

Food-dependent exercise-induced anaphylaxis to pistachio

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Summary. We report the case of a 16 year-old male who, 30 minutes after beginning to play football with previous ingestion of pistachio nuts, experienced an anaphylactic reaction. Prick-by-prick test with roasted pistachios was negative. Specific IgE antibodies to pistachio, cashew nuts and mango were negative. An open oral challenge test with pistachio in resting conditions was negative. Treadmill ergonometric stress in a fasting state and 60 minutes after a meal without pistachio gave negative results. A specific food exercise challenge 60 minutes after ingestion of 50 g pistachio nuts was positive, showing mild diffuse erythema and small wheals in face and thorax. To the best of our knowledge, this is the first described case of specific food dependent exercise-induced anaphylaxis to pistachio. Negative allergologic tests is an unusual condition, since most cases appear to be IgE-mediated. In this case, a positive specific food exercise challenge test provided a definite diagnosis

Key words: Anaphylaxis, exercise, food, pistachio hypersensitivity.

Resumen. Se notifica el caso de un varón de 16 años que, al cabo de 30 minutos de empezar a jugar un partido de fútbol y tras la ingestión previa de pistachos, experimentó una reacción anafiláctica. El prick-prick con pistachos tostados dio negativo. Los anticuerpos IgE específicos frente a pistacho, anacardo y mango dieron un resultado negativo. Una prueba de provocación oral abierta con pistacho en condiciones de reposo fue negativa. La prueba de esfuerzo en tapiz rodante en ayunas y 60 minutos después de una comida sin pistachos, dio resultados negativos. Una prueba de ejercicio con ingesta previa de alimentos específicos realizada al cabo de 60 minutos de haber ingerido 50 g de pistachos fue positiva: mostró un eritema difuso leve y pequeños habones en la cara y el pecho. Según los conocimientos de que disponemos, éste es el primer caso descrito de anafilaxia al pistacho inducida por ejercicio dependiente de alimentos específicos. Las pruebas alergológicas con resultado negativo son poco habituales ya que, según parece, la mayoría de casos están mediados por IgE. En este caso, una prueba de ejercicio con ingesta previa de alimentos específicos positiva proporcionó el diagnóstico definitivo.

Palabras clave: Anafilaxia, ejercicio, alimentos, pistacho, hipersensibilidad.

Introduction

The pistachio tree (*Pistacia vera*) is native to western Asia and Asia Minor. Although known as a nut, the fruit of the pistachio is botanically a drupe, the edible portion of which is the seed. Pistachio nuts are considered one of the prime edible nuts, along with almonds, macadamias and cashews. World production has increased >300% since 1980, with nearly every country experiencing large increases. Pistachio nut belongs to the Anacardiaceae family. Some members of this family, such as pistachio,

cashew nut and mango, have been reported to cause IgE-mediated allergic reactions [1,2], and allergenic cross-reactivity has been described among them [3].

Specific food-dependent exercise-induced anaphylaxis (SFDEIA) has been associated with cereals, seafood, peanut, tree nuts, eggs, milk and vegetables. An IgE-mediated mechanism is suggested in light of the skin prick tests (SPT) and/or specific IgE results against the implicated foods. Nevertheless, no reaction occurs in the absence of exercise, and other non-immunologic mechanisms have been hypothesized [4].

Case report

We report the case of a 16 year-old male with mild seasonal rhinoconjunctivitis, who immediately after ingestion of some roasted pistachio nuts went to play football. About 30 minutes after beginning to run, he developed pruritus, diffuse warmth, facial and hand erythema followed by generalized urticaria, edema of the eyelids, dyspnea and short-term unconsciousness. He was treated with antihistamines and methylprednisolone and recovered within 2 hours. He could eat pistachio (up to 30-35 units) without subsequent physical exertion. The physical examination was normal. Laboratory tests, hematology, biochemistry, urinalysis and complement levels, all were normal. Total serum IgE was 28 KU/l.

