Asthma is a common disease characterized by clinical airflow obstruction that can usually be reversed after a simple bronchodilator treatment. Many physicians, and even some patients, tend to view acute exacerbation of this disease as an annoyance that will pass, rather than a potentially life-threatening event. Nevertheless, several reports indicate that asthma mortality has increased during the last few decades, although the absolute number of deaths is still relatively small [1–4]. To prevent death from asthma, it is important to identify patients who are at risk of a fatal attack. The purpose of this study was to evaluate the clinical features of fatal asthma and to identify the possible warning signs associated with a fatal asthma attack.

**Key Words:** fatal asthma, near-fatal asthma, dead on arrival  

**PATIENTS AND METHODS**

This retrospective study included adult patients (age >15 years) who died of an acute asthma attack during a 15-year period from January 1989 to December 2003 at National Cheng Kung University Medical Center, a tertiary-care medical center in southern Taiwan. Data collected from medical records included asthma history, date of attack, and clinical characteristics such as age, gender, duration between onset of symptoms and fatal attack, patterns of decompensation, and history of previous admissions due to near-fatal attacks. Data on parameters associated with the fatal attack, including blood pressure, heart rate, respiratory rate, arterial blood gas analysis, and potassium level were also collected.

We defined patients as having asthma if they had had a previous diagnosis of asthma by a physician and presented with at least one of the following two conditions: (1) subjective evidence of variable wheezing and/or...
breathlessness and a response to asthma treatment; and (2) objective evidence of 20% reversibility in peak expiratory flow recording or forced expiratory volume in 1 second by spirometry (with 200 mL incremental improvement following bronchodilator administration). A near-fatal attack was defined as a severe attack with loss of consciousness or an attack requiring intubation and ventilator support.

Patients were divided into three groups according to their patterns of decompensation during the fatal attack, using Wasserfallen’s classification [5]. The first group included patients with an extremely rapid deterioration, leading to intubation and mechanical ventilation within 3 hours after the onset of the first symptoms. The second group included patients with gradual decompensation (crescendo phase), evolving over several days before institution of mechanical ventilation. The third group included patients with acute deterioration that occurred after a few days of unstable asthma. For comparison, the patterns of decompensation of patients with previous near-fatal attacks were also studied, noting the duration between the onset of symptoms and endotracheal intubation or disturbed consciousness.

RESULTS

Twelve patients had fatal asthma in our hospital from 1989 to 2003. The age range of the patients was 18–89 years (mean 52.1 years). Nine patients (9/12, 75%) were men and three (3/12, 25%) were women. The average duration between onset of symptoms and endotracheal intubation was 41 minutes (range, 20–60 min) for patients in group 1 (n = 4), 2 days (range, 1–3 days) in group 2 (n = 2), and 4.9 days (range, 1–20 days) in group 3 (n = 6). The proportion of young patients (< 35 years old) was higher among those in group 3 (3/6, 50%) than among those in group 2 (0/2) and group 1 (0/4).

Clinical features

All patients had a long history of asthma (mean 25 years, range 12–40 years). Patients in group 2 had the longest asthma history (median 29 years, range 17–40 years), followed by those in group 1 (median 25 years, range 20–30 years) and group 3 (median 24 years, range 12–40 years). The overall mean number of admissions to the hospital per subject during the past 12 months was 0.8. All patients in groups 1 and 2 had one or more near-fatal attacks before their fatal attacks. The mean number of near-fatal attacks was 1.5. Six patients had suffered a total of nine previous near-fatal attacks, and eight of these attacks were severe enough to require intubation, whereas one had the manifestation of disturbed consciousness. By contrast, only one near-fatal attack was noted among patients in group 3, and the mean number of previous near-fatal attacks was 0.17 (1/6).

Only six of these 12 patients (50%) had regular follow-up in our outpatient clinic. Seven patients (7/12, 58%) had previous near-fatal attacks before their fatal attacks. In most of them (5/7, 71%) the pattern of decompensation during the fatal attack was similar to that in a previous near-fatal attack (Table).

Fatal attack features

Eight of the fatal attacks (four patients in group 1 and four patients in group 3) occurred outside the hospital before arrival in the emergency room (ER). These patients’ deaths were considered due to asthma because of histories of comparable asthma attacks and respiratory failure noted in their medical records. Among the remaining four cases, the fatal attack occurred after the patient had arrived in the ER. Three patients developed respiratory arrest within 1 hour after arrival. Cardiovascular collapse developed soon after respiratory arrest, and these patients died despite rapid intubation and resuscitation. One patient died of asthma due to a severe attack of asthma during treatment for asthma in the hospital 3 days after admission. Three of these four deaths occurred before 1993.

Case presentations

All six patients who had regular follow-up in our outpatient clinic received treatment with inhaled steroids (equivalent to beclomethasone 400–1,200 μg/day), short-acting inhaled β₂-bronchodilators, and oral long-acting theophylline treatment. Two of them had moderate persistent asthma, and four had severe persistent asthma as defined by GINA (Global Initiative for Asthma) guideline criteria [6]. Two of the four patients with severe persistent asthma also received prednisolone 5–10 mg daily.

