

The perfect storm: the best conditions for making pollinic patients' symptoms worse

J. M. Igea*, M. Lázaro

Key words: atmospheric pressure; climate changes; dry storm; emergency visits; pollen levels; pollinosis; wind.

During spring time, one of the best types of weather conditions favouring pollinosis symptoms appears to be dry storms. Recently, we had the opportunity of studying one of these. It was a well-remembered dry storm for pollinic patients, who referred to it as 'the perfect storm', i.e. the ideal weather conditions to make their symptoms as bad as they could remember.

The study was carried out in Salamanca (Spain), a city with a continental climate where anthesis peak of most allergenic plants occurs from mid-May to mid-June. The study period was 29 May 2002 to 4 June 2002.

To register the aggravation of pollinosis, we reviewed the medical records of patients who attended the three major emergency departments of the city during the study period for pollinosis.

The pollen count was made with a volumetric spore trap (Burkard Manufacturing Co. Ltd, England). The slides corresponding to the period of study were scanned transversally at 2-h intervals. Meteorological recordings were obtained from the National Meteorological Institute.

Finally, the relationship between variables was carried out by means of Pearson's R, seeking the best possible

adjustment by linear or polynomial regression. A P-value < 0.05 was considered to be significant.

Between 29 May 2002 to 4 June 2002 in Salamanca, 90 patients were examined in emergency departments for pollinosis, of whom 31 sought assistance in the 24 h following the storm (Fig. 1A), which corroborates the reports of our pollinic patients.

The circadian periodicity of some important allergenic pollens observed during stable sunny weather was lost during our study period. In the evening of 1 June 2000, after the dry storm, a peak of pollen levels was observed at the same time as a peak in visits to emergency departments for pollinosis (Fig. 1B), but we observed other higher peak pollen levels in the period of study not accompanied by increases in emergency visits. In fact, there was no significant correlation between the levels of any pollen and emergency visits.

Climatologically, the period of study was characterized by low atmospheric pressure (Fig. 1E). Temperature and relative humidity showed the habitual circadian pattern (Fig. 1E). Only a slight decrease in temperature was observed during the last two days of the study period (the cold front of the storm). The only factor that showed a clear variation related to dry storm and increase in emergency visits for pollinosis was wind speed. Whereas in the rest of the study period, wind speed fluctuated following a circadian pattern under a value of 3.5 m/s, dry storm was characterized by a sharp increase in wind speed (to 8 m/s). Within hours of this peak wind speed, pollinic patients visited the local emergency departments (Fig. 1A).

No significant correlations were found between meteorological variables and pollen levels.

During the passage of one dry storm through the city we observed that the only factor clearly associated with an increase of emergency visits for pollinosis

was an increase in wind speed in the previous hours. Therefore, we infer that wind affects pollinosis symptoms by a different mechanism from merely pollen transport, at least during a dry storm. Other authors have attributed epidemics of asthma during thunderstorms to rainfall, wind, lightning, and other factors (1–3); but all the storms involved were different from that observed here because of the presence of rainfalls.

Taylor et al. (4) recently demonstrated that after a cycle of wetting and drying followed by wind disturbance, grasses produced an aerosol of particles; the allergenicity of these aerosols has been demonstrated by other authors (5, 6). In the days previous to the dry storm, there were no rainfalls, but we observed high relative humidity throughout the study period, which perhaps played a role in releasing micronic allergenic particles.

In conclusion, it seems that dry storms – 'perfect storms' – establish ideal conditions to trigger pollen allergic symptoms during spring time. In these conditions, pollen level is not the only factor which determines the symptomatology of pollinic patients.

