

## Dual Anaphylaxis Triggered by Cannabis and Tomato: A Case Report

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### Abstract

**Introduction and objectives:** Cannabis allergy is increasingly associated with systemic allergic reactions, including anaphylaxis, frequently mediated by non-specific lipid transfer proteins. This report describes a clinically significant case of dual anaphylaxis linked to cannabis exposure and tomato ingestion.

**Materials and methods:** The clinical history and allergy evaluation of a 23-year-old male were reviewed. The diagnostic work-up included skin prick testing, prick-by-prick testing with recreational cannabis, serum specific immunoglobulin E assessment by component-resolved diagnostics, and basophil activation testing.

**Results:** The first episode was severe and occurred without an immediately identifiable trigger, while a

second milder episode followed accidental tomato ingestion. The patient showed sensitization to multiple lipid transfer proteins, including Can s 3, the lipid transfer protein of Cannabis sativa. Prick-by-prick testing with cannabis was strongly positive, and basophil activation testing confirmed marked reactivity to tomato. Complete symptom remission followed cannabis avoidance.

**Conclusions:** This case supports cannabis as a potential primary sensitizer in lipid transfer protein-mediated allergy and underlines the need to investigate cannabis exposure in unexplained or atypical anaphylaxis.

**Keywords:** Anaphylaxis; Cannabis allergy; Cross-reactivity; Lipid transfer protein; Tomato allergy

**Abbreviations and Acronyms:** BAT: Basophil Activation Test; CA: Cannabis Allergy; CBD: Cannabidiol;  $\Delta$ 9-THC:  $\Delta$ 9-Tetrahydrocannabinol; nsLTP: non-Specific Lipid Transfer Protein; OAS: Oral Allergy Syndrome

## Introduction

*Cannabis sativa* is an annual plant of the Cannabinaceae family, widely used for industrial, recreational, and medicinal purposes [1]. Its major phytochemicals include  $\Delta$ 9-Tetrahydrocannabinol ( $\Delta$ 9-THC), the principal psychoactive compound, and Cannabidiol (CBD), both exhibiting psychoactive activity to varying degrees [2,3]. With increasing global accessibility and the liberalization of cannabis-based products, reports of allergic reactions to cannabis have become more frequent [4]. The first clinical case of Cannabis Allergy (CA) was documented in 1971 [5]. In a recent survey of 445 allergists, 192 (43.1%) reported evaluating patients with suspected cannabis allergy, highlighting its emerging relevance in clinical practice [6]. A Spanish cohort study estimated the prevalence of cannabis allergy at 0.4% among patients presenting with respiratory and/or cutaneous symptoms [7]. Epidemiological estimates vary across regions, likely reflecting differences in national legislation regarding cannabis use. The incidence of CA appears to be rising in parallel with evolving legal frameworks [8]. Allergic reactions have also been reported in occupational settings, including among cultivators, laboratory personnel, pharmaceutical employees, and hemp industry workers [9,10].

To date, five *Cannabis sativa* allergens have been identified and officially recognized by the WHO/IUIS Allergen Nomenclature Sub-Committee: Can s 2, a profilin; Can s 3, a non-Specific Lipid

Transfer Protein (nsLTP); Can s 4, an Oxygen-Evolving Enhancer Protein 2 (OEEP2); Can s 7, a Thaumatin-like protein [11]; and Can s 5, a PR-10 protein homologous to Bet v 1 [12-14]. Among these, Can s 3 is considered the most clinically relevant due to its structural homology with other plant-derived nsLTPs, predisposing to cross-reactivity with botanically unrelated foods [15]. Can s 3 is also present in cannabis pollen [13]. The clinical significance of Can s 2, Can s 4, Can s 5, and Can s 7 remains uncertain [16]. Cannabis allergy can be life-threatening and carries a high risk of cross-reactivity. Exposure may occur via inhalation, direct contact, ingestion of hemp seeds or cannabis-containing products, or medical use [8,17]. Symptoms typically develop rapidly, predominantly affecting the respiratory tract (rhinoconjunctivitis, asthma), followed by cutaneous manifestations (pruritus, urticaria, angioedema) [4,10,19]. Gastrointestinal and cardiovascular involvement has also been described [18]. Importantly, anaphylaxis occurs in up to 20% of sensitized individuals, with at least one fatal case reported after parenteral administration [20].

