

Case Report

ALLERGY TO *CANNABIS SATIVA*: AN UNUSUAL TYPE OF 'WEED' ALLERGY

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INTRODUCTION

Cannabis sativa is a herb indigenous to Central Asia and the Indian subcontinent but it can be found growing worldwide. Ancient archaeological evidence dating back to the Neolithic period, shows that cannabis is one of the world's oldest cultivated crops widely used for food, rope and fabric, as well as recreational, medicinal and religious purposes. In recent years, many governments have debated the illegal status of *Cannabis sativa*. As a result, many countries, including South Africa, have legalised or decriminalised its use. The United Nation's World Drug Report estimates that 4% of the global population use cannabis recreationally, and this seems to be steadily increasing.¹ *Cannabis sativa* allergy is of particular relevance given the growing popular interest in the potential health benefits that might be derived from cannabis in the form of hemp, hemp seeds, cannabis oil and other forms.

Keywords: *Cannabis sativa*, weed allergy, cannabis-fruit/vegetable syndrome

CASE REPORT

PA is a 43-year-old female with mild persistent asthma (on inhaled corticosteroid/long-acting B2 agonist combination therapy), allergic rhinitis (AR) and atopic eczema. As a young child living in Canada, she had IgE-mediated allergic reactions to cow's milk, which she outgrew by late adolescence. Her asthma was triggered by ragweed pollen and cat exposure clinically, proven with a skin-prick test (SPT) and specific IgE tests.

As an adult, she had three episodes of anaphylaxis requiring adrenaline. The first occurred in 2005 when she developed urticaria, angioedema, vomiting and wheezing after eating hazelnuts. In 2007, she had similar severe reactions to kiwifruit

and strawberry. She has milder oral allergy-type symptoms with nectarine and peach.

PA presented to a Cape Town Emergency Unit with acute anaphylaxis. She had been smoking a cannabis cigarette, and after a few inhalations, developed pruritis of her mouth and throat. Within minutes, she developed generalised urticaria, angioedema of her lips, tongue and eyes, erythema of her body and AR. She took two chlorpheniramine tablets and had her partner drive her to the hospital.

On arrival at the emergency unit, she developed breathing difficulty and was given intramuscular adrenaline, intravenous



Fresh *Cannabis sativa* leaves



Fresh *Cannabis sativa* leaf extract



Dried *Cannabis sativa* bud extract

antihistamine and cortisone and nebulised. She responded well to this treatment. She was observed for period and then discharged.

She attended an allergy clinic a few weeks thereafter. Her examination was normal except for mild AR and keratosis pilaris. Pulmonary function tests were within normal limits. Further history was then obtained regarding the cannabis allergy. For many years preceding the anaphylaxis episode, PA recalled developing a blocked, itchy nose each time she smoked cannabis. On one occasion, she had a generalised pruritis and erythema after smoking. She developed localised urticaria after handling cannabis, while rolling the cigarettes. More recently, she described an itchy, swollen mouth and throat after chewing absentmindedly on the cannabis stalks.

SPTs were performed and included in the panel were those for crude cannabis extract, both fresh and dried. Results were as follows:

TABLE I: SKIN-PRICK TESTS

ALLERGEN	SIZE IN MILLIMETRES
Cat	7 mm
Hazelnut	5 mm
Strawberry (fresh, prick-prick method)	4 mm
Kiwi (fresh, prick-prick method)	3 mm
Cannabis (fresh, prick-prick method)	17 mm – with pseudopodia
Cannabis (dried, prick-prick method))	11 mm
Negative control	0 mm
Positive control (histamine 10 mg/mL)	5 mm