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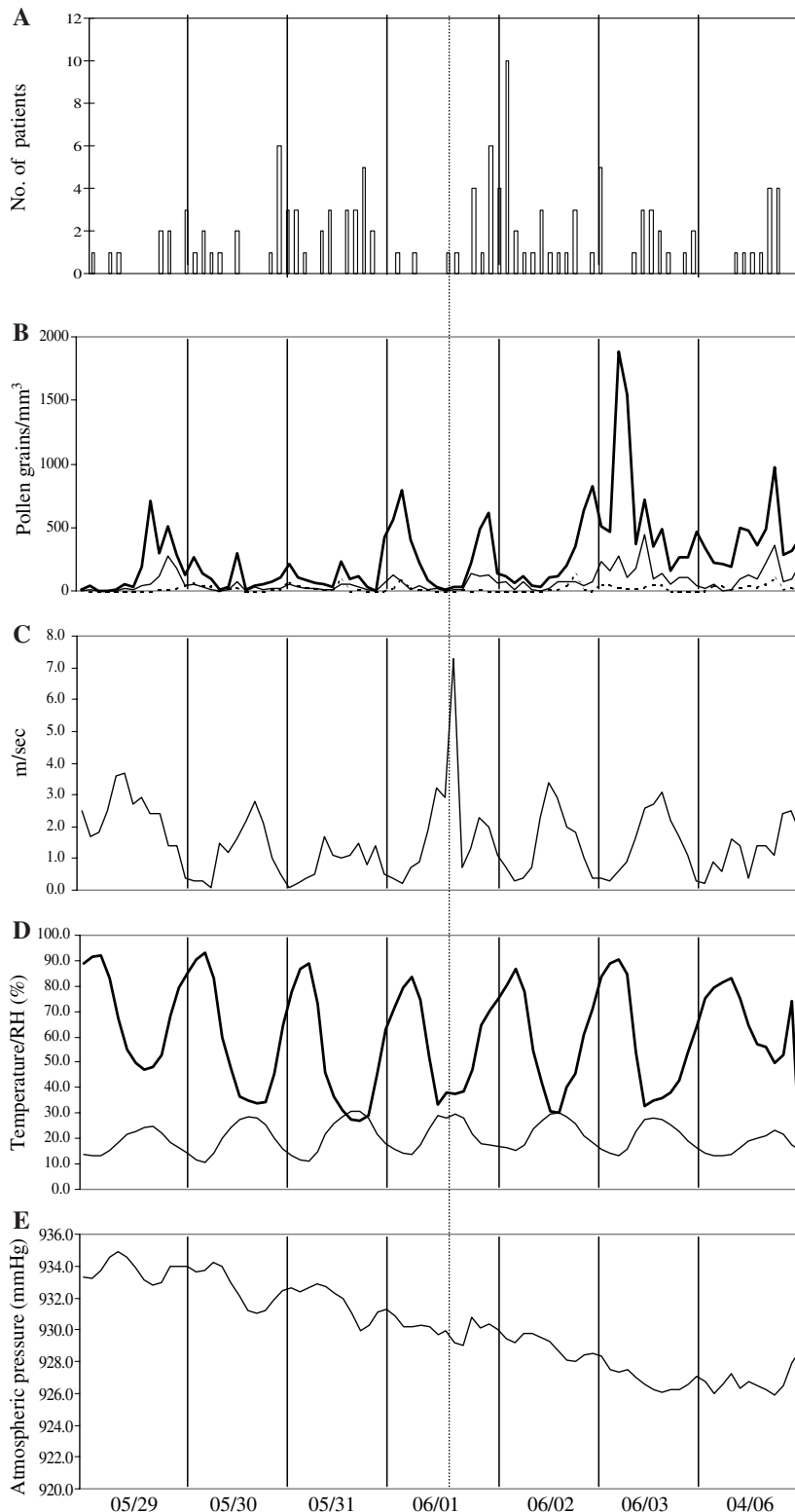


Figure 1. Chart showing number of patients who attended the emergency departments of the city for pollinosis (A), air-borne pollen levels (—, total; —, grass; - - -, *Olea*) (B), wind speed (C), temperature and relative humidity (RH) (D), and atmospheric pressure (E) between 00:00 hours of 29 May 2002 and 24:00 hours of 4 June 2002 in Salamanca, Spain. The vertical dashed line represents the time at which the dry storm took place.

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Anaphylaxis due to caffeine

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Key words: anaphylaxis; caffeine; coffee; cola drink.

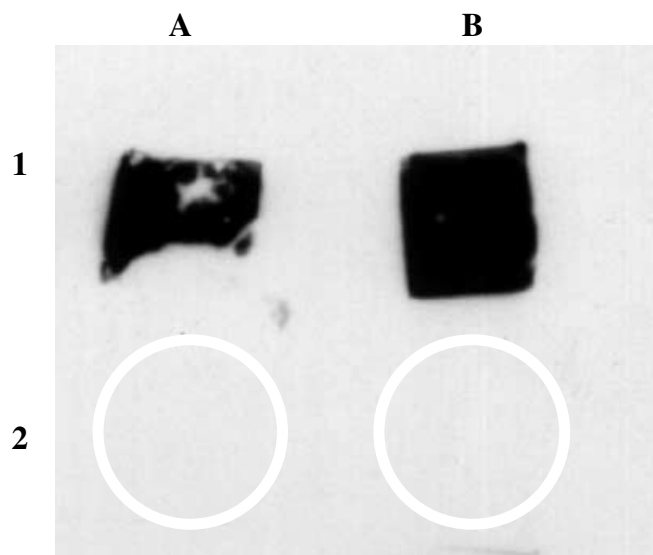
Caffeine ($C_8H_{10}O_2N_4 \cdot H_2O$) is an alkaloid found in the seeds of the coffee, tea, and cocoa plants.

This xanthine derivative is one of the most popular natural stimulants. Caffeine increases arterial tension,

stimulates the central nervous system, promotes urine formation and increases the activity of the heart and lungs.

The maximum blood concentration of caffeine, reached within 30–45 min of ingestion, is reduced to half within 3–6 h.

Anaphylaxis due to caffeine is IgE-mediated and dose-dependent.



1: Patient, 2: Control (-),
A: Coke, B: Caffeine 60 µg

Figure 1. Dot-blot analysis.

Caffeine is consumed daily by millions of people; nevertheless, sensitization to caffeine hardly occurs. A cup of coffee contains between 100 and 150 mg of caffeine (1), while a cola beverage has only 23 mg.

We report the case of a 21-year-old atopic male, who presented anaphylactic reactions related to caffeine. The first episode occurred when he was 9 years of age, 30 min after he had a cup of coffee. He developed pruritus of the soles and palms, generalized urticaria, cough, wheezing and shortness of breath. These symptoms appeared every time he had more than two cokes, unless on a fast. He never drank coffee again. He tolerated coke without caffeine, tea, chocolate, beer and whisky.