Diagnosis relies on a careful clinical history supported by *in vivo* tests, such as prick-by-prick with raw plant material (flowers or leaves) or homemade crude extracts, as well as *in vitro* assays. Currently, a singleplex assay for specific IgE to cannabis extract and a multiplex platform for specific IgE to Can s 3 are available [4,8,10]. Tomato (*Solanum lycopersicum*) is one of the most widely consumed vegetables worldwide. Tomato allergy prevalence ranges from 1.5% in Northern Europe [21] to 16% in Italian adults [22], with a European average of ~4.9% [23]. Higher rates are reported in Southern Europe, particularly Italy and Spain [24,25]. Clinical manifestations of tomato allergy commonly

involve Oral Allergy Syndrome (OAS), with itching or swelling of the lips, tongue, and pharyngeal mucosa. Cutaneous symptoms, including erythema, pruritus, and urticaria, are frequent, particularly after direct contact or ingestion. Gastrointestinal and cardiovascular involvement has also been reported [24,26,27], and systemic reactions including anaphylaxis have been documented [28,35]. Tomato allergy is often associated with pollen-food allergy syndrome and involves multiple panallergens: Sola l 1, a profiling [29]; Sola l 2, a Beta-fructofuranosidase [30]; Sola l 4, a PR-10 protein homologous to Bet v 1; Sola l 5, a cyclophilin; Sola l 3 and Sola l 7, type 1 nsLTPs [28,31]; and Sola l 6, a type 2 nsLTP [32]. Positive skin prick tests with commercial tomato extracts are frequent in LTP-monosensitized individuals [33]. and in vitro diagnostics include specific IgE to tomato extract (singleplex) or to Sola l 6 (multiplex).

### Case Presentation

We report a case of a 23-year-old male who experienced two episodes of anaphylaxis. The first, most severe, was characterized by urticaria/angioedema, dyspnea, hypotension, and transient loss of consciousness, requiring three intramuscular doses of epinephrine, systemic corticosteroids, antihistamines, and supplemental oxygen. No immediate trigger was evident, as the

patient had not ingested food or medications in the preceding 3–4 hours. The second episode, two months later, was milder and associated with accidental tomato ingestion. The patient had previously eliminated tomato due to episodes of lip edema and occasional respiratory distress immediately after consumption, which had only partially resolved with avoidance. No other foods were implicated.

### Materials and Methods

At the Allergy Unit of Buccheri La Ferla Hospital (Palermo), skin prick testing revealed strong reactivity to tomato, peanut, walnut, hazelnut, peach, and celery, with weak reactivity to shellfish (without clinical correlation). Inhalant testing was positive for cypress, mugwort, olive pollen, and house dust mites. Further work-up included multiplex IgE testing (ALEX2, MADx—Macro Array Diagnostics, Wien, Austria), singleplex IgE to Pru p 7 (ImmunoCAP, ThermoFisher, Uppsala, Sweden), and baseline tryptase (ImmunoCAP; 4.3 µg/L). Testing confirmed sensitization to nsLTPs, including Can s 3, the cannabis nsLTP (Table 1). Prick-by-prick testing with the patient’s own recreational cannabis produced a strong positive reaction (wheal 9 mm; histamine 7 mm; negative control 0 mm) Written informed consent was obtained from the patient for publication of this case report.

