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Epidemiological description and analysis of Enterovirus-related Admissions in One Taipei Municipal Hospital

Abstract

In this study, the medical histories of inpatients of one Taipei municipal hospital with illness caused by enterovirus between 1998 and 2000 were analyzed. In addition, criteria of hospital pediatricians for admission of patients with uncomplicated enterovirus infections were surveyed and analyzed with a semi-structured questionnaire. The case number was 442. The results showed that there was no gender difference between enterovirus-infected patients in the three years. More than ninety percent of patients were less than five years old, and the average age was two years old. Forty-four percent of patients were admitted through the emergency department, and the admission duration was about five days. As to the route of admission, in 1998 when there was an epidemic of enteroviral infection in Taiwan, the percentage of patients admitted through the emergency department and the duration of their hospitalization were significantly higher than that in 1999 and 2000 ($p < 0.01$ respectively). Comparing the diagnoses of each year, the percentage of patients with hand-foot-mouth disease

was highest in 1998, and lowest in 1999. The main symptoms of the patients were anorexia, fever, and blisters or ulcers on the oral mucosa. The percentage of patients with herpangina was highest in 1999, and lowest in 2000. The major symptoms in order of frequency of presentation were fever, oral blisters or ulcers, and anorexia.

In addition, between 1999 and 2000 there was a difference in trend between case numbers from the sentinel surveillance reports and the numbers of admission through the outpatient and emergency departments ($p < 0.05$). After admissions through the emergency department were excluded, there was still a difference in trend between case numbers from sentinel surveillance reports and numbers of admitted patients ($p < 0.05$). The case numbers from sentinel surveillance reports and number of admissions were more in 2000 than in 1999. In 2000, 36.0% of patients were admitted through the emergency department, especially in the 17th to the 33rd weeks and the 38th to the 41st weeks. Factors including: admissions through the emergency department not being included in numbers of enterovirus-related outpatient department patients on sentinel surveillance reports, reports not conforming to the admission case definition, errors in sentinel surveillance weekly reports, and changes in admission criteria by doctors are possible causes of the difference in trend between the numbers of sentinel surveillance reports and those of admissions in 2000. Criteria determining a doctor's consideration for patient admission in order of descending importance were: 1. inability to swallow and profound lethargy, 2. persistent fever, 3. rapid disease progression or symptoms that were not compatible to epidemic type and to which special attention was required, 4. high fever, 5. parental request, 6. no improvement after seeking treatment at more than two hospitals, and 7. the availability of hospital beds.

Introduction

In 1998, an enterovirus epidemic in Taiwan caused social panic and alarm. Public health bureaus therefore declared an emergency status, and established teams for emergency management. Hospitals and related research institutes also took preventive measures to stop the epidemic from spreading. These measures were quite effective, and the most important among them was the enterovirus-related case monitoring system, which included three report systems. They were: (1) sentinel surveillance report system: gathering and reporting to the CDC weekly the number of patients seeking medical attention due to hand-foot-mouth disease or herpangina; (2) severe complicated enterovirus infection case report system: cases of severe complicated enterovirus infection who had symptoms including typical hand-foot-mouth disease or herpangina or other symptoms compatible with the epidemic type and complicated by encephalitis, paralysis of extremities, myocarditis, disseminated infantile infection or other symptoms requiring intensive medical care were reported; disseminated infantile infection occurred in infants less than six months of age; its symptoms included acute hepatitis, myocarditis, death due to cardiorespiratory failure or multiple organ failure; hospitals had to report immediately to public health bureaus if cases of severe complicated enterovirus infection were detected; Public health bureaus continued to follow up, monitor, and identify the cases thereafter; (3) enterovirus-related admission report system: new cases admitted due to hand-foot-mouth disease or herpangina were reported to public health bureaus by the infection control divisions of various hospitals. Since weekly case numbers of the sentinel surveillance system and those of the admission report system showed a difference in trend, it was necessary to investigate the causes of this phenomenon. In this study, enterovirus-related admissions and OPD patients of a

Taipei municipal hospital were investigated in order to show the possible causes of difference in trend and to demonstrate a profile of enterovirus-related admissions.

