

Anaphylaxis Due to Senna (*Cassia Angustifolia*)

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Senna (*Cassia angustifolia*) is a scrub plant belonging to the *Fabaceae* family, widely used as a medicinal plant due to its laxative effects associated to sennosides; and as a colouring agent in hair dyes, because of its content in anthraquinones [1]. It is a frequent component of herbal teas marketed for weight loss.

We report a 19-year-old man who presented with rhinoconjunctivitis, dyspnea, disfiguring facial edema and disseminated hives ten minutes after eating rice with clams, fried eggs, lettuce, and yoghurt, followed by a Delgaxan Plus® infusion (Pompadour Ibérica, Alicante, Spain); the latter is an herbal mixture containing artichoke, horsetail, peppermint and senna. There were no other drugs or cofactors associated to the episode. This recovered promptly with intramuscular epinephrine and intravenous metilprednisolone and dexchlorpheniramine.

Allergologic workup consisted of: A) Skin prick-tests with all the foods involved, common inhalant allergens and vegetal panallergens such as natural profilin/Pho d 2 and peach LTP/Pru p 3, besides natural latex and *Anisakis* extracts. B) Skin tests (prick-prick) with Delgaxan infusion and its separate components: artichoke, horsetail, mint and *Cassia* leaves. C) Determinations of blood cell count, biochemistry, tryptase, total and specific IgE, and C3-C4. D) Oral challenge tests with ingested food and components of the infusion. E) SDS-PAGE

immunoblotting with extracts from *Cassia* leaf and Delgaxan infusion. Informed consent was obtained from the patient for all *in vitro* and *in vivo* tests.

Skin tests were positive to Delgaxan and senna leaf extracts in the patient, and negative in twenty-two healthy and atopic controls. Skin tests were negative to artichoke, horsetail, and peppermint; to egg and milk proteins; and to rice, clam, mussel, shrimp, codfish, *Anisakis*, lettuce, wheat, corn, lentil, peanut, walnut, soy, peach, kiwi, latex, and native profilin and LTP extracts. Prick-tests with inhalant allergens were positive to *Dermatophagoides* and negative to storage mites, molds, cat and dog dander, and a variety of pollens, including *Fagaceae*. There was subsequent oral tolerance to rice, clams, egg, and dairy products; as well as to artichoke, horsetail and peppermint.

Laboratory results were normal. Total IgE was 118 kU/L. Specific IgE to mint, Bet v 1, Bet v 2, Pru p 3, Tri a 14, and alpha-gal were <0.1 kU_A/L. Immunoblotting showed IgE-binding bands of 66, 23 and 16,5 kDa in *Cassia* extract, and bands of 23 and 16,5 kDa in Delgaxan extract (Figure 1). The patient disallowed an oral challenge test with senna.

Very few reactions to senna have been reported. European Medicine Agency (EMA) Committee on Herbal Medicine Products, in its monograph on senna [2], mentions some hypersensitivity reactions (pruritus, urticaria) without associated specific bibliography. Isolated cases of occupational allergy (asthma and rhinoconjunctivitis) have been reported in workers in the phytopharmaceutical industry [1, 3-5]; one of these patients tolerated intake of laxative senna infusions [5], while in others an eventual oral tolerance is unknown. In two of these reports, several IgE-binding bands were detected by SDS-PAGE immunoblotting with *Cassia* leaves [1, 4] and powder extracts [1], mainly in the range between 16 and 28 kDa. Two of the bands detected with our patient's serum have similar molecular weights than previously reported by Helin et al [4], but not so similar to the ones reported by Carneiro-Leao et al [1].

Furthermore, 11 IgE-reactive proteins from *Cassia siamea* pollen have also been identified in the range between 181 kDa and <29 kDa [6].

C. angustifolia belongs to the *Fabaceae* family, as the legumes ingested regularly in the Mediterranean diet. However, in our patient, there was no serum cross-reactive IgEs among proteins from senna and edible legumes: skin tests were negative and he tolerates the habitual intake of lentils, chickpeas and peas. Thus, an eventual implication of storage proteins seems very unlikely; in fact, these are specific of seed tissue, and are not usually expressed in plant leaves. Moreover, our patient shows negative tests against profilins, so we consider discarded that the 16.5 kDa band detected in *C. angustifolia* extract correspond to this protein family. The same can be stated for PR-10 proteins, for our patient showed negative tests to *Fagaceae* pollens and Bet v 1.

Interestingly, the IgE-band of highest molecular weight observed in senna leaves' extract was not detected in the Delgaxan infusion extract, so the persisting two bands of lower weight seem to be the cause of anaphylaxis. We think that the senna 66 kDa band might correspond to an aggregate of smaller IgE-binding proteins that do not appear in Delgaxan extract, because of a lower concentration of these proteins in it; or due to the effect of heating or other eventual processes during manufacture.

In summary, we report an anaphylactic reaction due to *Cassia angustifolia* contained in Delgaxan Plus® infusion, hitherto considered "innocent" by our patient. The etiology is demonstrated by a) positive prick-prick tests with *Cassia* leaf and the multi-herbal preparation in the patient, and negative in 22 controls; and b) IgE-binding bands of the same molecular weight detected in both extracts from *Cassia* leaf and Delgaxan infusion. To our knowledge, this is the first report of an anaphylactic reaction by ingestion of senna, since all other reported cases are from professional allergy due to inhalation of this plant in work settings. Moreover, at least in one of these cases there was a natural tolerance of senna infusions and laxatives [4].

Sensitization via inhalation or ingestion might occur through different proteins. Also, as is the case with cereal flours, the same protein might cause allergy by inhalation, but tolerating its ingestion, and vice versa; e.g. wheat LTP Tri a 19 in baker's asthma and in some patients with food allergy to wheat.

One of the objectives of this case is to highlight the growing consumption of apparently harmless natural herbs and dietary supplements in complementary medicine environment [7]. Despite a documented frequency of toxic or immunologic reactions and drug interactions [8], this issue is often forgotten in the clinical record, even among allergists [9]. As usual, an adequate anamnesis can lead to a more accurate diagnosis and prevent future anaphylaxes.

Conflicts of interest: None of the authors declares to have conflicts to disclose.

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FIGURE LEGENDS

Figure 1

SDS-PAGE Immunoblotting. A) *Cassia angustifolia* leaf extract B) Infusion powder extract. Lane P: patient serum, Lane C: control serum (pool of sera from non-atopic subjects), Lane M: Molecular mass standard.