Brief histories are given here of four patients who came to the hospital and then died in the ER or ward.

Case 5

This 78-year-old man had had asthma for 40 years and had been regularly followed in our hospital for 3 years. He was treated with inhaled beclomethasone 1,200 μg/day, an oral long-acting β₂-agonist, theophylline, and prednisolone 10 mg daily. However, his asthma was poorly controlled,
and he had six ER admissions and six hospitalizations in the 3 years before his fatal attack. During his fatal attack he had gradual decompensation for 2 days, and was admitted to the general ward. On admission his consciousness was clear; blood pressure, 130/80 mmHg; heart rate, 96 beats/minute; and respiratory rate, 32 breaths/minute. Arterial blood gas values were: pH 7.356; PaCO$_2$ 60 mmHg; PaO$_2$ 46 mmHg; and HCO$_3^-$ 34 mEq/L (on nasal cannula oxygen 2 L/min). Nebulized bronchodilators, intravenous aminophylline, and intravenous methylprednisolone 40 mg were given every 6 hours, but his condition did not improve. He refused intensive care admission and intubation with ventilator support because of his having a prolonged illness. Severe dyspnea with respiratory arrest occurred in the general ward, followed by cardiovascular collapse on the second day of hospitalization. Resuscitation was not successful.

Case 6
A 45-year-old woman had received regular medical control for allergic asthma for 8 years at our hospital. Her latest medications were: budesonide 800 μg/day; inhaled salmeterol 50 mg twice daily; aminophylline 225 mg twice daily; and fenoterol two inhalations as needed. Her condition had been stable until she came to the ER this time because of progressive dyspnea for 1 day after an upper respiratory infection. On arrival her consciousness was clear; blood pressure, 161/102 mmHg; heart rate, 160 beats/minute; and respiratory rate, 40 breaths/minute. Arterial blood gas values were: pH 7.240; PaCO$_2$ 50.4 mmHg; PaO$_2$ 79 mmHg; and HCO$_3^-$ 21.8 mEq/L. Initial treatment included: oxygen; one inhalation each of nebulized terbutaline and ipratropium; intravenous hydrocortisone 200 mg; and aminophylline infusion. However, her condition did not improve, and respiratory arrest occurred 1 hour after arrival in the ER. She was intubated, but resuscitation was not successful.

Case 9
A 55-year-old man had irregular control of asthma. He had increased dyspnea and wheezing for 1 day, with acute deterioration about 1 hour before arrival in the ER. On arrival his consciousness was clear; blood pressure, 161/102 mmHg; heart rate, 160 beats/minute; and respiratory rate, 40 breaths/minute. Arterial blood gases were not measured because his condition was considered relatively stable. Initial treatment included: oxygen; one dose of nebulized budesonide 800 μg; and intravenous aminophylline and methylprednisolone.
terbutaline 0.5 mg; and methylprednisolone 40 mg intravenously. Fenoterol and beclomethasone metered-dose inhalations were used by the patient in the ER. Unfortunately, severe dyspnea and respiratory arrest developed suddenly within 1 hour after arrival in the ER, and resuscitation was unsuccessful.

Case 10
An 18-year-old man had no history of regular medical treatment for asthma. He had had an acute attack about 2 hours before arrival in the ER. On arrival in the ER his vital signs were: blood pressure, 120/70 mmHg; heart rate, 112 beats/minute; and respiratory rate, 38 breaths/minute. Initial treatment included: oxygen; subcutaneous epinephrine 0.3 mg; three doses nebulized terbutaline 0.5 mg at 20-minute intervals; and intravenous hydrocortisone 200 mg. After the treatment, arterial blood gases were pH 7.051 and PaCO₂ 84.9 mmHg. Intubation was performed about 1 hour after ER admission. Persistent cyanosis, bradycardia, and hypotension developed, and he died 2 hours later.

**DISCUSSION**

In most cases of severe life-threatening asthma, the attack develops against a background of poorly controlled disease. However, in 10–20% of cases of fatal or near-fatal asthma, the onset seems to be sudden and unexpected, with death sometimes occurring within a few hours. These episodes have been termed “sudden asphyxic asthma” [5]. The duration of these fatal attacks can be extremely short, and patients frequently die outside of the hospital—sometimes before they can call for medical help [5,7-9].

In this study of 12 patients with fatal asthma, four patients suffered from sudden asphyxic attacks (group 1). They presented with rapid progressive deterioration, leading to acute respiratory failure within 3 hours of the onset of symptoms. The average duration of the fatal attack was 41 minutes, and ranged from 20 minutes to 1 hour. All four patients died outside of the hospital. It is difficult to prevent death from sudden asphyxic asthma, either because the fatal attacks are so sudden and progress so rapidly that appropriate medical help cannot be summoned in time, or because there is an unavoidable delay in the arrival of help [1]. Educating patients, who are at risk of fatal attacks, and their families in the use of subcutaneous epinephrine may be the only method to prevent fatalities from these attacks [10].

