Clinical Analysis of Anaphylaxis Patients in an Emergency Medical Center

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ABSTRACT Clinical analysis was conducted for 26 patients who were transferred and admitted for emergency treatment of anaphylaxis in a secondary healthcare setting in Toho University Omori Medical Center during the two years between September 2003 and August 2005. Possible triggering factors for anaphylaxis were foods in 12 patients, drugs in 11 patients, and other factors (bee sting and rat and hamster bites) in three patients. The foods included fish for seven patients; meat, soba or buckwheat noodles, and citrus fruits for one patient each; and other foods for two patients. Five of the patients tested had positive results for a specific radioallergosorbent test (RAST). Drugs were all oral agents including non-steroidal anti-inflammatory drugs (NSAID) in eight patients and antibiotics in three patients. The results from a drug lymphocyte stimulation test (DLST) were positive for only two of the patients. All patients experienced cutaneous and respiratory symptoms. Seven patients experienced symptoms of disturbance of consciousness, and nine patients experienced symptoms of shock, either drug-induced (five patients) or food-induced (four patients). No significant difference was observed between the two groups. Nineteen of the 26 patients had a history of allergies. Although the rate is significantly higher than the general population, the patients experiencing symptoms of shock included three cases of drug-induced shock without a history of allergies. This reaffirms the importance of paying special attention to drug-induced anaphylactoid reactions that may cause sudden symptoms of shock in a patient without a history of allergies. Thirteen patients were treated with epinephrine (0.5 ± 0.4 mg) and 24 patients with corticosteroids. The outcome was good for all patients, and no biphasic anaphylaxis was observed. Although corticosteroids are not a first-line agent, they may play a role in the prevention of biphasic anaphylaxis.

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Introduction

Anaphylaxis is an acute systemic allergic reaction characterized by rapid onset after exposure to a causative substance¹⁻³⁾. As patients with anaphylaxis transferred emergently mostly have severe symptoms, they are more frequently treated by an emergency physician than allergist, which suggests the importance of the initial treatment. For this reason, treatment of anaphylaxis needs to be provided in compliance with international guidelines⁴⁾. Phy-

sicians in charge of the initial emergency treatment are and will be required to implement appropriate first-aid measures for patients with anaphylaxis. The biphasic reaction of anaphylaxis is a recurrence of anaphylaxis symptoms after an initial reaction. Because many reports have recommended that patients with anaphylaxis should be observed for 8 to 24 hours to monitor for biphasic reactions, it is important for an emergency physician to understand biphasic reactions. Although there have been occasional reports analyzing patients with anaphylaxis, recently only a few reports about the emergency transfer of adult patients with severe symptoms involving biphasic reaction have been published in Japan⁵⁾. Therefore, the purposes of this retrospective study were to: 1) analyze the clinical data of adult patients with anaphylaxis who were admitted to an emergency unit; 2) report several characteristics observed in these patients; and 3) assess the

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Table1. Etiology of anaphylaxis.

Cause	No (%)
Food	12 (46)
Medication	11 (42)
Bee sting	1 (4)
Rat bite	1 (4)
Hamster bite	1 (4)
Total	26 (100)

Table2. Clinical signs and symptom of anaphylaxis.

Signs/Symptoms	No (%)
Urticaria, angioedema, flushed skin	26 (100)
Shortness of breath, dyspnea, wheezing	26 (100)
Hypotension	9 (35)
Nausea, vomiting, diarrhea	8 (31)
Syncope	7 (27)
Laryngeal edema, tongue swelling	6 (23)

biphasic reaction.

Subjects

Clinical analysis was conducted for 26 patients with anaphylaxis who were transferred and admitted for emergency treatment at the Toho University Omori Medical Center between September 2003 and August 2005. We studied 12 male patients and 14 female patients aged 17 to 69. Anaphylaxis includes in a broad sense an anaphylactic reaction caused by a type 1 IgE-mediated allergy and an anaphylactoid reaction induced by direct stimulation of mast cell degranulation. Because there is not much significance in their clinical differentiation, both are treated as anaphylaxis in this study.