Prick test was positive to caffeine extract (10 mg/ml) which was negative in 10 control subjects. Prick tests were negative to coke with and without caffeine. Total IgE measured was 178 kU/l. No specific IgE was detected to green coffee, tea and malt, by Pharmacia CAP system. We used a dot-blot technique for detecting specific IgE and the results were positive to caffeine and coke with caffeine, and negative to coke without caffeine (Fig. 1).

Oral challenge was not performed due to the severity of symptoms.

In conclusion, a case of allergy to caffeine is presented based on clinical

symptoms and specific IgE determination by cutaneous test and dot-blott studies. The symptoms, as described in other reports, are dose-dependent (2).

Despite its high consumption, there are few cases of adverse reactions till date (1–5). Perhaps caffeine is an infradiagnosed hidden allergen that causes some cases of urticaria of unknown origin (6).

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Contact urticaria by angler fish

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Key words: allergy; angler fish; contact urticaria; fish allergy; food allergy.

Angler fish belonging to the order Lofiformes, family Lophidae is a commonly consumed fish. Although positive skin-prick tests to fish are often seen in food handlers with good tolerance to fish ingestion, no cases of professional contact urticaria caused by isolated allergy to angler fish have been reported.

A 27-year-old man, with a history of rhinitis and conjunctivitis because of sensitization to pollens and oral allergy syndrome to melon and nuts, developed contact urticaria after handling raw angler fish. The patient had been a cook for 10 years and for the last 2 years he had had pruriginous, papular, erythematous eruptions few minutes after skin contact with raw angler fish. The handling of cooked angler fish and other fishes induced no reaction. He had no symptoms after oral intake of fish too.

Skin-prick test with commercial extracts were positive to pollens, melon and nuts, and were negative to different fishes (cod, sole, turbot, anchovy, trout),

A case of professional contact urticaria caused by isolated allergy to angler fish.

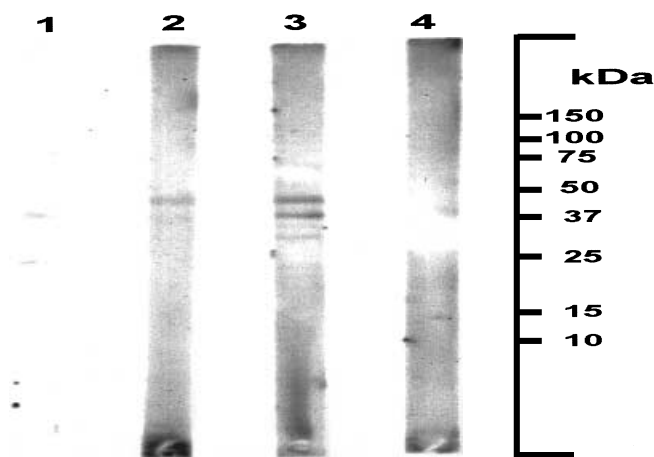


Figure 1. IgE immunoblotting. Lane 1, negative control; lane 2, hake with patient's serum; lane 3, raw angler fish with patient's serum; lane 4, cooked angler fish with patient's serum.

shellfish and anisakis. Prick-by-prick test showed positive reaction to raw angler fish, and negative to cooked angler fish. The handling tests were negative to cooked angler fish, and positive to raw angler fish with immediate development of urticaria in areas of contact. Total serum IgE was 216 kU/L.

Fish extracts (angler fish and hake) were extracted in phosphate buffered saline (PBS) by mixing 10 g of extract in 100 ml of PBS. Raw angler fish and hake were extracted at 4°C, and cooked angler fish at 80°C. After it had been stirred for 90 min, the solution was centrifuged and then passed through a Millipore filter (0.22 µm), with a final dilution of 1/10 w/v. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis of fish extracts and IgE immunoblotting with the patient's serum were performed.

IgE immunoblotting (Fig. 1) showed specific recognition of several bands by the patient's IgE. In raw angler fish, and faintly in hake, bands between 37 and 50 kDa were observed. No bands were seen in cooked angler fish.

In the majority of allergic reactions to fish the responsible allergens are low molecular weight heat-resistant proteins that belong to the parvalbumins (1–3), and the reactions occur after fish ingestion.

It has been reported that fish antigens of > 40 kDa molecular weight are more heat-sensitive (4, 5), and are probably responsible for isolated contact urticaria without allergic symptoms after oral intake (6). These allergens are not well characterized.

In conclusion, this patient has contact urticaria for isolated allergy to angler fish, with a good tolerance to its ingestion. This study demonstrates a type-I hypersensitivity to heat-sensitive angler fish allergens.

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Anaphylactic reaction to manioc: cross-reactivity to latex

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Key words: food allergy; manioc; cross-reactivity; latex.

The association of latex allergy and allergy to plant-derived foods is called latex-fruit syndrome. An increasing number of plant sources have been associated with this potentially life-threatening syndrome.

Anaphylaxis to manioc due to cross-reactivity with latex.

Manioc (*Manihot esculenta*) is a highly important food in South America (native to Brazil) and Africa. The tuber, also known as cassava root, can be eaten fried, cooked, toasted or raw (flour), being the source of most of the daily carbohydrate intake for large populations in the tropics. Mainly eaten as a substitute for potato, this food is slowly entering European dietary habits. To our knowledge, there is no report in the literature of any allergic reaction to manioc.

