The presence of potential barley allergens and proteins from *S. cerevisiae* have been described in beer through proteomic studies (nonspecific lipid transfer protein [nsLTP], gliadins, glutelins, trypsin \( \alpha \)-amylase inhibitors, serpins) [3,4], and some have been shown to trigger allergic reactions, as follows: nsLTP (9 kDa), protein Z (45 kDa) [5], and protein Z-type serpin (20–25 kDa) [6]. Similarly, sensitization to yeast [7] has been described as the cause of allergy to beer, cider, and wine.

The patient was a 33-year-old woman with a personal history of allergic rhinoconjunctivitis and exercise-induced asthma who had been experiencing episodes of anaphylaxis (ocular pruritus, eyelid angioedema, globus sensation, dysphonia, diarrhea, urticaria, and dizziness) with no associated exercise over a period of 3 years. These reactions resolved with self-administered epinephrine. She related the episodes to ingestion of beer with chips or olives. Occasionally, she had experienced milder symptoms after drinking red and white wine. She tolerates other alcoholic beverages, cereals (including bread), grapes, nuts, and all kinds of food.

Beer and wine are the most widely consumed alcoholic beverages in the world. Wine is made from fermented grape juice and beer is brewed from fermented cereal grains (most commonly malted barley). Hops are also used to flavor beer. Both beverages are produced by fermentation with yeasts (*Saccharomyces cerevisiae* or *Saccharomyces carlsbergensis*). Hypersensitivity reactions to beer or wine are rare and have been attributed mainly to grains [1] and grapes. Proteins from barley are the most common cause of beer allergy [2].

Figure. I, SDS-PAGE Immunoblotting. A, Franziskaner beer extract. B, Chimay beer extract. C, *Saccharomyces cerevisiae* extract. Lane P, patient’s serum; Lane C, control serum (pool of sera from nonatopic individuals); Lane S, anti–Pru p 3 rabbit serum; Lane C\(_1\), unimmunized rabbit serum; Lane M, molecular mass standard. II. SDS-PAGE immunoblotting-inhibition. Solid phase: Chimay beer extract. Lane C, control serum (pool of sera from nonatopic individuals); Lanes 1–4, patient serum preincubated with Chimay beer extract (lane 1), with Franziskaner beer extract (lane 2), with *S. cerevisiae* extract (lane 3), and with lamb extract (lane 4).
Dermatophagoides pteronyssinus (3×3), Lepidoglyphus destructor (3×3), Alternaria alternata (3×3), and Aspergillus fumigatus (7×8). SPTs were positive with beer extracts, as follows: Heineken, 5×5; San Miguel, 4×4; Chimay, 6×5; Franziskaner (from wheat), 5×5; red wine, 7×7; white wine, 8×6; S cerevisiae, 7×6; raw S cerevisiae, 6×6; cooked S cerevisiae 6×6; Penicillium nalgiovense, 7×6; and mushrooms, 8×8. The results of SPTs performed with cereal extracts (wheat, barley, corn), fruits (apple, peer, peach, red and white grape), and Pru p 3 (peach nsLTP) were negative.

Total serum IgE (ImmunoCAP, Thermo Fisher) was 178 kU/L, and the results for specific IgE were as follows: 4.51 to S cerevisiae, 4.29 to Penicillium chrysogenum (Penicillium notatum), 3.93 to A fumigatus, 3.87 to Candida albicans, 1.93 to Cladosporium herbarum, 1.93 to A alternata, 4.24 to rPru p 3, and 3.96 to rMal d 3. Specific IgE <0.10 was recorded for cereals (barley, oat, maize, malt, hop, rye, wheat, rTri a 19, rTri a 14), rAlt a 1, rAsp f 2, rAsp f 4, and rAsp f 6.

SDS-PAGE immunoblotting was carried out under reducing conditions (with mercaptoethanol) as described by Lammeli [8], with Franziskaner and Chimay extracts, S cerevisiae extract, and the patient’s serum. In order to study the possible involvement of the cereal nsLTP in the allergic reaction due to beer ingestion, the beer extracts were also incubated with rabbit serum against Pru p 3.

A similar profile of IgE-reactive bands was detected in both beer extracts, the main ones being bands of around 97 kDa, 80 kDa, 55 kDa, 40 kDa, 32 kDa, and 17 kDa. In the S cerevisiae extract, a high intensity IgE-binding zone was revealed between 100 kDa and 29 kDa, as was a band of around 17 kDa. The anti–Pru p 3 rabbit serum revealed a band around 17 kDa. The anti–Pru p 3 rabbit serum revealed a band around 17 kDa.