Results

Possible anaphylaxis triggering factors were foods for 12 patients, drugs for 11 patients, and other factors (bee, rat, and hamster) in three patients (**Table 1**). The foods included fish for seven patients; meats, soba or buckwheat noodles, and citrus fruits for one patient; and other factors for two patients. The results of a specific RAST were positive for five of the patients. The mean serum IgE level was high with 420 ± 430 U/ml. All drug-induced cases were caused by oral agents, including NSAIDs for eight patients and antibiotics for three patients. The results of a DLST were positive for two patients. The period between exposure and onset of symptoms ranged from a few minutes to less than an hour, accounting for 24 ± 28 minutes and 15 ± 18 minutes in the food-induced and drug-induced cases, respectively. There was no significant difference among them. Cutaneous and respiratory symptoms were observed in all patients. Twenty-four patients experienced symptoms of hypoxemia and were treated with oxygen. No tracheal intubation was required. Seven patients experienced symptoms of disturbance of consciousness, and nine patients experienced symptoms of shock, either drug-

induced (five patients) or food-induced (four patients) (**Table 2**). Nine of 12 food-induced cases and 7 of 11 drug-induced cases were associated with a history of allergies, that is, 19 of 26 cases in total. Food allergies were the most prevalent among patients with a history of allergies.

Thirteen patients were treated with epinephrine (0.5 ± 0.4 mg) and 24 patients with steroids, and three patients with antihistamine. Epinephrine was administered at the mean dose of 0.5 ± 0.4 mg subcutaneously in nine patients, intramuscularly in one patient, and intravenously in three patients. Hydrocortisone sodium succinates were administered intravenously in eighteen patients at the mean dose of 466 ± 216 mg (300-1000mg). Methylprednisolone sodium succinates were administered intravenously in three patients at the dose of 300, 500, and 1000 mg. Betamethasone was administered intravenously in two patients at the dose of 2 and 8 mg. Prednisolone was administered intravenously in a patient at the dose of 60 mg. The outcomes were good, and no biphasic reactions were observed in any patients.

Discussion

This analysis included 26 patients with anaphylaxis who were transferred to a secondary healthcare setting due to dyspnea, which is one of the severe symptoms of anaphylaxis. The primary symptoms of anaphylaxis are cutaneous such as urticaria and angioedema observed in more than 90% of patients, followed by respiratory symptoms such as dyspnea^{6,7)}. It is a coincidence of this study that urticaria and angioedema were observed in all patients.

In this study, detailed questioning was conducted to estimate specific factors because it is extremely difficult to obtain allergen screening such as a loading test as the risks of each test are high. Although the results of a specific RAST were positive for only five patients with food-induced anaphylaxis, triggering factors were estimated based on a reasonable temporal relationship between the onset of symptoms and exposure to drugs, foods, and other

factors. The reason why no idiopathic anaphylaxis was observed in this study, even though 37% of patients were thought to have idiopathic anaphylaxis in a recent report, is uncertain⁷⁾. However, the detailed questioning could be very important to estimate causative factors in this study. In a recent Japanese report, the probable cause of anaphylaxis was identified in 29 subjects (100%) of 29 patients, and foods were thought to cause anaphylaxis in 16 subjects (55%), and medications appeared to cause anaphylaxis in 13 subjects (45%)⁸⁾. These observations were similar to the results in this study.

A history of allergies was observed in 19 of 26 patients including 8 of 12 food-induced cases and 7 of 11 drug-induced cases. There was no significant difference. However, it should be noted that three patients without a history of allergies presented severe symptoms, such as loss of consciousness and shock. High risk anaphylaxis is generally related to food/drug allergies, bronchial asthma, and atopic diathesis, as well as administration of beta-blockers^{9,10)}. None of the triggers were observed in these three patients. As some cases of drug-induced anaphylactoid reaction may not involve sensitization at onset, it is possible that the first exposure triggers the onset of the clinical syndrome. There are no preventive measures for avoiding unexpected anaphylactic shock in routine medical practice. Here, we are reaffirmed that the risk of anaphylaxis should be kept in mind whenever drugs are administered to patients with or without a history of allergies.

A recent report has suggested that the length of time before the onset of symptoms is reduced and the number of severe clinical symptoms are increased in patients with drug-induced anaphylaxis compared with food-induced cases in Japan⁸⁾. Although the results of our study indicated a tendency for a reduced length of time before the onset of symptoms in drug-induced anaphylaxis, no significant difference was observed. In addition, four patients experienced food-induced shock that developed rapidly. It is suggested that food-induced anaphylaxis also occurs rapidly in severe cases.