We report a case of a 51-year-old woman, born in Mozambique, with a previous history of bronchial asthma and multiple pelvic-abdominal surgeries (last one performed 9 years ago), who, over the last 2 years, has experienced several episodes of anaphylactic reactions

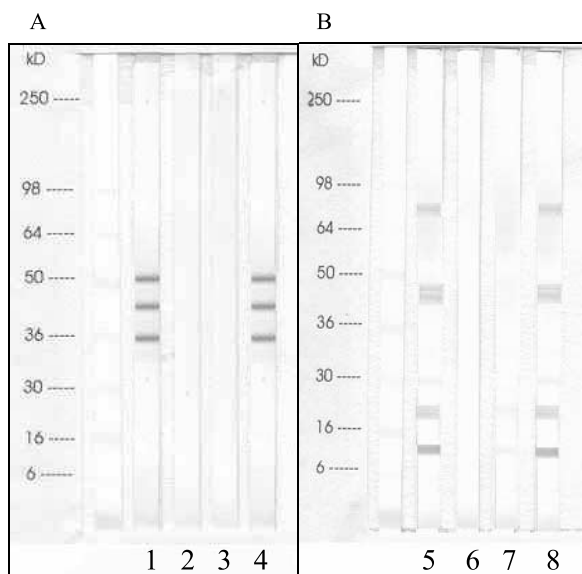


Figure 1. Panel A: Manioc AlaBLOT® IgE Assay: IgE binding to manioc allergens was completely inhibited by latex and manioc extract (100%). Lane 1, non-inhibited; lane 2, inhibited with manioc extract; lane 3, inhibited with latex extract; lane 4, inhibited with dog epithelium extract (as negative control). Panel B: Latex AlaBLOT® IgE Assay: IgE binding to latex allergens was partially inhibited (83%) by manioc extract (10 µl of manioc extract, concentration of 10 mg protein/ml) and completely inhibited by latex extract (100%). Lane 5, non-inhibited; lane 6, inhibited with latex extract; lane 7, inhibited with manioc extract; lane 8, inhibited with dog epithelium extract (as negative control).

immediately after eating foods cross-reacting with latex (chestnut, kiwi, passion fruit, papaya, mango, peach, fig, melon, tomato and spinach) (1). One year ago the patient also had an anaphylactic reaction, with generalized urticaria, bronchospasm and laryngeal oedema, 30 min after eating boiled manioc. Later she had a similar reaction immediately after eating a small amount of raw manioc (tapioca flour). Both reactions required treatment with subcutaneous epinephrine, intravenous corticosteroids and antihistamines, and the symptoms subsided 24 h later. Since then she has avoided these foods. Previously, she used to eat these foods, namely manioc (which she had been eating since childhood), with no adverse reaction. She denied any exposure to latex for the last 4 years.

The patient was referred to the Immunoallergy Department. Skin-prick tests (SPT) to commercial latex extract were strongly positive (Stallergènes, France). SPT to foods with known cross-reactivity with latex were positive to chestnut, mango, spinach and potato (commercial extract), peach, kiwi, passion fruit, papaya, fig, melon and tomato (fresh food). SPT to fresh

manioc, raw and cooked, were also strongly positive. We also tested 10 atopic patients, followed-up in our department, with fresh raw and cooked manioc, as controls, all being negative. Serum total IgE (AlaSTAT®, DPC-Amerlab) was 118 kU/l and latex-specific IgE (Immulite® 2000, DPC-Amerlab) was 67.4 kU/l (class 5). The challenge test with latex glove was strongly positive (anaphylactic reaction after 10 min hand contact). An oral challenge with manioc was not performed as the patient had severe anaphylactic reactions after eating this food.

Sodium dodecyl sulphate-polyacrylamide gel electrophoresis immunoblotting was performed with manioc and latex extracts (DPC, Los Angeles, USA). The immunoblotting analysis (AlaBLOT® Specific IgE Procedure, DPC) showed three protein bands of around 35, 42–44 and 50 kDa to crude manioc extract. In inhibition assay, IgE binding to manioc allergens was completely inhibited (100%) by latex extract (AlaBLOT® Inhibition Assay Procedure, DPC) (Fig.1 – lane 3).

IgE immunoblotting analysis demonstrated the existence of six protein bands of around 13–14, 17–18, 26–27, 42–44,

59–60 and 70 kDa to latex. Inhibition of this reactivity was partially obtained with manioc extract (83%) (Fig.1 – lane 7). Manioc extract completely inhibited IgE binding to 42–44 kDa band, probably corresponding to patatin-like latex protein *Hev b7*, previously identified as responsible for cross-reactivity with potato and tomato; patatin was recently confirmed as a potential food allergen (2).

In conclusion, this case report represents the first description of an IgE-mediated allergic reaction to manioc. Cross-reactivity between manioc and latex was proved by inhibition analysis, and manioc should be added to the growing list of foods involved in the latex-fruit syndrome.

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Kiss-induced facial urticaria and angioedema in a child allergic to fish

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Key words: children; fish; food allergy; kissing.

An account of the elicitation of urticaria and angioedema on the face of a 2-year-

old girl allergic to fish when kissed on the cheek by her grandfather, who had eaten fish 2 h earlier has been given.