In order to determine whether S cerevisiae was the allergic source of the IgE-reactive proteins detected in beer extracts, an immunoblotting-inhibition assay was carried out with Chimay beer extract in the solid phase and beer extracts and S cerevisiae extract as inhibitors. Both beer extracts and S cerevisiae extract produced total inhibition of IgE-binding in Chimay beer extract.

Airola et al. [9] reported a case of allergy to S cerevisiae in a patient who experienced anaphylactic reactions to beer, red wine, and sauces, suggesting that the reaction may have been due to cross-reactivity with antigens from fungi to which the patient was sensitized (C herbarum, A alternata, A fumigatus, P notatum, Malassezia furfur, and mushroom).

Proteins ranging from 5 to 100 kDa have been described in beer and include mainly albumins, globulins, serpin, amylase inhibitors, lipid-binding proteins, chaperones, and enzymes. During the manufacturing process, proteins can also be modified. The proteins most frequently found in beer are serpin-Z-4 (45 kDa) and LTP (9 kDa) [10]. The result of SDS-PAGE immunoblotting suggests that these proteins were not involved in the present case, as they were not recognized by the patient’s serum. S cerevisiae proteins of 97 kDa, 80 kDa, 55 kDa, 40 kDa, 32 kDa, and 17 kDa, which have not been previously reported, might be the responsible for the patient’s condition.

We present a case of beer and wine allergy caused by allergy to S cerevisiae, which is used in the fermentation of both beverages. When this allergenic source is heated, it does not cause allergy symptoms. Given that the patient in the present report tolerates bread, we believe that some S cerevisiae allergens can be inactivated with heat. She had a previous history of respiratory allergy due to A alternata and subsequently developed anaphylactic reactions after drinking beer and wine. Therefore, we think that the primary sensitization could be due to environmental fungi. More research will be necessary to identify and characterize the allergenic proteins of S cerevisiae.

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Conflicts of Interest

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References

Cutaneous B-cell Lymphoma at the Injection Site of Airborne Allergen Immunotherapy: Progression to Cutaneous Metastasis

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Injection site reactions in subcutaneous immunotherapy (SCIT) with airborne allergens are common, with up to 86% of patients experiencing this adverse effect [1]. Delayed local reactions are often self-limiting, although they can sometimes be persistent owing to granulomatous foreign body reactions or, rarely, to cutaneous pseudolymphoma (CPL).

In 1974, Bernstein et al [2] reported the first case of CPL induced by a hyposensitizing vaccine against mites and bacteria. Since then, several cases of B-cell CPL have been published with tetanus, meningoencephalitis, and hepatitis vaccines [3,4] and hyposensitizing extracts [5,6]. Given that aluminum hydroxide was present as an adjuvant in most cases [3,4,6], it is thought to have a causal role. However, cases in which this adjuvant was not present have been described [7].

CPL affecting vaccine injection sites tends to have a benign course and rarely progresses to lymphoma [8,9]. The reported causes were influenza and anthrax vaccines, and one of the patients died [8].

We present the case of a patient who developed CPL at the injection site of a hyposensitizing extract of pollens with aluminum hydroxide that progressed to primary cutaneous B-cell follicular center lymphoma (CBFCL).

A 42-year-old woman diagnosed with rhinoconjunctivitis and asthma due to pollen allergy was treated with monthly injections of a hyposensitizing depot pollen extract for 4 years. The extract contained aluminum hydroxide as an adjuvant. The patient did not present any local or systemic adverse reactions, and her seasonal respiratory symptoms improved.

Four years after the end of the hyposensitizing treatment, she presented itchy, papulonodular lesions on the external aspect of both arms, exactly in the areas where the vaccine was injected. Aluminum hydroxide–induced granulomas were suspected, and treatment with topical corticosteroids was started. However, the lesions progressed, and a skin biopsy was performed. The histopathological examination revealed a CD20+ B-cell follicular center lymphoma, consistent with primary cutaneous B-cell follicular center lymphoma, which was confirmed by immunohistochemistry.

We discuss the rare case of a patient who developed primary cutaneous B-cell follicular center lymphoma at the injection site of a hyposensitizing extract of pollens with aluminum hydroxide that progressed to cutaneous metastasis.

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