazine-mediated anaphylaxis was made. These findings were supported by histologic confirmation of the urticaria and documented mast cell activation as shown by elevated methylhistamine (165.6 $\mu\text{mol/mol}$ kreat, ref range 0.0–150.0) upon urinary analysis.

Since specific IgE against procabazine is not commercially available and intracutaneous testing is not possible due to the chemotoxic properties of procabazine, we performed a procabazine basophil activation test (BAT). Peripheral blood of the patient was stimulated with different concentrations of procabazine (1 $\mu\text{g/ml}$ –1 mg/ml), and CD63 and CD203 expression on the basophils was measured (Figure 1A). Upon stimulation with procabazine, there was a clear basophil activation as shown by upregulation of CD63, suggesting sensitization to procabazine.

While desensitization protocols are available for immediate DHR against several other chemotherapeutics,⁴ no such protocols exist for procabazine. We developed a novel desensitization schedule for immediate procabazine-related DHR (Figure 1B). Three oral solutions of 0.1 mg/ml, 1 mg/ml, and 10 mg/ml were prepared. Procabazine was incrementally administered in 12 steps over one day using concomitant antiallergic medication. The reintroduction was well tolerated, and the remaining two cycles of PCV chemotherapy could be successfully administered. Posttherapy MRI did not show signs of glioma recurrence, and the patient felt well enough to resume his work duties.

The novelty of these findings is twofold: First, to our knowledge, the successful use of BAT for procabazine has not been described previously. Reliable *in vitro* diagnostics for procabazine DHM are currently not available but would facilitate further analysis of procabazine-mediated DHM while avoiding unnecessary exposure of patients to the drug.

Limiting factors are that BAT is laborious and can be performed on fresh peripheral blood samples only, so other feasible options should be explored; and second, this is the first description of a successful desensitization for a severe, immediate procabazine-mediated DHR. It is important to remember that the desensitization effect is temporary, and hence, the 12-step schedule should be repeated at every cycle. Nevertheless, this schedule allowed the patient to receive his full dose of procabazine without adverse events and therefore shows potential for validation in other patients with immediate procabazine-mediated DHM.

KEYWORDS

anaphylaxis, basophil activation test, desensitization, procabazine

CONFLICT OF INTEREST

All authors declare they have nothing to disclose with regard to this manuscript.

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