The patient had been affected with atopic dermatitis (AD)

since she was 2 months of age. At 13 months, she presented urticaria and angioedema when first exposed to egg. The Radioallergen sorbent test (RAST's) performed at that time (CAP System, Pharmacia, Uppsala, Sweden) were positive for egg (albumen 2.41 kU/l; yolk 0.74 kU/l) and negative (<0.35 kU/l) for milk, α -lactalbumin (LA), β -lactoglobulin (LG), casein, wheat, cod, *Dermatophagoides pteronyssinus* and *D. Farinae*, cat.

At 19 months, she was rushed to our first-aid station in a severe anaphylactic state induced a few minutes after her first exposure to fish (Mediterranean bream: *Dentex dentex*). Further examinations following her discharge disclosed moderate AD (ADASi score 9) (1) and RASTs now positive for egg (albumen 7.36 kU/l; yolk 0.74 kU/l), α -LA, β -LG, casein (0.6, 0.62 and 0.63 kU/l), wheat (1.19 kU/l), cod (20.5 kU/l), bream (15.4 kU/l), soy (2.33 kU/l) and numerous other inhalants. Other challenges revealed allergy to cow's milk (urticaria, sneezing and vomiting), wheat (urticaria, angioedema and sneezing) and rice (immediate vomiting, recurrence of AD and persistent diarrhoea). Since then, she had never ingested fish, nor had fish been cooked in her home for fear of reactions to the vapours thus produced.

At 25 months of age, she went to her grandfather's house. He, however, had eaten bream 2 h earlier. When he kissed her on the cheek, urticaria and angioedema appeared after a few minutes and quickly spread to the whole of the face. Regression followed oral antihistamine and cortisone management.

Elicitation of facial urticaria has been reported in two infants with cow's milk allergy when kissed on the cheek by their mother and sister soon after drinking

Facial urticaria and angioedema were elicited in a 2-year-old girl allergic to fish when kissed on the cheek by her grandfather, who had eaten fish 2 h earlier.

milk (2). Anaphylactic reactions have also been described in adults allergic to peanuts (3), fish, fruit or vegetables (4, 5) when kissed by their partners minutes or even hours after eating the food. The striking feature in our case is the long interval between the grandfather's meal and his kiss. The presence of tiny particles of fish on his lips may have been sufficient to trigger a reaction in a sensitized subject with a prior history of severe anaphylaxis caused by ingestion of bream.

Kissing may thus give rise to allergic reactions due to contact with such food and also constitute a risk factor for general reactions. Care must therefore be taken in kissing such children after eating foods to which they are highly allergic.

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Delayed systemic reactions with flare-ups of previously negative intradermal skin tests to heparin

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Key words: drug allergy; heparin; lepirudin; nandroparin; enoxaparin.

Immunologically mediated adverse reactions to heparin are not frequent (1-3). We describe two cases of delayed reactions with flare-ups of previously negative intradermal skin tests to enoxaparin and nandroparin after the controlled administration of heparin as a challenged test.

Case 1. This was a 41-year-old woman who presented erythematous papular lesions of the upper body, arms and legs 12-18 h after the administration of the sixth dose of nandroparin. This patient was receiving prophylactic treatment for knee surgery and experienced itching around the injection site 4-6 h after the last administration of nandroparin.

Case 2. This was a 68-year-old woman who presented swelling and erythema in the application area and on the face and hands, during treatment with nandroparin and enoxaparin for a thrombophlebitis in the left leg.

Skin prick and intradermal tests were conducted 3 weeks after the reaction using commercial sodium heparin, enoxaparin and nandroparin diluted to 1 : 1, 1 : 10 and 1 : 100. The application sites were evaluated after 20 and 90 minutes and after 4, 24, 48 and 96 h. Five subjects, who had previously well tolerated heparin were used as controls.

Patch tests were performed in both cases with sodium heparin, enoxaparin and nandroparin using 'as is'.

Delayed reactions with flare up to intradermal skin test to heparins and tolerance to lepirudin in two patients.

Skin prick, intradermal and patch tests were negative in both cases and controls at all time intervals.

One week after the skin tests, a challenge test was conducted with sodium heparin, nandroparin and lepirudin in the first case and with sodium heparin and lepirudin in the second.

Twenty-four hours after the challenge test with nandroparin, the first case developed a maculo-papular rash on the upper body and induration at the sites where intradermal tests had been conducted 1 week earlier with enoxaparin and nandroparin. Cutaneous biopsies, taken from the flare-ups originating at the sites of the challenge tests demonstrated hydropic changes to the basement membrane with the formation of micro-vesicles and queratinocytic necrosis with deposition of capillary C3. Provocation tests with sodium heparin and lepidurin were negative.

In the second case, 24 h after the challenge test with sodium heparin, the patient presented generalized cutaneous erythema and induration of the areas where intradermal skin tests had been conducted the previous week with enoxaparin. The biopsy of these nodules presented perivascular linfocytic infiltrate, espongiosis and isolated eosinophils. The provocation test to lepirudin was negative.

Lepidurin could be a safe alternative treatment for patients with immunologically mediated reactions to heparin because of the difference in chemical composition. However, reactions to hirudins in patients clinically sensitive to heparin have also been published (3).

Cases 1 and 2 presented positive provocation tests to nandroparin and to sodium heparin, respectively. In both cases, flare-ups occurred in the areas where previously negative intradermal skin tests with low molecular weight heparins had been performed. Although intradermal skin tests in both patients were negative even after 96 h, the reactions which occurred after the challenge test, could have been provoked by residual amounts of heparin under the skin, further suggesting an nonimmediate (delayed) immunologically mediated mechanism. As previously described, in both cases, we observed good tolerance to lepidurin (2, 3).

