Rare disease

Exercise-induced anaphylaxis

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Summary

A 23-year-old man presented with acute flushing, pruritus and warmth followed by collapse after vigorous exercise in a gymnasium. After resting for 30 min and receiving a rapid infusion of 0.9% sodium chloride, he was finally stable. He admitted that he had a similar experience 5 years earlier during exercise. Based on the patient's history, his symptoms were attributed to exercise-induced anaphylaxis. None of his episodes was associated with any suspicious co-triggers of anaphylaxis. He was successfully discharged from hospital without any complications after receiving guidance on how to prevent this condition.

BACKGROUND

Anaphylaxis is one of the acute conditions that frontline physicians may encounter on a daily basis. In exercise-induced anaphylaxis, anaphylaxis occurs in association with physical exercise.¹ Symptoms are those of typical anaphylaxis including extreme fatigue, warmth, flushing, urticaria and pruritus. In the advanced stages, angioedema, upper airway obstruction and collapse are observed.^{1–3} These symptoms may occur at any stage of exercise. We believe that knowledge of this disease as a differential diagnosis of anaphylaxis is very important because a better understanding of this condition will enable clinicians to make correct diagnosis, properly educate patients and ultimately realise a better outcome for the patients.

CASE PRESENTATION

A 23-year-old medical student presented with acute flushing followed by collapse that occurred during a basketball game in the gymnasium. On the morning in question, the patient had an appointment with his friends to play basketball. He overslept and ran to the school gymnasium without having breakfast. At the gym, 3 min after starting the game, he suddenly experienced generalised pruritus beginning at his neck. He also felt warmth, fatigue and abdominal discomfort. He denied experiencing facial swelling, chest pain, dyspnoea, nausea or diarrhoea. He also denied any history except for a similar experience of symptoms 5 years earlier while jogging on a sunny spring day in a nearby park. He was not on any medication and was not allergic to any drug or food. His last meal was dinner at the university dormitory the previous evening.

INVESTIGATIONS

On examination, his pulse was 88 beats/min and blood pressure was 94/65 mm Hg. A generalised flushing over his upper trunk and extremities was observed. His heart-beat was normal, and lungs were clear for auscultation bilaterally.

DIFFERENTIAL DIAGNOSIS

- ▶ Systemic mastocytosis
- ▶ Cold-induced anaphylaxis
- ▶ Exercise-associated laryngoesophageal reflux
- ▶ Cardiovascular disorders
- ▶ Cholinergic urticaria
- ▶ Hypoglycaemia (unusual presentation).

TREATMENT

After resting for 30 min following a rapid infusion of 500 ml of 0.9% sodium chloride at the emergency room, his symptoms diminished and finally disappeared.

OUTCOME AND FOLLOW-UP

The patient was discharged after his symptoms disappeared. He was followed up 7 days after discharge; no symptoms recurred. According to his history, the patient's previous experience was the same as the episode he experienced this time, which was related to the lack of any food intake prior to the exercise and onset of the symptoms. The patient was advised to exercise with companions and to be alert to the early symptoms including fatigue, flushing and pruritus. He was also advised to stop exercise immediately and lie down if the symptoms occurred and to prepare for intramuscular injection of adrenaline if the symptoms persisted or worsened.

DISCUSSION

Exercise-induced anaphylaxis is a disorder usually observed in young adults, characterised by symptoms of anaphylaxis triggered by physical activity. Typical symptoms include generalised fatigue, diffuse warmth, flushing, pruritus and urticaria.^{1–3} The symptoms commonly occur during exercise, and his symptoms actually occurred during the game. These symptoms usually improve immediately after cessation of exercise. However, if the exercise is continued, the symptoms progress to more severe and even fatal conditions including hypotension, laryngeal oedema with upper airway obstruction and anaphylactic shock. A subset of patients have food-dependent,

exercise-induced anaphylaxis, in which symptoms develop when starting exercise within a few hours of eating.^{3 4} The diagnosis of exercise-induced anaphylaxis is based on the clinical presentation of the patient consistent with anaphylaxis in the setting of physical activity and exclusion of other differential diagnoses. The typical signs and symptoms of the disease mentioned above will raise the clinical index of suspicion of the diagnosis. With regard to the patient's history, he was a young man who showed typical symptoms including generalised fatigue, diffuse warmth and flushing pruritus after exercise. This presentation is very much compatible with exercise-induced anaphylaxis.