Materials and Methods

Admission Data Collection

A questionnaire for patients with enterovirus-related admissions was first designed. Then data including age, gender, address, route and date of admission, date of discharge, primary diagnosis, secondary diagnosis, and clinical symptoms of patients with enterovirus-related admissions between June 1998 and December 2000 was collected for the infection control division of a Taipei municipal hospital. Moreover, criteria of hospital pediatricians for the admission of uncomplicated enterovirus-infected patients were also investigated with another semi-structured questionnaire.

Collecting case numbers of enterovirus-related OPD patients

Weekly case numbers of OPD patients with enterovirus-related illness, hand-foot-mouth disease, and herpangina were supplied by the sentinel surveillance system of the Disease Monitor Group of the CDC.

Data Analysis

Data gathered from questionnaires was processed using Epi-Info software, debugged, and their accuracy was confirmed. Statistical analyses including Chi-Square test, Wilcoxon Rank Sum test, and Chi-Square for trend were then performed.

Results

A total of 442 admissions between June 1998 and December 2000 in a municipal hospital were collected (Table 1). There were 224 male and 218 female patients. Their routes of admission included 247 (56.0%) cases through the OPD, and 195 (44.0%) through the emergency department. The duration of hospital admission ranged from one day to 41 days, and the median stay was five days. The age of patients ranged from one week to 36 years old, and the peak ages were two years of age (35.7%) and followed by one year of age (20.6%). The principal diagnoses included 336 cases of herpangina (76.0%), 78 cases of hand-foot-mouth disease (17.6%), 6 cases of aseptic meningitis (1.3%), 2 cases of hand-foot-mouth disease complicated by aseptic meningitis (0.5%), and 2 cases of herpangina complicated by aseptic meningitis(0.5%). There were 18 (4.1%) cases with diagnoses not compatible with the reporting case definition. The distribution of six cases of aseptic meningitis cases was 1 in 1999 and 5 in 2000. The two cases of hand-foot-mouth disease complicated by aseptic meningitis were both admitted in 2000. The distribution of two cases of herpangina complicated by aseptic meningitis was one in 1998 and one in 2000.

Next, the profiles of admitted enterovirus-related cases between June and December of each year were compared (Table 2). In 1998 when there was an enterovirus epidemic, the admission rate of enterovirus-related cases was higher than that in 1999 and 2000. There was no statistical significance between gender, median of age and numbers of admission ($p > 0.05$, respectively). As to routes of admission, in 1998 the percentage of admissions through the emergency department and the days of hospitalization were significantly higher than those in 1999 and 2000 ($p < 0.01$). The percentage of hand-foot-mouth disease was 25.0% in 1998, 4.3% in 1999 and 22.8% in 2000. The percentages in 1998 and 2000

were significantly higher than that in 1999 ($p < 0.001$, respectively), and there was no significant difference between the percentage in 1998 and that in 2000 ($p > 0.05$). The percentage of herpangina was 69.5% in 1998, 91.5% in 1999, and 53.5% in 2000. The percentage in 1999 was significantly higher than that in 1998 and 2000 ($p < 0.05$, respectively).

Table 3 shows the profiles of admitted hand-foot-mouth disease patients between June and December in the years 1998 to 2000. There were no significant differences between gender, median of age, and route of admission among hand-foot-mouth disease patients in those three years ($p > 0.05$). The median duration of admission was significantly higher in 1998 than in 1999 and 2000 ($p < 0.05$). The major symptoms in 1998 were anorexia (90.6%), fever (78.1%), and oral ulcers or blisters (78.1%), in 1999 oral ulcers or blisters (100.0%), fever, skin rash and blisters (75.0%, respectively), and in 2000 oral ulcers or blisters (92.3%), anorexia (84.6%) and fever (80.8%).

The profiles of herpangina patients between June and December of each year are shown in Table 4. In those three years, there was no difference in gender ratio, or median age of patient. ($p> 0.05$). As to routes of admission, the number of patients admitted through the emergency department was significantly higher in 1998 than in 1999 and 2000 ($p < 0.01$). In addition, in 1998 the major symptoms were fever (93.3%), oral blisters or ulcers (91.0%), and anorexia (80.9%). In 1999, the major symptoms were fever (97.7%), oral blisters or ulcers (80.2%), and anorexia (61.6%). In 2000, the major symptoms were fever (97.4%), oral blisters or ulcers (85.7%), and anorexia (79.2%). The major symptoms and their rate of occurrence were the same in those three years.