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Effects of a nitro compound patch on neuropathy in Churg-Strauss syndrome

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Key words: Churg-Strauss syndrome; neuropathy.

A 54-year-old woman with bronchial asthma experienced heel pain on the right heel and skin eruption on both the legs, and 2 months later developed peroneal palsy (foot-drop) and numbness of the right lower leg. She had been treated for asthma with inhaled steroid, theophylline, and a β_2 -agonist (tulobuterol) patch. Further examination revealed eosinophilic pneumonia, peptic ulcers in the

stomach, duodenum, and colon, and congestive heart failure. Biopsies of the skin, lung, and colon showed eosinophilic inflammation, and she was diagnosed with Churg-Strauss syndrome. Treatment with corticosteroid improved the lesions of the skin, digestive system, and lungs. Because of the persistence of neuropathy and heart failure, cyclophosphamide was added to her corticosteroid therapy, and her heart condition gradually improved. However, her peroneal palsy persisted for 3 months. Transdermal isosorbide dinitrate (ISDN) patches were applied to all toes of the affected leg to treat the numbness, and she soon began to feel warmth in the affected leg. She was able to contract the muscles of the leg within 24 h, and then was gradually able to move the foot and the numbness disappeared within 2–3 weeks. Six months after the beginning of treatment with the ISDN patches, she was able to move the affected leg similar to the contralateral leg. When she missed applying the patches, she felt a mild numbness of the leg.

With the application of the ISDN patches on the affected toes, the skin temperature of the affected leg (at the instep) increased from 25.7 to 35.8°C, and that of the contralateral site simultaneously warmed up from 32.7 to 35.1°C. Also, the application of the ISDN patches to the contralateral site increased the skin temperature of both legs. We examined the effect of the ISDN patch on the fibular nerve conduction velocity. The conduction velocity of the fibular nerve increased from 38.5 to 44.0 m/s, while that of the contralateral site showed no significant change (from 46.5 to 46.2 m/s).

In this patient, local application of an ISDN patch improved the peroneal nerve lesion. Transdermal nitroglycerin to the affected side has been used successfully to treat Raynaud's syndrome and was reported to increase the finger blood flow bilaterally (1). In this patient, the skin temperature of the bilateral legs increased by ISDN patches to the affected side only. The application of nitroglycerin to the forearm is reported to raise the skin temperature bilaterally (2). Thus, ISDN patches may increase blood flow to the legs via local and systemic vasodilating effects. Meanwhile, the topical application of nitroglycerin is reported to reduce hyperalgesia and block neurogenic inflamma-

Churg-Strauss syndrome and nitro compound.

tion (3). An ISDN patch improved the foot-drop and increased the nerve conduction velocity. As the ISDN patch is a nitric oxide donor, it may stimulate the cyclic-GMP pathway, and increase the postsynaptic neuron cyclic GMP level (4). Thus, ISDN patches may affect nerve conduction via an increase in neural cyclic GMP, in addition to directing the vasodilating effect, in neuropathy caused by Churg-Strauss syndrome.

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Amoxicillin-induced aseptic meningo-encephalitis

O. Thauinat*, J. Gilquin, I. Lazareth, P. Priollet

Key words: adverse event; amoxicillin; meningitis aseptic; plasma cell.

Drug-induced aseptic menngitis (DIAM) is a rare adverse effect of several drugs.

The major causative agents are nonsteroidal anti-inflammatory drugs, antibiotics, intravenous immunoglobulin and OKT3 monoclonal antibodies (1).

Among antibiotics, cotrimoxazole seems to be the main cause of DIAM in human immuno deficiency virus (HIV)-infected patients. Only three cases of amoxicillin-induced aseptic menningitis have already been reported, in the last 2 years (2–4). We report a new case of this rare adverse event and discuss its pathogenesis.

An 86-year-old man was treated with amoxicillin–clavulanic acid 1 g b.i.d before skin grafting for varicose ulcers of the legs for 2 days, when he presented an extrapyramidal stiffness with fever and confusion followed by a coma with a Cheyne-Stokes respiration. There was no focal deficit and a computed tomography of the head was normal. Cerebrospinal fluid (CSF) analysis revealed pleiocytosis with 18 leukocytes/mm³ (57% of typical plasma cells), increased proteins (0.6 g/l) and normal glucose. No bacterial micro-organisms were found, interferon-alpha level was normal and herpes virus polymerase chain reaction was negative. As there was no improvement after 2 days of treatment with an increased dose of intravenous amoxicillin (3 g t.i.d), a DIAM was considered and the amoxicillin administration was withdrawn. The patient improved rapidly without any after-effects within 4 days. CSF examination was normal, 4 days after the discontinuation of the drug. An analysis of his medical history revealed an episode of extrapyramidal syndrome and somnolence consecutive to a course of amoxicillin therapy, 3 years ago. No lumbar puncture had been performed, but all symptoms had resolved quickly after withdrawal of the antibiotic.