The initial treatment should include maintenance of respiratory and circulatory functions and prevention of the progress of allergic reactions. As is well known, epinephrine is a first-line agent for anaphylaxis¹¹⁾. In this study, 13 of 26 patients were treated with epinephrine and did not present with persistent anaphylaxis, which is occasionally observed. Epinephrine was administered at a dose of 0.1 mg to a maximum dose of 1 mg subcutaneously in nine patients, intramuscularly in one patient, and intrave-

nously in three patients. No patients experienced adverse effects, such as arrhythmia and elevated blood pressure. According to international guidelines for treatment of anaphylaxis, subcutaneous infusion of epinephrine is not effective in severe cases and intramuscular injection should be provided every five minutes⁴⁾. The 13 patients treated with epinephrine in this study included patients with severe anaphylaxis presenting shock or disturbance of consciousness who were treated at a higher dose of 0.5 to 1 mg. Intravenous administration was provided for three patients, which is considered rather frequent. Physicians should continue to seek optimal treatment for each pathological condition based on sufficient knowledge of treatment guidelines.

In this study, inpatient treatment is provided for all patients for follow-up observation. Although biphasic anaphylaxis generally occurs in 10% to 20% of patients in 8 to 12 hours after resolution of the initial symptoms, no biphasic anaphylaxis was observed in this study^{12,13)}. This is primarily attributable to the effects of inflammatory cells by leukocyte chemotactic factors. The clinical characteristics of biphasic anaphylaxis development have not been elucidated. Some reports have indicated that it was prevalent in patients who were orally administered a beta-blocker or an antigen or those with dyspnea or symptoms of shock. Another characteristic has also been suggested in a previous report in which increased incidence was observed in patients treated with insufficient epinephrine at initial treatment¹⁴⁾. Another report indicated that biphasic reactions were less likely to present with dyspnea¹⁵⁾.

Administration of corticosteroids as the initial treatment is not evidently linked to prevention of biphasic anaphylaxis¹³⁾. On the other hand, another study suggested that corticosteroids might be beneficial in preventing severity of biphasic anaphylaxis¹⁶⁾. Since administration of steroids is not effective for maintenance of respiratory and circulatory functions in the initial treatment, and it may trigger anaphylaxis, careful consideration is required for administration of corticosteroids¹⁷⁾. It remains unclear whether corticosteroids given for the initial treatment can prevent biphasic anaphylaxis. However, the absence of or a dose of corticosteroids that is too small given for the initial event may affect the incidence of biphasic anaphylaxis¹⁴⁾. Considering that the incidence of biphasic anaphylaxis was not observed in any patient in this study, it is highly likely that the initial treatment with corticosteroids prevented the incidence of biphasic anaphylaxis. In this study, hydrocortisone sodium succinate was administered intravenously in most patients at a dose of

about 500 mg just after diagnosis of anaphylaxis. It is suggested that early and appropriate doses of corticosteroids may play a role in prevention of biphasic anaphylaxis. However, it is difficult to estimate the effects of different kinds of corticosteroids because our study suffers from the limitations of data in a retrospective analysis. A prospective study, which would be able to estimate the benefit of corticosteroid with biphasic anaphylaxis, will be needed in the future.

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原著論文

救急搬送されたアナフィラキシー 26 症例の臨床的検討

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要旨 2003年9月より2005年8月までの2年間に東邦大学医療センター大森病院に2次救急搬送され、入院加療を行ったアナフィラキシー症例26例に臨床的検討を加えた。アナフィラキシーを引き起こしたと考えられる誘因物質は、食物12例、薬物11例、その他3例（ハチ、ラット、ハムスター）であった。食物では魚介類が7例、肉類1例、そば1例、かんきつ類1例、その他2例であった。このうち特異的 radioallergosorbent test (RAST) の陽性例は5例であった。薬物は全て内服薬であり、非ステロイド系消炎鎮痛剤が8例、抗生物質が3例であった。このうち drug lymphocyte stimulation 試験 (DSLIT) の陽性例は2例であった。症状は皮膚症状および呼吸器症状は全例に認められた。意識障害は7例、ショックは9例に認められ、そのうち5例が薬剤性、4例が食事性であり、特に有意差は認めなかった。アレルギー歴は26例中19例に認められ、一般に比べ有意に高率であるが、ショックを呈した症例のうち3例はアレルギー歴を認めない薬剤性であった。薬剤性アナフィラキシー様反応は過去にアレルギー歴がなく、突然のショック状態になることがあり、特に注意が必要であることが再認識される。治療はエピネフリン投与 ($0.5 \pm 0.4\text{mg}$) が13例、ステロイド投与は24例であった。予後は全例良好であり、遅発性反応は認められなかった。ステロイドの投与は第一選択薬ではないが遅発相予防としては有益と考えられる。(日救急医学会誌 2006; 17: 137-41)

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