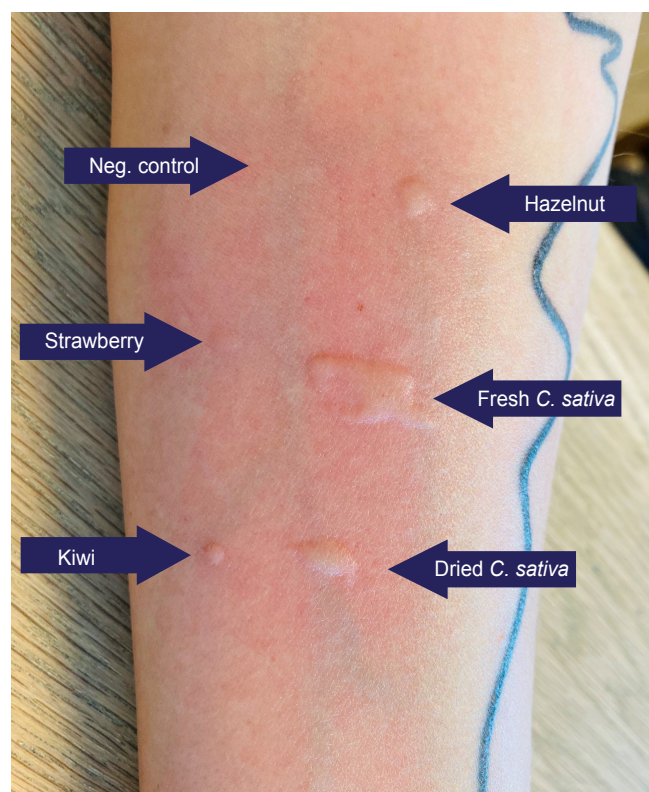
Her IgE for hemp was sent to the laboratory but the results were not yet available at the time of publication. An ISAC test was performed and was positive for lipid transfer protein, PR-10 protein, ragweed, Thaumatin-like protein as well as rCan f 1 (dog), uteroglobin (cat) and acidic glycoprotein (*Alternaria*). PA was advised to avoid hazelnut, kiwi and strawberry as well as cannabis in all its forms.

DISCUSSION

CLINICAL MANIFESTATIONS

Allergy to *Cannabis sativa* has been reported previously and may manifest with mild to life-threatening reactions, including anaphylaxis.² Various routes of exposure may lead to symptoms and these include cutaneous exposure, pollen inhalation, smoke exposure (either direct or second-hand), ingestion and intravenous use.

Direct cutaneous contact with the plant may cause urticaria, pruritis and angioedema.³ Allergic rhinoconjunctivitis, hypersensitivity pneumonitis and bronchoconstriction have been reported with cannabis pollen as an aeroallergen as well as with smoking cannabis. Cannabis pollen is 23–28 microns in diameter and is typically found in late summer and early autumn in areas where it is cultivated. It is a relevant aeroallergen in



Skin-prick test (Note: the cat and positive control tests are outside of this frame, but were performed)

central India, Pakistan, southern Europe and the United States. Oral ingestion may also cause hypersensitivity reactions.^{3,4}

Cross-reactivity has been investigated between *Cannabis sativa* and other plants. The 'cannabis-fruit/vegetable syndrome' has been reported in individuals who present with hypersensitivity reactions after smoking cannabis or when exposed to second-hand smoke. Hypersensitivity reactions in these individuals have been reported with various LTP containing foods such as tomato, apple, cherry, peach, almonds, hazelnut and chestnut.^{5,6}

Unlike the more well-known birch pollen-related food-pollen syndrome, cannabis-fruit/vegetable syndrome can be bidirectional (i.e. sensitisation to the nsLTP in the fruit or vegetable can cause sensitisation to cannabis, as well as the other way around). Cannabis-fruit/vegetable syndrome often presents with more severe symptoms than food-pollen syndrome, including anaphylaxis due to fruit and vegetables that were previously tolerated.²

Occupational exposure to cannabis has been reported in cannabis growers, commercial hemp industry workers and laboratory workers. Symptoms reported include asthma, contact dermatitis and rhinoconjunctivitis.^{3,7,8}

