

Letter

Systemic mastocytosis presenting as occupational IgE-mediated anaphylaxis to pine processionary caterpillar

Mastocytosis is characterized by the accumulation of clonal mast cells (MCs) in organs such as skin, bone marrow (BM), and the gastrointestinal tract. Patients with systemic mastocytosis often have symptoms related to the mediator release of MCs, including anaphylaxis in 22% to 49% of the cases.^{1,2} The frequency of anaphylaxis among patients with indolent systemic mastocytosis without skin lesions (ISMs[−]) is higher than that found in patients with skin involvement (ISMs⁺).^{2–4}

The most common trigger for anaphylaxis in patients with ISMs[−] is Hymenoptera venom sting.^{3,4} These patients are predominantly males who present with severe systemic reactions to Hymenoptera venom characterized by cardiovascular collapse in the absence of pruritus, urticaria, or angioedema, remaining otherwise asymptomatic. They typically have a low BM MC burden together with low (even normal) serum baseline tryptase levels.^{3,4} In contrast to the well-known association between Hymenoptera venom anaphylaxis and systemic mastocytosis, anaphylaxis caused by other insects has been rarely described in patients with mastocytosis.⁴ We report a case of occupational IgE-mediated severe anaphylaxis attributable to pine processionary caterpillar (PPC) as the clinical presentation of an underlying ISMs[−].

A 54-year-old, male pine-resin worker was treated at the emergency department for local pruritus and erythema, dyspnea, wheezing, dizziness, loss of consciousness, and sphincter relaxation 10 minutes after direct skin contact on his neck with 1 PPC during work, which required parenteral epinephrine, corticosteroids, and dexchlorpheniramine. Foods, drugs, and other potential triggers for anaphylaxis were ruled out on an exhaustive anamnesis. Physical examination did not reveal urticaria pigmentosa, adenopathy, or organomegaly. A complete blood cell count, biochemical analyses, thyroid function tests, serum immunoglobulin levels, antinuclear antibody levels, and complement were normal. Initial allergy workup revealed the following: serum baseline tryptase (ImmunoCAP Tryptase, Thermo Fisher Scientific, Uppsala, Sweden), 37.1 µg/L; total serum IgE, 72 kU/L; positive skin prick test (SPT) results for a whole-body PPC extract (Laboratorios Bial-Aristegui, Bilbao, Spain⁵; wheal, 4 × 3 mm; erythema, 7 × 5 mm; histamine, 3 × 3 mm); and negative SPT results for a battery of common food extracts, together with no detectable (<0.35 kU/L) serum specific IgE antibodies to *Anisakis simplex*, *Ascaris lumbricoides*, and

Echinococcus granulosus. The SPT result for whole-body PPC extract was negative in 30 controls (atopic and nonatopic).

The Spanish Network on Mastocytosis (REMA) score was applied, resulting into a score of +4 (ie, male [+1], syncope [+3], pruritus [−2], and serum baseline tryptase >25 µg/L [+2]), which translated a high probability of systemic mastocytosis.^{3,4} In view of these results, the patient was referred to the Instituto de Estudios de Mastocitosis de Castilla La Mancha for a complete BM study, which included cytomorphologic and histologic evaluation, flow cytometry immunophenotyping of BM MCs, and molecular analysis of the D816V *c-KIT* mutation on fluorescence-activated cell sorting–purified hematopoietic cell lines, including MCs, eosinophils, and CD34⁺ progenitor cells. This study revealed an increase of MCs in BM smears and sections with the presence of more than 15 MC aggregates. These cells accounted for 0.675% of all BM nucleated cells and revealed an aberrant CD25⁺/CD2⁺ immunophenotype. The D816V *c-KIT* mutation was detected in fluorescence-activated cell sorting–purified BM MCs and tested negative in other BM hematopoietic cells. Abdominal ultrasonography and dual-energy X-ray absorptiometry scan revealed mild hepatic steatosis and osteopenia in the lumbar spine and femoral neck, respectively.

The patient was diagnosed as having ISMs[−] associated with anaphylaxis attributable to sensitization to PPC. Although the reaction occurred immediately after direct skin contact with PPC, because of the high risk of reexposure because of his job, the patient was warned to carry an epinephrine autoinjector and to use adequate protective equipment at work to minimize the probability of future skin/inhaled contacts with PPC.

