CASE REPORT

Exercise-induced anaphylaxis in an elderly patient

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SUMMARY

A 75-year-old Japanese woman presented with acute flushing pruritus and a feeling of diffuse warmth followed by collapse while dancing. After resting for 30 min and receiving a rapid infusion of 0.9% sodium chloride, her condition stabilised. She admitted that she had a similar experience 2 years earlier while dancing. Based on her history, her symptoms were attributed to exercise-induced anaphylaxis. None of the episodes was associated with any other suspicious cotriggers of anaphylaxis. She was successfully discharged from the clinic without any complications after receiving careful guidance on how to prevent this condition.

BACKGROUND

Anaphylaxis is an acute and life-threatening condition that many physicians have experienced or might encounter on a daily basis. Exercise-induced anaphylaxis (EIAN) is characterised by anaphylaxis in the setting of physical exercise.¹ Typical anaphylactic symptoms include sudden fatigue, warmth, flushing, generalised urticaria and pruritus. In the advanced stages, acute angioedema, upper airway obstruction and collapse are observed.¹⁻³ These symptoms can occur at any time during exercise and occasionally occur just after physical exercise. Recognition of this disease is significant because increased awareness of this condition will enable physicians to make an accurate diagnosis, adequately educate patients and ultimately realise a better outcome for the patient and their quality of life.

CASE PRESENTATION

A 75-year-old Japanese woman presented with acute flushing pruritus and a feeling of diffuse warmth followed by collapse while dancing at the studio contained within her home. That morning, she had arranged to go dancing with her friends. She performed the household chores and then ran to the dance studio, without eating breakfast. At the studio, 10 min after beginning to dance, she experienced sudden generalised pruritus that began in her neck, coincident with fatigue, diffuse warmth and abdominal discomfort. She did not experience facial oedema, chest pain, dyspnoea, nausea or diarrhoea. She did not have any relevant medical history except for a similar experience that occurred 2 years earlier while dancing on a sunny autumn day in another studio. She was not under medication and had no known food or drug allergies. She had no relevant family history. She had no illnesses and underwent yearly check-ups. She had last eaten a meal the previous evening at home.

DIFFERENTIAL DIAGNOSIS

- ▶ Cholinergic urticaria
- ▶ Systemic mastocytosis
- ▶ Hypertryptasemia
- ▶ Cold-induced anaphylaxis
- ▶ Exercise-associated reflux
- ▶ Cardiovascular events
- ▶ Exercise-induced bronchoconstriction
- ▶ Hypoglycaemia
- ▶ Neoplasmatic disorder
- ▶ Postural orthostatic tachycardia syndrome (POTS)
- ▶ Primary food allergy exacerbation by exercise

TREATMENT

After resting for 30 min following a rapid infusion of 500 mL of 0.9% sodium chloride at the emergency room, her symptoms improved and finally resolved.

OUTCOME AND FOLLOW-UP

The patient went home once her symptoms resolved. She was followed up for 7 days but did not experience any recurring symptoms. According to her history, the recent episode was the same as the patient's previous experience, which was related to the absence of food intake before exercise leading to the onset of symptoms. The patient was advised to exercise with companions and to be alert to the early symptoms including excessive fatigue, flushing and pruritus. She was also advised to stop exercise immediately and lie down if the symptoms of anaphylaxis occurred and to prepare for intramuscular injection of epinephrine and call an ambulance if the symptoms persisted or worsened.

DISCUSSION

EIAN is a rare disorder that is usually observed in adolescents and young adults but may occasionally affect older adults.³ EIAN is characterised by symptoms of anaphylaxis triggered by physical exertion.³ Typical symptoms include sudden fatigue, diffuse warmth and/or flushing, generalised pruritus and urticaria.¹⁻³ These symptoms commonly occur during exercise, and her symptoms occurred while dancing. Cessation of exercise usually improves or resolves the symptoms.⁴ However, if exercising is not discontinued, then the symptoms progress to more severe and even fatal events including hypotension, laryngeal oedema with upper airway obstruction and anaphylactic shock. Some subsets of patients have food-dependent EIAN, in which symptoms develop during exercise performed within a few hours of eating.^{5,6}

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In most cases, a clinical diagnosis of EIAN is based largely on a meticulous history taking of events and exclusion of differential diagnoses. The typical signs and symptoms of EIAN, mentioned above, increase the clinical possibility of an EIAN diagnosis. With regard to the patient's history, she was an elderly woman who showed typical symptoms including sudden fatigue, diffuse warmth and flushing pruritus after exercise. Her presentation was indicative of EIAN.