This observation meets the criteria of DIAM (1): temporal relationship with the drug intake (including a positive reintroduction test), CSF pleiocytosis, negative testing for micro-organisms,

We report a case of amoxicillin-induced aseptic meningo-encephalitis with infiltration of cerebrospinal fluid by plasma cells.

absence of other explanation and complete resolution following discontinuation of the drug.

Among antibiotics responsible for aseptic meningitis, amoxicillin is only quoted three times, all in the last 2 years. Considering the lack of specific characteristics allowing the distinction between DIAM and infectious process, one can wonder if the frequency of this pathology is not underestimated.

Three unusual features are worth being noticed: (i) Absence of underlying condition such as HIV infection or connective tissue disease (1). (ii) Although uncommon in DIAM, encephalitic involvement has already been noticed in a previous report of amoxicillin-induced aseptic meningitis (2), and could be a specific feature. (iii) Instead of neutrophils, the CSF pleiocytosis consisted mostly in typical plasma cells. This might be a clue to clarify the pathogenesis of amoxicillin-induced meningoencephalitis.

The pathogenesis of DIAM is not well understood. As for the antibiotics, the prior exposure to the drug, the more severe symptoms on drug re-exposure, the cellular changes of CSF and the resolution of symptoms following discontinuation of the drug are all suggestive of a hypersensitivity reaction. Among immunological hypersensitivity mechanisms, type III and type IV are more likely to be involved. In type III, pre-existing autoantibodies combine with the drug resulting in complement fixation and development of acute meningitis. Bernstein (5) suggested that the drug combines with a CSF protein that acts as a hapten, explaining the restricted localization of the inflammatory response to the meningeal compartment.

This first report of a CSF plasma cell population appearing during a DIAM and disappearing with drug withdrawal pleads for type III hypersensitivity involvement in amoxicillin-induced aseptic meningitis.

DIAM is a rare adverse effect of several drugs. Amoxicillin seems to induced reversible meningoencephalitis by a type III hypersensitivity mechanism, although more researches is needed to definitely conclude about the pathogenesis.

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Severe hypotension complicating primary angioplasty: allergy to abciximab

C. Hawkins*, P. Gatenby, D. McGill

Key words: abciximab; allergy; anaphylaxis; adverse reaction.

Chimeric antibodies were devised to reduce the risk of hypersensitivity reactions but there are reports in the literature of complications following their administration

(1). We describe the case of a man with anaphylaxis secondary to abciximab with an immediate hypersensitivity response demonstrated on intradermal testing.

A 50-year-old man was admitted with an acute inferior myocardial infarct.

Coronary angiogram revealed an occluded right coronary artery. Angioplasty with stenting to the right coronary artery was immediately performed. Within 7 min of commencing an intravenous abciximab infusion, the patient became hypotensive (systolic blood pressure 50 mmHg). Crystalloid, aramine 3 mg, atropine 600 µg and metoclopramide 10 mg were administered. Urgent coronary angiogram, ventriculogram and echocardiogram did not reveal a cause. An erythematous rash and facial angioedema developed. The abciximab infusion was stopped, hydrocortisone 200 mg administered and an adrenaline infusion commenced with haemodynamic stabilization. A repeat coronary angiogram revealed a good angiographic result. Serum tryptase performed 9 h after the abciximab infusion was elevated at 71.2 ng/ml (normal reference range 0–15), and 24 h later it had normalized to 10.1 ng/ml.

The patient then had a skin prick and an intradermal testing to abciximab. Skin-prick testing to abciximab was negative. Intradermal administration was associated with a 5 × 5 mm wheal. No reaction was observed in a control subject.

Abciximab is a chimeric monoclonal antibody fragment (c7E3 Fab) that binds to the glycoprotein 11b/11a receptor and integrin $\alpha_v\beta_3$ (2) modulating platelet aggregation. A concern in the use of chimeric, human monoclonal antibodies is the potential for the development of an immune response to variable portions within the antigen binding site. Following the first administration of abciximab, low-titer, IgG human antichimeric antibodies (HACA) were detected in 6–7% of patients (3). No episodes of anaphylaxis were recorded. The Reopro Readministration Registry was established to assess the risks of further infusions of abciximab (4). At the completion of the trial, 1342 patients had received two or more infusions of abciximab with no hypersensitivity responses recorded (J. Tcheng, personal communication). Up to August 1998, 22 of 454 patients were found to have positive HACA titers at baseline with a further 82 of 432 developing positive titers after subsequent infusions (5).

On review of MEDLINE, EMBASE, Current Contents and CINAHL databases only one other possible case of ana-

phylaxis to abciximab has been reported (6). A case report documented the development of exanthematous rash and facial angioedema 9 days after intradermal infusion of abciximab (7). The Australian Drug Reactions Advisory Committee (ADRAC) has been notified of three cases of anaphylaxis following administration of abciximab (L. Henshaw, personal communication). The clinical scenario, raised serum tryptase and positive intradermal testing would support our case as being consistent with a type I mediated hypersensitivity response to abciximab. While the use of iodinated contrast media is associated with anaphylactoid reactions attributable to mast cell degranulation (8), iopamidol was re-administered without further hypotension. It is not clear why he developed such a reaction. He had not received chimeric monoclonal antibodies in the past, nor was there any history suggestive of a potential source of sensitization.

