

Case report

Occupational IgE-mediated rhinitis caused by ninhydrin

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Ninhydrin is a laboratory chemical used as a reagent in the detection of free amino and carboxyl groups in proteins and peptides. We present the case of a laboratory technician who developed symptoms of rhinitis when handling papers immersed in a solution containing ninhydrin. Prick tests for ninhydrin and ninhydrin RAST were positive. The inhalation provocation test in an exposure chamber gave an immediate nasal response. A positive prick test to ninhydrin, an elevated level of specific IgE antibodies to ninhydrin, and the RAST inhibition test confirmed an IgE-mediated type I allergic reaction. We are not aware of any other report of ninhydrin as a cause of IgE-mediated allergy.

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Many different allergens can cause occupational rhinitis. Most cases of occupational allergic rhinitis are caused by proteins, but low-molecular-weight chemicals can also induce sensitization (1–4). Ninhydrin (CAS 485-47-2; 2,2-dihydroxy-1,3-indanedione; 1,2,3-triketohydrindene hydrate), discovered by Ruhemann in 1911, is a laboratory chemical used widely as a reagent for the detection of free amino and carboxyl groups in proteins and peptides, yielding a blue color under proper conditions (5). Ninhydrin is a white to brownish powder that is freely soluble in water. It is also available as a 0.2% spray reagent in ethanol. Apart from its use in chromatography, ninhydrin is also used in the morphologic detection of fingerprints on paper. The use of ninhydrin in the binding of urea and creatinine in dialysate regeneration has been studied (6). Ninhydrin has been reported to cause allergic contact eczema (7). However, we have not found any report of ninhydrin as a cause of IgE-mediated allergy in the literature. We present a patient who developed occupational IgE-mediated rhinitis from exposure to ninhydrin.

Case report

The patient was a 40-year-old woman without atopy. She was otherwise healthy, did not smoke, and used no other medication except an ointment for psoriasis on her elbows and scalp. She had

worked for 12 years as a technician in a crime laboratory. For 2–4 days per week, 3–5 h each time, her task was to detect fingerprints on papers or tapes that were first immersed in a solution of ninhydrin, glacial acetic acid, ethanol, and Freon (Arklone®). The solution was prepared as follows: 25 g of ninhydrin, 50 ml of glacial acetic acid, and 100 ml of ethanol were mixed. A volume of 15 ml of the solution was mixed with 500 ml of Arklone. The papers were immersed in this solution and then placed in a heating cupboard at a temperature of 80°C for 6 min. After the papers were taken from the cupboard, they were allowed to dry for a short period. Earlier only the immersion, but for the last 2 years the whole procedure has been done in a fume cupboard. After the procedure, the patient, who wore cotton gloves, checked the documents to detect fingerprints.

During the past 3 years, the patient had suffered symptoms of rhinorrhea and nasal blockage when she had mixed the solution or handled the immersed papers. In the beginning, she had no symptoms while doing other tasks, or during weekends or holidays. Later she began to have some nasal blockage also during weekends. She had had no eye or bronchial symptoms, or symptoms of dermatitis.

Investigations

Skin prick tests. Skin prick tests were done, read, and scored as previously described (8). They

included tests with common environmental allergens (Allergologisk Laboratorium A/S, Denmark), ninhydrin 0.05% and 0.125% water solutions, and a 2% ninhydrin-HSA solution. The 2% ninhydrin-HSA solution was prepared as follows: 200 mg of HSA (human serum albumin) and 100 mg of ninhydrin were dissolved in 40 ml of phosphate-buffered saline (PBS) and stirred for 1 h at room temperature. A 10-ml portion of the mixture was transferred to a Nanosept® N10 (Intersept Ltd, UK) sample concentrator chamber in order to concentrate the ninhydrin HSA and to separate it from free ninhydrin. The mixture was concentrated to a volume of 1 ml. A volume of 9 ml of PBS was added to the chamber. The concentration procedure was repeated and the solution was diluted to 2.5 ml with PBS. This 2% (w/v) HSA solution was used for skin prick tests.

Specific IgE determinations. The total IgE was determined by the Pharmacia CAP system IgE RIA (Kabi Pharmacia, Sweden). RAST disks for specific IgE determination were prepared as follows: 10 ml of conjugate mixture was concentrated to a volume of 1 ml, and 9 ml of 0.1 M NaHCO_3 buffer was added to the chamber. The concentration procedure was repeated, and the solution was diluted to 2.5 ml with 0.1 M NaHCO_3 . A volume of 100 μl of the solution of 2% ninhydrin HSA was added to each cyano-genbromide-activated paper disk according to the method of Ceska et al. (9). For specific IgE determination, the Phadebas® RAST technique (Pharmacia Diagnostics, Sweden) was used.

RAST inhibition studies were carried out by the method of Yman et al. (10). Serial dilutions (20, 2, 0.02, and 0.0002 mg/ml) of ninhydrin HSA conjugates in PBS were allowed to react with the patient's serum (20 μl of conjugate dilution plus 50 μl of serum) overnight at 4°C. The mixtures were then used for RAST determination. PBS (20 μl in 50 μl of serum) was used to obtain the noninhibited results. The degree of reduction of serum RAST values after absorption was expressed as an inhibition percentage.