If clinical history is suggestive, skin testing or in vitro testing for food-specific IgE should be performed.⁷ In this case, she had skipped breakfast and had not eaten for more than 12 hours before exercise; therefore, any association between anaphylaxis and food intake would be unlikely. An exercise challenge test, such as the Standard Bruce protocol for stress testing (with added spirometry before and during the test), could be used, but the test is not required for diagnosis. A positive result in the exercise challenge test could be used to confirm the diagnosis, but a negative result would not completely exclude the diagnosis.⁸

As differential diagnoses in the present case, cholinergic urticaria, systemic mastocytosis, cold-induced anaphylaxis, exercise-associated laryngoesophageal reflux, cardiovascular events, exercise-induced bronchoconstriction, hypoglycaemia, neoplastic disorder, POTS and hypertryptasemia were considered. In addition, the differential diagnosis of food-dependent EIAN included a primary food allergy exacerbated by exercise.

Cholinergic urticaria is a form of physical urticaria that is elicited by elevated core body temperature due to exercise or exposure to intrinsic or extrinsic factors (eg, spicy foods, hot showers or strong emotion).⁹ Typical presentations of the affected skin include small punctate weals with surrounding erythema, whereas systemic symptoms can occur if cutaneous mast cell mediators are released in sufficient amounts to diffuse to the systemic circulation.¹⁰ Weal size is one clue used to differentiate EIAN from cholinergic urticaria, although the case is not always clear-cut. EIAN weals are usually large (10–15 mm in diameter), whereas those of cholinergic urticaria are typically small (1–3 mm in diameter) and punctate.⁹ However, cholinergic urticaria-associated weals may increase in size as symptoms progress.

Mastocytosis (limited to the skin), especially systemic mastocytosis (involving extracutaneous tissues), can mimic anaphylaxis.¹¹ In this condition, patients are susceptible to anaphylaxis triggered by a variety of stimuli, including exercise, which is caused by pathological mast cell accumulation in the tissues. Patients with systemic mastocytosis often have persistent elevations of serum mature tryptase. In contrast, in patients with anaphylaxis, abnormal serum tryptase elevations return to normal after recovery and symptom resolution.¹¹ In the present case, the patient did not have elevated serum tryptase or characteristic skin findings of systemic mastocytosis, which ruled out mastocytosis.

Up to 6% of the general population may have hypertryptasemia which is due to duplication or triplication of the alpha-tryptase gene TPSAB1.¹² The cause and relevance of such increases are unknown. Patients with this genotype can present with multisystem complaints including flushing and POTS-like symptoms. More severe or recurrent anaphylaxis episodes have not been recognised with this condition. The patient had a normal tryptase.

Cold-induced anaphylaxis could be mistakenly diagnosed with EIAN.¹³ Cold ambient conditions are considered to be the sole or a cotrigger of EIAN. However, the patient indicated that she was not exposed to cold ambient conditions. She had woken in the morning and had been busy performing household chores. After that, she ran through the corridors to the dance studio within

her home. According to her, neither the house corridors nor the studio was cold.

Exercise-induced laryngopharyngeal reflux can mimic symptoms of EIAN including flushing as well as throat discomfort and chest tightness.¹⁴ However, the generalised pruritus and spontaneous symptom escalations in the patient did not correlate with exercise-induced laryngopharyngeal reflux.