Two reports show that more airway remodeling, more bronchoconstriction, and more mucus plugs in submucosal glands are found in patients with fatal asthma than in those with nonfatal asthma [11,12]. More bronchoconstriction is noted in short-course (< 3 hours) fatal asthma, whereas more mucus accumulation is found in long-course (> 8 hours) fatal asthma [11]. Retrospective analyses have also highlighted several clinical characteristics of patients who died of asthma [13-18]. Crane et al reported that a history of admission for asthma in the preceding 12 months was the strongest single indicator of risk for subsequent death from asthma [14], whereas Rea et al reported that a history of a near-fatal attack that required hospitalization and mechanical ventilation was the strongest single predictor of subsequent fatal attack [16]. All four patients who died from sudden asphyxic asthma had these two important clinical characteristics. Most of them had a history of admission for asthma in the preceding 12 months, and all of them had a history of a near-fatal attack. We also found that the patterns of decompensation in previous near-fatal attacks and fatal attacks were similar in these patients.

A previous study suggested that reduced chemosensitivity to hypoxia and blunted perception of dyspnea may predispose patients to fatal asthmatic attacks [19]. This may explain why these patients experienced a relatively mild or asymptomatic state of asthma until minutes or a few hours before their death. Measurements of airway narrowing, such as peak-flow monitoring, are required to assess a patient’s actual condition. Thus, identification of high-risk patients who have a history of a near-fatal attack of sudden asphyxic asthma and early detection of an unstable condition by peak-flow meter are essential.

Inadequate assessment, observation, and treatment have also been reported as contributors to fatal asthma attacks [1,17,18]. Two patients in our study suffered from progressive deterioration over several days (group 2). One of these patients developed respiratory arrest about 1 hour after her arrival in the ER, whereas the other developed respiratory arrest in the general ward 3 days after admission. Both patients died soon after the onset of respiratory arrest, despite intubation and resuscitation. Inadequate close observation and delayed intubation were considered to contribute to the death of these two patients.

A history of recent admission for asthma and near-fatal attack seems to be an important risk factor for fatal asthma attack [18]. Among the six patients with acute deterioration after unstable asthma (group 3), 50% (3/6) were younger than 35 years of age, and 5 had had no previous near-fatal attack.
attacks. Among these six patients, the mean duration of symptoms was 4.9 days. Four of these patients died outside the hospital, and two died within 1 hour after arrival in the ER. One of these two patients had not received adequate treatment, because the severity of the asthma was underestimated. The other patient had disturbed consciousness on arrival, and sudden respiratory and cardiopulmonary arrest developed soon thereafter. To prevent death in patients such as these, adequate assessment and treatment, careful monitoring of the response to medical treatment, and early intubation with ventilator support are essential soon after admission to the ER. It should be mentioned that three of the four patient deaths in the ER occurred before 1993, when GINA and Heart Lung and Blood Institutes asthma management guidelines were not yet available.

In conclusion, nearly all patients with fatal asthma in this study died outside of the hospital or within 1 hour after admission to the ER. A history of a near-fatal attack should be considered a warning sign that a similar life-threatening attack may recur. Some fatal attacks occurred without a previous episode of severe attack, and these fatal attacks were more frequent in younger patients. Better patient education for management of acute attacks, especially for high-risk patients, and better physician training in the management and close observation of these patients in the ER, especially during the first hour, may prevent or reduce fatal asthmatic attacks.

REFERENCES

氣喘死亡病例之臨床表現

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為了要了解致死性氣喘發作之情形，我們回溯分析從 1989 至 2003 年共 15 年間在本院因氣喘發作致死之病例。在此期間一共有 12 位主因為急性氣喘致死之病例，包括 8 位到院前死亡及 3 位患者在至急診處後一小時內死亡。此些 12 位患者根據此次致死性發作之臨床情形可區分為下列三種類型包括：第一型：3 小時內急性惡化至死亡有 4 個病例；第二型：2) 在幾天內逐步惡化至死亡有 2 個病例；第三型：3) 在幾天之不穩定期後突然急性惡化有六位病例。所有第一型及第二型之患者皆有前病史有六位病例，而六位第三型之患者僅有一位有以前瀕臨死亡發作之病史。在所有七位曾有以前瀕臨死亡發作病史之患者，五位之此次致死性氣喘發作之類型和以前之發作類型是一樣的。分析時也同時發現第三型之患者較年輕，一半 (3/6) 之患者年齡在 35 歲以下。我們總結發現幾乎所有之致死性氣喘皆是到院前死亡或至急診處一小時內死亡，且患者之急性氣喘發作致死之臨床表現和以前曾有之瀕臨死亡氣喘發作之模式非常相似。我們認為加強氣喘患者之衛教讓其了解急性發作之危險及儘早至急診處就醫，及急診處醫師足夠之治療與嚴謹監視病情之變化將可減少氣喘之致死性發作。

關鍵詞：致死性氣喘，瀕臨死亡氣喘，到院死亡

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