Nine months later, after the aforementioned job security instructions, no further anaphylaxis had been observed and the serum baseline tryptase level remained high (40.2 µg/L). At that time, additional allergy studies using whole-body PPC extracts were performed: (1) basophil activation test⁶ revealed 0% activated basophils in basal conditions, 89.5% in response to anti-IgE and 86.5% in response to PPC extract; (2) the level of serum specific IgE antibodies to PPC (enzyme allergosorbent test [EAST]; Hytec Specific IgE EIA kit, Hycor Biomedical Ltd, Garden Grove, California) was less than 0.35 kU/L but greater than the value obtained with a pool of sera from nonatopic individuals (negative control); and (3) sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting assay with and without 2-mercaptoethanol revealed 2 IgE-binding bands of approximately 35- and 55-kDa molecular weight in both electrophoretic conditions (Fig 1 and eAppendix).

PPC (*Thaumetopoea pityocampa*) is a Lepidoptera of the Thaumetopoeidae family, commonly found in Europe forests, particularly in Mediterranean areas. PPC has urticating hairs that

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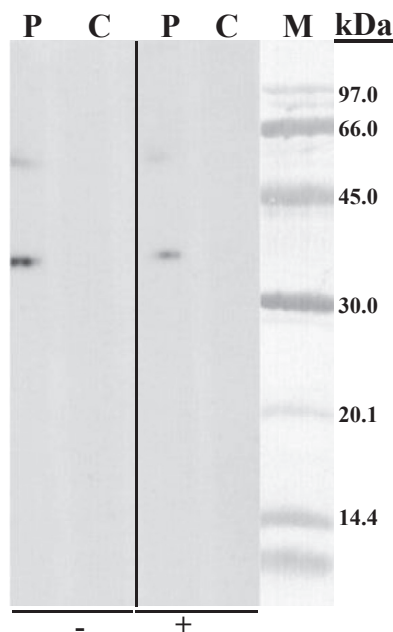


Figure 1. Sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting assay (without and with 2-mercaptoethanol) revealing 2 IgE-binding proteins. Lane P, patient serum; lane C, control serum; lane M, molecular mass marker; plus sign, positive; and minus sign, negative.

frequently induce local reactions, such as contact dermatitis, urticaria, or keratitis and, more rarely, systemic symptoms, including anaphylaxis, mostly in the context of occupational exposures.^{7–10} Although an irritant mechanism can be involved in local reactions, IgE-mediated hypersensitivity has been demonstrated, particularly in patients with anaphylaxis, by SPT, enzyme allergosorbent test, and sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting.⁷ Several allergens with different molecular weights have been reported so far,^{7–9} among which a 15-kDa protein called thaumetopoein (Thau p 1) has been suggested to be one of the most clinically relevant allergens.^{7,8} Although both IgE-binding bands of approximately 35 and 55 kDa detected with the serum of our patient have been already described,⁹ these have not been previously reported to be detected within the same patient serum. Noteworthy, our results indicate that basophil activation test might be also a complementary method that supports the hypersensitivity to PPC in this patient.

Similarly to other patients with ISMs[−] (eg, ISMs[−] associated with Hymenoptera venom anaphylaxis), the implication of PPC as the culprit trigger of anaphylaxis in our patient is supported by the demonstration of specific IgE to PPC together with the temporal association between the exposure to PPC and the development of symptoms and also by the absence of further anaphylactic episode while the patient has been using adequate protection to avoid new contacts to PPC. To the best of our knowledge, this is the first report on the coexistence of systemic mastocytosis and anaphylaxis attributable to PPC. Moreover, this case highlights the utility of the REMA score as a predicting tool for ISMs[−],^{3,4} even if the culprit elicitor of anaphylaxis has not been previously recognized in patients with mastocytosis.

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Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2016.07.002>.

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eAppendix. Sodium Dodecyl Sulfate–Polyacrylamide Gel Electrophoresis and Immunoblotting

Sodium dodecyl sulfate–polyacrylamide gel electrophoresis was performed according to the method of Laemmli. The samples were prepared in 0.125 M Tris hydrochloride (pH 6.8) and were dissociated with 0.1% sodium dodecyl sulfate and 5% β -mercaptoethanol at 100°C for 5 minutes. Proteins were electrophoretically transferred to polyvinylidene difluoride membrane (Immobilon-P membranes, Millipore Corp, Bedford, Massachusetts) essentially

as described by Towin et al. The membrane was blocked with 9% (wt/vol) defatted dry milk in Tris-buffered saline (1 hour at 37°C) and incubated with 0.5 mL of patient's serum (16 hours at 4°C); after being washed with Tris-buffered saline, the membrane was incubated with antihuman IgE–horseradish peroxidase conjugate and developed with a chemiluminescence method recommended by the manufacturer (Amersham ECL-Prime Western Blotting reagent, GE Healthcare, Little Chalfont, United Kingdom). A pool of sera from nonatopic patients was used as negative control.