**Table 1:** Patient’s molecular sensitization assessed using the ALEX2 test.

Allergen (IUIS)	Source	Family/protein	Platform	sIgE (kUA/L)
Ara h 9	Arachis hypogaea	nsLTP1	ALEX <sup>2</sup>	9.20
Can s 3	Cannabis sativa	nsLTP1	ALEX <sup>2</sup>	1.67
Pru p 3	Prunus persica	nsLTP1	ALEX <sup>2</sup>	10.14
Sola l 6	Solanum lycopersicum	nsLTP2	ALEX <sup>2</sup>	2.45

Par j 2	Parietaria judaica	nsLTP	ALEX <sup>2</sup>	26.64
Pla a 3	Platanus acerifolia	nsLTP1	ALEX <sup>2</sup>	10.78
Mal d 3	Malus domestica	nsLTP1	ALEX <sup>2</sup>	9.26
Art v 3	Artemisia vulgaris	nsLTP1	ALEX <sup>2</sup>	8.89
Cry j 1	Cryptomeria japonica	Pectate lyase	ALEX <sup>2</sup>	8.65
Zea m 14	Zea mays	nsLTP1	ALEX <sup>2</sup>	8.63
Api g 2	Apium graveolens	nsLTP1	ALEX <sup>2</sup>	8.47
Cup a 1	Cupressus arizonica	Pectate lyase	ALEX <sup>2</sup>	5.99
Fra a 1+3	Fragaria × ananassa	PR-10 + nsLTP	ALEX <sup>2</sup>	5.99
Cor a 8	Corylus avellana	nsLTP1	ALEX <sup>2</sup>	5.03
Pla a 2	Platanus acerifolia	Polygalacturonase	ALEX <sup>2</sup>	4.11
Jug r 3	Juglans regia	nsLTP1	ALEX <sup>2</sup>	3.73
Vit v 1	Vitis vinifera	nsLTP1	ALEX <sup>2</sup>	2.05
Bla g 9	Blattella germanica	Arginine kinase	ALEX <sup>2</sup>	1.96
Der p 20	Dermatophagoides pteronyssinus	Arginine kinase	ALEX <sup>2</sup>	1.34
Act d 10	Actinidia deliciosa	nsLTP1	ALEX <sup>2</sup>	1.32
Ole e 1	Olea europaea	Olee1 family	ALEX <sup>2</sup>	1.23
Fra e 1	Fraxinus excelsior	Olee1 family	ALEX <sup>2</sup>	1.03
Der p 2	Dermatophagoides pteronyssinus	NPC2 family	ALEX <sup>2</sup>	0.90
Der f 2	Dermatophagoides farinae	NPC2 family	ALEX <sup>2</sup>	0.67
Tri a 14	Triticum aestivum	nsLTP1	ALEX <sup>2</sup>	0.48

Note: positivity threshold assumed  $\geq 0.30$  kUA/L. Total IgE: 328.00 kU/L

## Results

Following cannabis avoidance, the patient remained symptom-free. Because he declined further in vivo testing, a Basophil Activation Test (BAT) was performed for tomato using the Flow CAST method (Bühlmann Diagnostics, Switzerland), demonstrating 45.2% basophil activation and a stimulation index of 23.7 (positivity thresholds:  $>15\%$  and  $SI >2$ ), confirming strong reactivity.

## Discussions

The combination of a positive cannabis prick-by-prick test, specific IgE to Can s 3, and symptom resolution after cannabis avoidance strongly supports its causal role, even though challenge testing was not performed. BAT was not feasible for cannabis, as no validated commercial preparations exist. Both reactions were associated with nsLTP sensitization. Structural identity between Sola l 3 and Can s 3 is 64.4%, supporting plausible IgE co-recognition [15],

whereas identity with Sola l 6 (nsLTP2) is lower (Table 2).

**Table 2:** Matrix identity of the allergenic molecules Sola l 6, Sola l 3, Can s 3, and Pru p 3.



Percentage identity values were calculated from pairwise alignments of the full-length amino acid sequences using standard bioinformatic tools.