Cardiovascular events can cause sudden fatigue, dyspnoea, chest pain, syncope or sudden death during exercise. These events may be due to structural abnormalities or arrhythmias such as coronary artery disease, myocarditis, idiopathic cardiomyopathy, mitral valve prolapse, long QT syndrome or Brugada syndrome. Specific cardiological examinations or tests such as electrocardiography or echocardiography could be performed to diagnose these disorders. However, EIAN is usually differentiated from cardiovascular events due to the presence of pruritus, warmth, urticaria or laryngeal oedema in EIAN. The patient exhibited generalised pruritus and diffuse warmth but did not exhibit urticaria or laryngeal oedema.

Exercise-induced bronchoconstriction presents with symptoms that are limited to the airways and occasionally occurs in patients with asthma.¹⁵ However, generalised pruritus and the worsening symptoms in the patient were not indicative of exercise-induced bronchoconstriction.

Hypoglycaemia has an unusual presentation that can mimic EIAN. Hypoglycaemia would present as generalised fatigue, palpitations and other symptoms associated with the autonomic nervous system. The length of fasting, a medical history of diabetes or other metabolic conditions, as well as the blood glucose level, could provide clues for a diagnosis of hypoglycaemia. However, the skin symptoms and sudden-onset fatigue in this patient did not equate to hypoglycaemia.

In neoplastic disorders with endocrine activity such as carcinoid, pheochromocytoma, medullary carcinoma of the thyroid or pancreatic cell tumours, the release of bioactive substances might mimic EIAN.¹⁶ These disorders do not depend on exercise, but the release of bioactive substances could be triggered by exercise. However, in the present case, an asymptomatic period of 2 years and the rapid resolution of her symptoms following treatment are unlikely to be associated with a neoplastic disorder.

POTS can be defined as an excessive increase in heart rate (>30 beats per minute) when moving from a supine to upright posture with accompanying symptoms, such as a headache, tachycardia, abdominal discomfort, nausea and presyncope.¹⁷ Symptoms of POTS should develop within 10 min of posture change. However, rarely, POTS may occur in association with mast cell disorders. However, the generalised pruritus and the spontaneous symptom escalations in the patient do not match POTS occurring in association with a mast cell disorder.¹⁷ Additionally, she had not moved from a prone to upright position since waking earlier in the day.

Patients with food allergies may have reactions that are exacerbated by concomitant exertion.⁵ However, as mentioned above, she had not eaten recently, ruling out primary food allergy exacerbation by exercise.

If patients with allergies do not have an identifiable trigger (eg, food, pollen, alcohol or temperature) that can be avoided, they are strongly recommended to exercise with companions or in a supervised setting and to warm up before exercise.³ If patients notice symptoms at the early stage of anaphylaxis, they are recommended to stop exercising immediately. Additionally, patients are encouraged to identify an exercise schedule that is unlikely to precipitate symptoms. Such patients should carry an intramuscular epinephrine injector to treat sudden-onset,

persistent symptoms. For patients with frequent and severe symptoms, H1-receptor antagonists (antihistamines) might be useful for reducing the frequency and severity of symptoms and in helping the patient to modify their exercise regimen.²

The prognosis of patients with EIAN has been favourable except for a few fatal cases, in which critical comorbidity existed or the EIAN was underdiagnosed.^{18 19} In contrast, the majority of patients enjoy a good prognosis and experience fewer and less severe attacks over time.³ A good prognosis can be fostered by recognition of the early signs of anaphylaxis and modification of exercise habits with an awareness of potential cotriggers of anaphylaxis.

Learning points

- ▶ Exercise-induced anaphylaxis (EIAN) is characterised by anaphylaxis in the setting of physical exertion.
- ▶ The diagnosis of EIAN is based on the clinical history and exclusion of other disorders. Careful history taking to detect other cotriggers is essential.
- ▶ Patients must stop exercise immediately when experiencing the first signs of anaphylaxis. It is strongly recommended that they exercise with companions or in a supervised setting and that they carry an intramuscular epinephrine injector for progressive symptoms.
- ▶ Premedication of an H1-receptor antihistamine is possible for those with frequent or severe symptoms or symptoms elicited by mild exercise.
- ▶ The prognosis of patients with EIAN is favourable.

Competing interests None declared.

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