It is important to distinguish the symptoms of allergy from the known psychoactive and physiological effects that cannabis is known to produce, such as tachycardia, dry mouth, euphoria, psychomotor changes and anxiety. Cannabis smoke exposure, either by direct inhalation or second-hand smoke, may also

TABLE II: POTENTIAL CANNABIS SATIVA ALLERGENS

ALLERGEN	HOMOLOGUE	EXAMPLE
Can s 3 (LTP)	Pru p 3, Mal d 3, Cor a 8	peach, apple, hazelnut, mugwort
Thaumatococcus-like protein	Act d 2, Mal d 2, Cup a 3, Mus a 4	tomato, kiwi, apple, banana, cypress pollen
ribulose-1,5-bisphosphate carboxylase oxygenase		
Oxygen-evolving enhancer protein 2		

cause non-specific wheezing and cough. Conjunctival and nasopharyngeal injection may easily be misdiagnosed as allergy.

CANNABIS ALLERGENS

Can s 3 is the non-specific lipid transfer protein (nsLTP) that is considered the major allergen in cannabis.⁵ nsLTPs are heat-stable panallergens, ubiquitous throughout the plant kingdom especially in fruits and vegetables. They show extensive cross-reactivity among various plant foods and pollens. Other potential cannabis allergens include Thaumatococcus-like protein, ribulose-1,5-bisphosphate carboxylase oxygenase (RuBisCO) and oxygen-evolving enhancer protein 2, among others⁹ (see Table II).

DIAGNOSIS OF CANNABIS SATIVA ALLERGY

As with most allergies, the cornerstone of the diagnoses of *Cannabis sativa* allergy rests on the clinical history. This is especially true for this allergy due to the lack of standardised diagnostic tests.

Skin-prick testing, although used in clinical practice, is not currently standardised for *Cannabis sativa*.^{2,10} The various parts of the cannabis plant, including buds, flowers and leaves, are usually crushed into an extract and used via the prick-prick method. As a result of the differences in the various source material, this method displays marked variability.

A hemp-specific IgE antibody test has recently become available in South Africa. It is a crude hemp extract and shows 82% sensitivity and 32% specificity.¹⁰ A SPT using recombinant Can s 3-rich extract, a specific IgE Can s 3 assay and basophil activation tests with cannabis extract and Can s 3 have shown promising results but are not commercially available.^{6,10} The gold standard of direct challenge testing, although limited by legal

and ethical considerations, could theoretically be undertaken if the diagnosis is uncertain.

TREATMENT OF CANNABIS SATIVA ALLERGY

Avoidance is the usual recommended treatment. Occupational exposures and potential poor compliance in the context of substance abuse or addiction, may complicate this. One case report describes the use of omalizumab for an occupationally exposed patient with recurrent anaphylaxis¹¹ and a few reports have been published describing desensitisation with subcutaneous immunotherapy to reduce the symptoms of AR and asthma during cannabis pollen season.^{12,13} In this case, PA was an occasional recreational user and avoidance was not a hardship for her.

CONCLUSION

PA has severe cannabis-fruit/vegetable syndrome. She initially presented with anaphylaxis to hazelnut, kiwi and strawberry and mild oral-allergy syndrome to peach. Mild reactions to cannabis eventually culminated in an admission for anaphylaxis. She demonstrated extensive cross-reactivity with some of the typical foods associated with the cannabis fruit/vegetable syndrome both clinically and on skin-prick testing and IgE testing.

Cannabis allergy is likely to become more prevalent given its widespread and increasing use in recreational, medicinal, industrial and occupational arenas. The potential for severe reactions and the extensive cross-reactivity displayed, should be an incentive for the development of more reliable cannabis allergy diagnostic tests, both *in-vivo* and *in-vitro*.

DECLARATION OF CONFLICT OF INTEREST

The author declares no conflict of interest.

This article has been peer reviewed.

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