If indicated by clinical history, skin testing for specific immunoglobulin E to food should be performed.⁵ In our case, the patient did not have breakfast and had last eaten more than 10 h before exercise; therefore, any association between anaphylaxis and food intake was not likely to manifest. An exercise challenge test, such as the standard Bruce protocol for stress testing (including spirometry before and during the test), can be used, but the test is not required for diagnosis. A positive result from the exercise challenge test can be used to confirm the diagnosis, but a negative result does not necessarily exclude the diagnosis.⁶

As differential diagnoses, mastocytosis, especially systemic mastocytosis, mimics anaphylaxis.⁷ In this condition, patients are susceptible to anaphylaxis triggered by various stimuli, including exercise due to pathological mast cell accumulation in tissues. Persistent elevation of serum tryptase is observed in systemic mastocytosis, whereas in anaphylaxis tryptase levels return to the normal range after complete recovery from the symptoms. The serum tryptase level of this patient was within the normal range, which suggests that the patient probably did not have mastocytosis.

A cold ambient condition is considered to be the sole or a co-trigger of anaphylaxis in exercise-induced anaphylaxis.⁸ However, questioning of the patient revealed that he was not exposed to cold ambient conditions, because he woke up in his dormitory room and rushed through the corridors to the gymnasium. According to him, his room, the corridor connecting the dormitory to the gym and the interior of the gym were not cold.

Exercise-induced laryngopharyngeal reflux resembles exercise-induced anaphylaxis with regard to symptoms including flushing as well as throat and chest discomfort. However, pruritus and the spontaneous escalation of the symptoms observed in this patient do not match reflux.

Cardiovascular disorders can cause symptoms such as fatigue, dyspnoea, chest pain, syncope or sudden death during exercise. These disorders include structural abnormality and arrhythmias, such as hypertrophic cardiomyopathy, coronary artery disease, myocarditis, mitral valve prolapse, long QT syndrome or Brugada syndrome. Diagnosing these disorders would entail specific cardiological examination or tests such as electrocardiography or echocardiography, but in general, what differentiates anaphylaxis from these disorders is the presence of pruritus, warmth, urticaria or laryngeal oedema. This patient exhibited generalised pruritus and warmth, but did not exhibit urticaria or laryngeal oedema.

Cholinergic urticaria is a subtype of physical urticaria that is usually elicited by elevated core body temperature due to exercise or exposure to intrinsic or extrinsic factors that raise the temperature such as spicy foods, hot water or strong emotion. A typical symptom is the presence of small punctate wheals with surrounding erythema limited to the skin, whereas systemic symptoms can occur if cutaneous mast cell mediators are released into the systemic circulation.⁹ One clue to differentiate exercise-induced anaphylaxis from cholinergic urticaria is the size of the wheals, although this distinction is not always clear-cut. The wheals observed in anaphylaxis are >10 mm in diameter, whereas the wheals associated with cholinergic urticaria are usually small (<5 mm in diameter) and punctate. The diameter of the wheals associated with cholinergic urticaria may increase as symptoms progress.

Unusual presentation of hypoglycaemia may mimic exercise-induced anaphylaxis, showing symptoms of 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 level of blood glucose may provide clues to the diagnosis of hypoglycaemia.

If patients do not have a specific trigger (such as food, pollen or humidity) to be avoided, they are recommended to exercise with companions and to warm up before exercise³; if patients notice symptoms of the early stage of anaphylaxis, they are recommended to stop exercising immediately. At this point, they should be prepared for an intramuscular injection of adrenaline if the symptoms progress. For patients with frequent and severe symptoms, H1 antihistamines may prove helpful in reducing the frequency and severity of symptoms.²

The prognosis is favourable in general, except for a few fatal cases. In those fatal cases, either significant comorbidity existed or the exercise-induced anaphylaxis was not formally identified.^{10 11} In contrast, most people enjoy a good prognosis with no fatal complications, having fewer attacks over time.^{3 12} This good prognosis may be attributed to an early recognition of the early signs of anaphylaxis and the modification of exercise habits in addition to avoiding potential co-triggers of anaphylaxis.

Learning points

- ▶ Exercise-induced anaphylaxis is a type of anaphylaxis in which symptoms occur in response to physical exertion.
- ▶ The diagnosis is usually based on the clinical history and exclusion of other disorders. Careful history taking to look for other co-triggers is essential.
- ▶ Patients should stop exercise immediately if they experience the early signs of anaphylaxis and be prepared for intramuscular adrenaline injections if the symptoms progress.
- ▶ Administration of an H1 antihistamine may be suggested for patients with frequent/severe symptoms or for patients who are unable to avoid doing exercise.
- ▶ The prognosis is generally favourable.

Competing interests None.

Patient consent Obtained.

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