The primary sensitizer cannot be definitively established. Emerging evidence suggests that, in adults, food sensitization may occur outside the gastrointestinal tract [34-36]. For nsLTPs, primary sensitization via cannabis smoke exposure has been proposed [35,36]. In this case, cannabis may represent the initial sensitizer, with tomato triggering clinical reactions through IgE cross-recognition.

**Conclusion**

This case is noteworthy for three reasons:

Cannabis allergy is difficult to diagnose, due to underreporting and limited diagnostic tools.

Even in Mediterranean populations, where peach is commonly the primary nsLTP sensitizer, cannabis may play a key role.

The culprit food, tomato, is a less typical nsLTP-related allergen. These findings underscore the importance of considering cannabis sensitization,

particularly when the eliciting allergen is not apparent and nsLTP positivity is present.

### Conflict of Interest

E.S. reports consulting fees from DASIT S.p.A. and Diesse Diagnostica Senese S.p.A., and honoraria for lectures from Thermo Fisher Scientific and DASIT S.p.A. All other authors declare no conflicts of interest.

### Author Contributions

I.B. managed the patient and collected the clinical data. M.B. performed the allergy diagnostic work-up and contributed to data interpretation. D.V., E.S. and C.G.U. contributed to data interpretation. M.B. drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

### References

1. Solmi F. Cannabis use and mental health: a global perspective. *Lancet Psychiatry*. 2023;10(1):15-7.
2. Bonini SA, Premoli M, Tambaro S, Kumar A, Maccarinelli G, Memo M, et al. Cannabis sativa: a comprehensive ethnopharmacological review of a medicinal plant with a long history. *J Ethnopharmacol*. 2018;227:300-15.
3. Pisanti S, Bifulco M. Modern history of medical cannabis: from widespread use to prohibitionism and back. *Trends Pharmacol Sci*. 2019;40(3):174-84.
4. Skypala IJ. Cannabis allergy: what do we know? *Clin Exp Allergy*. 2022;52(4):452-62.

5. Liskow B, Liss JL, Parker CW. Allergy to marihuana. *Ann Intern Med*. 1971;75(4):571-3.
6. Zeiger RS, Silvers WS, Fleischer DM, et al. Cannabis allergy: a survey of allergists. *Ann Allergy Asthma Immunol*. 2022;128(2):168-74.
7. Larramendi CH, López-Matas MA, Ferrer A, et al. Prevalence of sensitization to Cannabis sativa. *Allergy*. 2013;68(12):1552-3.
8. Decuyper II, Van Gasse AL, Cop N, et al. Cannabis allergy: what the clinician needs to know. *Expert Rev Clin Immunol*. 2015;11(8):821-32.
9. Decuyper II, Green BJ. Occupational cannabis allergy. *Curr Opin Allergy Clin Immunol*. 2020;20(2):112-8.
10. Decuyper II, Van Gasse AL, Ebo DG. Cannabis allergy: beyond the joint. *J Allergy Clin Immunol Pract*. 2019;7(7):2331-6.
11. Ebo DG, Rihs HP, Mertens CH, Van Gasse AL, van der Poorten ML, Hagendorens MM, et al. Exploring the thaumatin-like protein as a candidate cannabis allergen in North-Western Europe. *Allergol Int*. 2024;79(1):257-9.
12. Ebo DG, Bridts CH, Verweij MM, De Knop KJ, Hagendorens MM, Stevens WJ. Sensitization profiles in cannabis allergy: a cross-reactivity study. *Allergy*. 2013;68(5):621-8.
13. Nayak AP, Green BJ, Beezhold DH. Cannabis pollen allergens and cross-reactivity. *Curr Allergy Asthma Rep*. 2023;23(2):67-74.