Type I hypersensitivity reactions may be an important cause of unexplained hypotension in interventional cardiology where gpIIb/IIIa inhibitors are used. Early identification enables the administration of appropriate treatment. Although there are reports of desensitization in patients who develop allergic reactions to other monoclonal antibodies (9), given the acute setting in which abciximab is administered this is unlikely to be practical. Desensitization could be considered in the event of further infusions.

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Can NSAIDs intolerance disappear? A study of three cases

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Key words: aspirin, asthma, bronchial provocation test, intolerance, NSAIDs.

The prevalence of NSAIDs intolerance (NI) is about 30% in asthma associated

with rhinosinusitis. The diagnosis is supported by clinical history and a positive oral challenge test

(1). In the last few years, bronchial and nasal provocation tests have been useful in the diagnosis of NI (2). NI usually remains throughout a patient's life, although occasionally some cases of NI abatement have been noted (3).

Case 1. A 57-year-old male, was diagnosed in 1983 with moderate intrinsic asthma and nasal polyps. In 1986 he suffered an episode of dyspnea and wheezing after ingestion of acetyl salicylic acid (ASA) (500 mg), and another similar episode after ingestion of 50 mg of diclofenac. During oral challenge test (OCT), 45 min after Ibuprofen (100 mg) administration, the patient presented dyspnea and a 22% decrease in FEV1. He was treated with budesonide 800 mcg/12 h for asthma previously, and currently he takes salbutamol occasionally.

Case 2. A 52-year-old male, was diagnosed in 1970 with severe intrinsic asthma and nasal polyps. In 1983, he suffered three episodes of dyspnea and wheezing after ingestion of ASA (500 mg). During OCT, 60 min after ASA (500 mg) administration, the patient presented rhinorrhea, dyspnea, coughing and a 35% decrease in FEV1. Currently, he is being treated with budesonide 400 mcg/12 h.

Case 3. A 36-year-old male, was diagnosed in 1973 with moderate intrinsic asthma and nasal polyps. In 1976, he suffered two episodes of dyspnea and wheezing after ingestion of ASA (500 mg). During OCT, 60 min after dipyrone (100 mg) intake, the patient presented rhinorrhea, dyspnea and a 20% decrease in FEV1. Currently, is being treated with budesonide 400 mcg/12 h.

In 1998, the patients came to our outpatient clinic to confirm the diagnosis of NI as they needed NSAIDs treatment. After written informed consent, we performed a bronchial provocation test with lysine acetyl salicylate (BPT-LAS) on the three patients, following a modified method of Phillips et al. (4). We consid-

We confirm the disappearance of NSAIDs intolerance in three asthmatics by bronchial and oral provocation test.

ered the test positive if, after challenge, FEV1 dropped off by 20% or more, and negative if the patient tolerated up to 10 inhalations of 180 mg/ml LAS. We also performed ASA-OCT that we considered as positive if FEV1 dropped off by 20% or more and/or respiratory symptoms appeared. The test was considered to be negative if the patient tolerated up to 1000 mg of ASA.

In the three patients, BPT-LAS and OCT with ASA were found to be negative. After this study, they have tolerated other NSAIDs.

We present three patients previously diagnosed of ASA-triad in whom we have proved the abatement of NI. The abatement of NI in these patients is in agreement with a reduction of their asthma symptoms and hence asthma medication. The performance of BPT-LAS is easy, safe and has been very useful in the follow-up of these patients. In view of these results, in some cases, it could be necessary to repeat the diagnostic tests of NI every time, in order to increase the possibilities of NSAIDs treatment.

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Rush desensitization to allopurinol

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Key words: allopurinol; desensitization; hypersensitivity to drugs.

Hypersensitivity to allopurinol is relatively uncommon (1, 2), but makes difficult the treatment of hyperuricemia in allergic patients suffering from gout as in many countries no alternative drugs are available.

For example, in Italy, sulfinpyrazone is no more available, and benzbromarone is not on the market. An option in patients who need allopurinol treatment is desensitization, first introduced in 1976 (3) and recently retrospectively evaluated in 32 patients treated

Desensitization to allopurinol may be performed by rush protocols.

with a slow oral desensitization regime with good results (4).

Here we report on a patient (male, 42 years) with tophaceous gout who had urticaria-angioedema a few days following the first treatment with allopurinol, and a further, more intense episode when the family doctor tried to resume the treatment after some months. The patient was admitted to our Rheumatology/Allergy Unit because of an acute gout attack, with a high serum urate level (11.3 mg/dl), and we decided to perform an oral desensitization to allopurinol. The protocol was derived from Fam et al. (4), with dose increase as follows: 50 – 100 – 200 – 500 mcg – 1 – 5 – 10 – 25 – 50 – 100 mg. The soluble suspension of allopurinol was prepared as described by Fam et al. Different from the original protocol, in which each dose is administered every 3 days and requires about 1 month, we used a rush schedule with doses up to 1 mg administered in the first day with a 1-h interval, while 5 and 10 mg were administered in the second day, 25 and 50 mg in the third day, and 100 mg in the fourth day. Then the patient assumed each day a 100-mg tablet and, after 1 week, the dose was increased to half tablet of 300 mg and finally to a 300-mg tablet. No reaction occurred during desensitization nor during subsequent treatment, and the serum urate level was lowered to 5.9 mg/dl after 1 month.

The present case demonstrates that oral desensitization with allopurinol can be successfully performed also by rush protocols, ensuring, in a short time, an effective treatment in patients with gout.

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