The trend of sentinel surveillance reports of a municipal hospital between 1999 and 2000, and the number of admissions, including admission through the

emergency department, are shown in Fig. 1. These two lines showed differences in trend, and they intersected at points. The trend of sentinel surveillance reports and the number of admissions, including admission through the emergency department, between 1999 and 2000, showed significant differences in trend ($p < 0.05$). Even when patients admitted through the emergency department was excluded, the line representing sentinel surveillance reports and that representing the number of admitted patients still intersected (Fig 2). There was significant discrepancy between the two lines between the 17th and 33rd weeks, and 38th and 41st weeks in 2000. The trend of sentinel surveillance reports of a municipal hospital between 1999 and 2000, and the number of admissions, excluding admissions through the emergency department, still were different significantly ($p < 0.05$).

Seven attending pediatricians were asked to fill in questionnaires. Their major criteria for the decision to admit enterovirus-infected patients were shown in Table 5. In order of importance, criteria used by doctors when considering admission were: 1. inability to swallow and lethargy; 2. persistent fever; 3. rapid disease progression or symptoms that were not compatible with epidemic types and to which special attention was required; 4. high fever; 5. parental request; 6. no improvement after treatment by more than two hospitals; and 7. the availability of hospital beds. When the standards of admission before and after 2000 were compared, 71.0% of doctors did not change their criteria for admission even after the initiation of the enterovirus-related admission weekly report system in June 1998; 14.0% of doctors were more aware of enterovirus-related symptoms after 2000.

Discussion

The various types of enterovirus are most prevalent in the temperate zone, and cause different clinical symptoms. In the US, there are thirty million people infected with enterovirus each year, and ten to fifteen million people have clinical symptoms [4-5]. The typical symptoms of enterovirus infection include blisters and ulcers on the oral mucosa, palms, and soles. In the initial stage of the disease, there are symptoms including fever, malaise, vomiting or abdominal discomfort. The most common disease manisfestations include herpangina, hand-foot-mouth disease, aseptic meningitis, encephalitis, intercostal myalgia, acute infantile myocarditis, adult pericarditis, acute lymph node pharyngitis, and fever complicated by rash. Enterovirus infection is commonly transmitted through the gastrointestinal or respiratory tract. The incubation period is two days to two weeks, and the average is three to five days. The disease course may last from seven to ten days. Most patients are under ten years old, and adults are sporadically affected. Most patients infected with enterovirus have mild symptoms or may even be asymptomatic. Only a few will have severe complications. Infants and children are five to eight times more susceptible to viral encephalitis [4、5、7]. The enterovirus epidemic in Taiwan in 1998 was mainly caused by enterovirus 71. This type of enterovirus primarily infects the central nervous system, causing neurological symptoms and complications in patients, and results in a high mortality rate [1、2、6、7]. In Taiwan, peaks of enterovirus infection occur from March to July and September to November, and during these periods public health bureaus will intensify their disease monitoring. The case numbers of patients with suspected enterovirus infection causing hand-foot-mouth disease and herpangina in regional and larger hospitals after the initiation of the enterovirus-related admission report system was 5,577 from June

to December in 1998. 405 of these patients suffered from severe infection with complications and 78 died of the disease [2,3]. In 1999, the number of admissions was 6,364, 34 of whom suffered from complications and severe infection and nine died [3]. In this study, there were 128 cases admitted during June and December in 1998 to a municipal hospital, more than 94 in 1999 and 114 in 2000 (Table 2).

There was no gender difference among enterovirus-related admissions between 1998 and 2000 to the municipal hospital, and more than 90% of patients were younger than five years old. Their duration of admission was about five days. Those who were admitted though the OPD were 1.3 times more in number than those who were admitted though the emergency department. When the proportion of hand-foot-mouth disease patients during June and December in those three years was compared, a peak was in 1998 and then in 2000. The proportion of patients with herpangina peaked in 1999. There were six patients having aseptic meningitis in those three years, one in 1999 and five in 2000; their ages were between one and ten years old with average age of five years old. Their duration of admission was four to twenty-six days with an average hospital stay of seven days. 66.7% of patients were admitted through the emergency department. The number of patients with herpangina complicated by aseptic meningitis was one in 1998 and one in 2000. The two patients with hand-foot-mouth disease complicated by aseptic meningitis were both admitted in 2000. Therefore, hand-foot-mouth disease or herpangina was more likely complicated by aseptic meningitis in 2000.