Inhalation provocation tests. The patient was exposed in a 6-m³ exposure chamber. Exposure to 100 g lactose for 30 min was used as a control provocation. On the next day, she handled papers containing ninhydrin for 30 min. In all provocations, the nasal response was followed by anterior rhinoscopy and nasal stats scoring. To exclude a possible reaction caused by the papers themselves, the provocation with papers without ninhydrin was repeated 1 week later, and on the next day a provocation with papers containing ninhydrin was repeated. This time acoustic rhinometry

(RHIN2000, S.R. Electronics ApS, Denmark) was also used for the follow-up. The nasal eosinophils were taken 2 h after the beginning of the ninhydrin provocation and after an exposure-free time of 4 days. Control inhalation provocation tests with ninhydrin-containing papers were done on four healthy, nonexposed volunteers.

Results

No positive reactions in the prick tests to the common environmental allergens were found. Ninhydrin tested as 0.05% and 0.125% water solutions gave a slight 1+ reaction. Ninhydrin tested as a 2% HSA conjugate gave a histamine-size reaction with pseudobodies. Skin prick tests with 2% ninhydrin-HSA conjugate for five nonexposed controls and with 0.125% ninhydrin water solution for seven nonexposed controls were all negative.

The patient's total IgE was low: 20 kU/l. Ninhydrin-specific IgE determination was done twice from the patient's serum, giving elevated values of 0.6 and 0.7 kU/l. RAST tests done with the sera of three non-ninhydrin-exposed subjects gave values <0.3 kU/l. The RAST inhibition value was 92% (Fig. 1).

After the exposure to 100 g lactose for 30 min, there was no clinically significant change in the nasal status. During the first ninhydrin provocation, the patient developed nasal symptoms similar to those at work, and a profuse increase in the degree of rhinorrhea and some increase on nasal blockage were noted. Despite her feelings of hoarseness, her laryngeal status remained unchanged.

After the provocation done with papers without ninhydrin, no change was seen in nasal status. The nasal volume (the volume of the right side plus the volume of the left side from the nasal tip to 52 mm) increased by 15%. In the provocation done with ninhydrin-containing papers, blockage of the nose and profuse rhinorrhea were seen. The measured nasal volume decreased by 35%. The nasal eosinophils taken after the provocation showed moderate eosinophilia (+ +/+). After an exposure-free period, the number of nasal eosinophils was decreased (-/+). In the ninhydrin provocation test on volunteers, none developed definitive symptoms of rhinitis or any change in their nasal status.

Discussion

Most cases of occupational rhinitis are caused by protein allergens (3). However, low-molecular-weight chemicals (e.g., nickel, reactive dyes, phthalic anhydrides, and diisocyanates) are also known to cause type I allergy (2-4).

Ninhydrin is known to be a local irritant causing

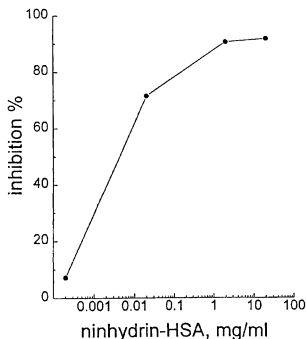


Fig. 1. RAST inhibition of ninhydrin HSA when tested with different ninhydrin-HSA-Conjugate concentrations.

redness of the skin. It is also a contact allergen. Schlacke & Fuchs (7) reported three patients undergoing patch testing who developed allergic contact eczema (type IV allergy) to ninhydrin-containing surgical marking-pen ink used to indicate test areas on the skin.

Our patient represents type I allergy to ninhydrin. She had been exposed to ninhydrin in her work for a total of 12 years, and she had developed immediate-type rhinitis symptoms during the past 3 years. The causal association between her rhinitis symptoms and ninhydrin was demonstrated by a provocation test in an exposure chamber.

Hapten-HSA conjugates are often necessary when skin prick tests are performed with chemical haptens (11), but the conjugates are more time-consuming and expensive than water solutions. Therefore, skin prick tests are often first done with water solutions in the case of water-soluble haptens. Such solutions are easy to prepare and may at least give a hint of prick test positivity (2).

The specificity of our patient's positive ninhydrin skin prick test results was shown by negative control skin tests. In agreement with investigations done with other chemical haptens (11), the elevated ninhydrin-specific IgE and the high RAST inhibition percentage verified the specificity of the ninhydrin skin prick test solutions. The patient's nasal eosinophilia after the provocation also confirmed that her immediate symptoms were caused by IgE-mediated allergy and not by unspecific nasal irritation.

Ninhydrin is a new chemical hapten which can include IgE-mediated occupational rhinitis. Our skin prick test results suggest that a 2% ninhydrin-HSA solution is suitable for skin prick tests when a type I allergy to ninhydrin is suspected.

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