14. Gamboa PM, Sanz ML, Lombardero M. Allergy to Cannabis sativa confirmed by skin testing. *J Investig Allergol Clin Immunol*. 2007;17(2):138-40.
15. Skypala IJ, Asero R, Barber D, et al. Non-specific lipid transfer proteins: allergen structure and function. *Allergy*. 2021;76(7):1921-34.
16. Loblundo S, Scala E, Villalta D. Minor cannabis allergens: clinical relevance and diagnostic limitations. *Curr Opin Allergy Clin Immunol*. 2023;23(4):285-91.
17. Stadtmayer G, Beyer K, Bardina L, et al. Anaphylaxis to ingestion of hempseed. *J Allergy Clin Immunol*. 2003;112(1):216-7.
18. Decuyper II, Rihs HP. Systemic manifestations of cannabis allergy: beyond respiratory symptoms. *Allergy*. 2019;74(9):1830-2.
19. Rojas Pérez-Ezquerro P, Sánchez-Morillas L, Reaño-Martos M, Laguna-Martínez JJ. Cannabis-induced urticaria and angioedema. *J Investig Allergol Clin Immunol*. 2015;25(1):67-9.
20. Gilbert S, Harris J. Fatal anaphylaxis following parenteral cannabis exposure. *Forensic Sci Med Pathol*. 2017;13(2):226-9.
21. Petersen BN, Asero R. Tomato allergy in Europe. *Clin Exp Allergy*. 1996;26(8):920-926.
22. Ortolani C, Pastorello EA, Farioli L, et al. IgE-mediated allergy from tomato. *J Allergy Clin Immunol*. 1989;83(3):620-6.
23. Burney PGJ, Potts J, Kummeling I, et al. The prevalence and distribution of food sensitization in Europe. *Allergy*. 2014;69(3):365-71.
24. Asero R. Tomato allergy: clinical features and cross-reactivity. *Eur Ann Allergy Clin Immunol*. 2009;41(4):119-22.
25. López-Matas MA, Larramendi CH, Ferrer A, et al. Tomato allergy: clinical features and geographic differences. *Allergy*. 2015;70(9):1154-60.
26. Zacharisen MC, Kurup VP, Fink JN. Food-induced systemic allergic reactions: clinical features and diagnosis. *Ann Allergy Asthma Immunol*. 2002;88(4):350-8.
27. Worm M, Moneret-Vautrin A, Scherer K, et al. First European data from the network of severe allergic reactions (NORA). *Allergy*. 2012;67(6):720-8.
28. Pravettoni V, Primavesi L, Piantanida M. Tomato allergy and lipid transfer proteins. *Allergy*. 2009;64(1):140-1.
29. Willeroider M, Fuchs H, Ballmer-Weber BK, et al. Cloning and molecular and immunological characterisation of two new food allergens, Cap a 2 and Lyc e 1, profilins from bell pepper and tomato. *Int Arch Allergy Immunol*. 2003;131(4):245-55.
30. Foetisch K, Westphal S, Lauer I, et al. Biological activity of IgE specific for cross-reactive carbohydrate determinants. *J Allergy Clin Immunol*. 2003;111(4):889-96.
31. Martín-Pedraza L, Mayorga C, Torres MJ, et al. nsLTPs as allergens. *Curr Opin Allergy Clin Immunol*. 2016;16(3):263-9.
32. Giangreco I, Ricciardi L, Alessandri C, et al. Tomato nsLTPs: molecular characterization. *Mol Nutr Food Res*. 2015;59(5):1033-42.
33. Asero R. In vitro diagnosis of lipid transfer protein allergy. *J Investig Allergol Clin Immunol*. 2002;12(1):31-5.

34. Akdis CA. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? *Nat Rev Immunol.* 2021;21(11):739-51.
35. Asero R, Antonicelli L. Does sensitization to foods in adults occur always in the gut? *Int Arch Allergy Immunol.* 2011;154(1):6-14.
36. Asero R, Pravettoni V, Villalta D, Scala E. Is gastrointestinal epithelial barrier dysfunction the only responsible for sensitization to food allergens? *Eur Ann Allergy Clin Immunol.* 2025;57(4):147-55.

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