When the data of sentinel surveillance reports and number of admissions to the hospital were compared, the possible causes of the different in trend may include: admissions through the emergency department not being included in numbers of enterovirus-related outpatient department patients in sentinel

surveillance reports, reports not conforming to admission case definition, errors in sentinel surveillance weekly reports, and changes in admission criteria by doctors. In the hospital, there was no significant change in the number of admissions between June and December in 1998 to 2000 ($p > 0.05$). Moreover, in that period, the rates of reports not conforming to the admission case definition were 4.7%, 3.2%, and 4.4% without any significant change. Nevertheless, when weekly numbers of these two data in 1999 were compared, their trends differed significantly ($p < 0.05$, Fig. 1). The differences in trend occurred in the 17^{th} to 19^{th} weeks, 21^{st} to 23^{rd} weeks, and 26^{th} to 33^{rd} weeks. In 2000, 34.4% of cases were admitted through the emergency department; among them 26.8% (15/56) had hand-foot-mouth disease and 1.8% (1/56) had hand-foot-mouth disease complicated by aseptic meningitis. After admission through the emergency department was excluded, there was still a significant difference in trend between surveillance weekly reports and number of admissions ($p < 0.05$, Fig. 2).

Since the data of all of the OPD patients and admission cases could be collected and compared in this hospital, its surveillance weekly reports should approximately reflect the numbers of enterovirus-infected patients in the OPD, though some errors might have occurred (Fig. 1, 2). Their admission cases were from the OPD and the emergency department. If the same proportion of OPD patients were admitted every week, then the trend between surveillance weekly reports and the number of admissions through OPD should be parallel. Nevertheless, as shown in Fig. 2, these two data were not parallel in trend, even after the number of admissions through the emergency department was included. These two lines, however, approximate at several weeks (Fig. 1). In Fig. 1 and Fig. 2, the number of admissions and surveillance weekly reports of enterovirus-infected patients in 2000 in the hospital were significantly higher than

those in 1999. In 2000, a significant proportion of patients were admitted through the emergency department (36.0%, Table 2), especially in the 17th to 33rd weeks, and the 38th to 41st weeks. In the hospital, patients admitted through the emergency department were not recorded at the OPD, and their reasons for admission through the emergency department, including rapid progression of disease, and severe clinical symptoms, therefore could not be traced. Since hospital patients came mainly from the nearby community, it is speculated that admissions through the emergency department were primarily due to rapid progression of disease or severe symptoms. Patients admitted through the emergency department were not included in the surveillance weekly reports, and this may be why there was a difference in trend between the surveillance weekly reports and the number of admissions. There may be other reasons for this difference in trend, and further investigation is required.

Next, data of enterovirus-related admissions through the emergency department was analyzed. During the 17th and 21st weeks of 2000, the average duration of hospital stay was six days, more than the average number of days of hospital stay in that year. During that period, 52.9% of cases were admitted through the emergency department (among them 33.3% had hand-foot-mouth disease and 22.2%) had aseptic meningitis.), higher than the 34.4% of cases in that year. There were no cases not conforming to the definition for report, and the percentage of non-conforming cases in that year was 4.3%. Hence, it is suspected that enterovirus-infected patients had more severe symptoms during that period. There was no significant difference in the duration of hospital stay during 24th and 26th weeks and that of the rest of the year. 38.1% of cases were admitted through the emergency department; among them 25.0% had hand-foot-mouth disease, and 75.0% had herpangina. The percentage of cases not conforming to case definition

was 9.5% during that period, and this may be the cause of the difference in trend. It is certain that during an epidemic of enterovirus infection associated with severe complications, such as caused by enterovirus 71, the percentage of admissions will be higher. Hence the difference in trend of reports was predictable and acceptable.

Compared with the criteria for admission before 2000, more than two out of three doctors did not change their criteria for admitting enterovirus-infected patients. In the enterovirus-related admission report system, the report records were sent to the public heath bureaus by Monday 10 AM by infection control nurses after gathering nursing records of enterovirus-related admissions on pediatrics wards. Since doctors did not verify the reports, there may have been cases not conforming to the definition.

In summary, the admission report system was of significant importance in analyzing the trend of enterovirus infection, especially since the data of severely infected and emergency patients could be acquired through this system. Moreover, since there were still cases not conforming to the report case definition, education of infection control personnel and doctors will be mandatory.

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