SPT with common inhalants were positive to timothy grass and artemisia. Prick-by-prick test with roasted pistachios was negative. Specific IgE antibodies to pistachio, cashew nut and mango (CAP-FEIA Pharmacia, Uppsala, Sweden) were negative (<0.35 KU/l). An open oral challenge test with pistachio in progressively increasing doses every 30 minutes (1, 3, 10 and 30 units) was negative. Treadmill ergonometric stress with the standard Bruce protocol was done under three different conditions on three different days. Initially, a fasting treadmill exercise challenge, following by an exercise challenge 60 minutes after a meal without the implicated food, and finally an exercise challenge 60 minutes after the ingestion of 50 g pistachio (equivalent to 35 units, the maximum amount tolerated by the patient without subsequent physical exertion) were performed. The patient gave his written consent before the challenge procedures. Challenge tests were performed in a room with immediate access to an intensive care unit. Intravenous access and equipment for resuscitation was available. Briefly, the patient runs on a treadmill to exhaustion. At timed stages during the test (every 3 minutes) the speed (Km/h) and grade of slope (%) of the treadmill are progressively increased. Electrocardiogram, oxygen saturation, blood pressure and heart rate were continuously monitored. Baseline pulmonary function measures of FEV1 and FVC were performed and repeated at 5, 10, 20 and 30 minutes after each challenge. If an objective reaction was developed, serum tryptase level (Tryptase UniCAP. Pharmacia) was drawn within 60 minutes after the onset of the reaction and compared with a baseline level obtained when the patient was asymptomatic.

Treadmill exercise challenge tests in fasting state and 60 minutes after a meal not containing pistachio were negative. Finally, specific food exercise challenge 60 minutes after pistachio intake was positive. The patient exercised for 18 minutes to a maximum effort of 202 beats per minute with normal blood pressure and oxygen saturation throughout the challenge. Basal spirometric measures and after finishing the test were normal. Thirty minutes after ending the exercise, the patient developed pruritus of the hands and forearms followed by mild diffuse erythema and small wheals in face and thorax.

The reaction resolved spontaneously in two hours. Baseline tryptase level was 3.26 µg/L and it did not increase within 60 minutes following the reaction (3.36 µg/L. Normal values 5.5- 13.5 µg/L).

Discussion

To the best of our knowledge, this is the first described case of specific food-dependent exercise-induced anaphylaxis to pistachio. Negative allergologic tests, as can be seen in our patient, are not a common fact, since most cases of SFDEIA described in the literature appear to be IgE-mediated. This condition has been usually associated to non-specific food-dependent exercise-induced anaphylaxis and it did not rule out the causative role of the implicated foods. Therefore, in this case, a positive specific food exercise challenge test provided definite diagnosis.

Just a mild cutaneous reaction, which resolved spontaneously, was observed under controlled conditions. Symptoms may not always be reproduced by the same amount and type of exercise, and associated adjuvant factors, such as the timing of the challenge and climatic conditions may be required to reproduce similar episodes in our patient [5]. Small wheals similar to those seen in cholinergic urticaria were observed. However, this possibility was ruled out because the patient exhibited a lack of symptomatic response to single exercise challenge and other increases in body temperature. It could be a case of a previously described variant type of exercise-induced anaphylaxis [6]. Elevation of tryptase (a product of mast cell activation) is associated with anaphylaxis and has been shown to correlate with the severity of the symptoms. In this case, serum tryptase did not increase, perhaps due to the low severity of the reaction.

Patients with pollinosis may develop allergy to certain fruits and vegetables. Cross-reaction between pistachio nuts and *Parietaria pollens* has been reported [7]. Mugwort hay fever has been associated with allergic reactions to the Compositae family of foods, but also with other foods such as the pistachio and tree nuts. CAP inhibition experiments showed the existence of common antigenic epitopes in pistachio and *Artemisia* pollen in one patient [8].

Artemisia seems not to play an important role in mild seasonal symptoms referred by our patient. *Artemisia* pollen accounts for a low proportion (0.1%) of the annual total pollen count in the atmosphere of Cáceres (Middle-western Spain). The pollination period occurs from late summer to early fall, and our patient suffered from symptoms in the spring months. Nevertheless, specific IgE to pistachio has not been found and this case cannot be explained by crossreactivity with *Artemisia*.

Certainly, we cannot totally assert that pistachio-specific IgE is absent. IgE-mediated sensitization is frequently not detected by using plant derived food allergenic extracts because of the lability of the responsible allergens. We prefer the prick-prick method,

which is usually more sensitive and reproducible than using extracts from more manufacturers [9]. In general, negative SPT responses with food allergens could exclude an IgE-mediated mechanism due to a high negative predictive value >95%. Nevertheless, the accuracy of skin prick test and *in vitro* IgE determinations with pistachio and most tree nuts is not established so far.

According to the revised nomenclature for allergy, in this case the role of IgE is unclear and it would be a case of food-dependent exercise-induced allergic anaphylaxis [10].

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