Taiwan has been experiencing a resurgence of measles since the beginning of 2009. We retrospectively reviewed the clinical presentations of eight confirmed measles cases during a nosocomial outbreak, in order to identify diagnostic clues. The exanthem was polymorphous and non-specific in terms of its morphology, distribution, sequence of appearance, and symptoms. The presence of cough and coryza as well as abnormal results of routine laboratory studies were also non-specific and unhelpful for the differential diagnosis of measles from other infectious diseases, adverse drug reactions, or autoimmune diseases. In our experience, the combination of exudative conjunctivitis with febrile exanthem is the most distinguishing feature of measles. Serologic studies can confirm the diagnosis within a few hours. Further measles outbreaks are possible in the near future as a result of increased international travel, immigration of foreign workers, and overseas marriages. Dermatologists must be proficient in the diagnosis of measles in order to prevent the potential morbidity and mortality associated with future outbreaks.

Introduction

The incidence of measles in Taiwan decreased dramatically after the introduction of routine immunization in 1978. With an average incidence rate of 0.04 confirmed cases per 100,000 inhabitants during the period of 1990–2008, measles had been regarded as “almost eradicated” in Taiwan. Most young physicians are therefore unfamiliar with this disease. However, the southern and northern parts of Taiwan have been experiencing a resurgence of measles since the beginning of 2009. It is important to diagnose and isolate measles patients as early as possible, to prevent the potential morbidity and mortality associated with an outbreak. We present eight confirmed measles cases from one referral center, with the aim of identifying clinical clues that might lead to its diagnosis.

Methods

Case definition

Eight patients with a diagnosis of confirmed measles in February 2009 were included. A confirmed case of measles was defined either as a laboratory-confirmed case (presence of immunoglobulin M (IgM) antibodies against measles virus or a positive polymerase chain reaction), or as a case that met the clinical definition (generalized rash for more than 3 days and a temperature above 38.0°C with one or more of the following symptoms, cough, coryza, Koplik’s spots and
Nosocomial measles outbreak in Taiwan

conjunctivitis), which was epidemiologically linked to a laboratory-confirmed case. We retrospectively reviewed the medical charts, laboratory data and photographs of skin rashes from these eight patients. Their parents were interviewed by telephone if key clinical data were unavailable from the charts.

Results

The index case (patient 1) in this nosocomial outbreak was a boy aged 5 years and 5 months old who had received only one measles vaccination at 9 months old. Ten days before the onset of symptoms, he had been admitted to a hospital in southern Taiwan where he might have come into contact with an imported measles case from China. A history of exposure to patient 1 can be traced for all the other seven children, either in the emergency department or during admission to the same ward.

Clinical presentations

Patient demographics and clinical presentations are summarized in Table 1. There were six boys and two girls. Their

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (mo) and sex</th>
<th>Cough/coryza/conjunctivitis</th>
<th>Exanthem (Koplik spots/mucositis)</th>
<th>Rash-developing sequence</th>
<th>Pruritus</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65 M</td>
<td>++/++</td>
<td>++/++</td>
<td>Trunk, limbs to face</td>
<td>+</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>2</td>
<td>18 M</td>
<td>++/++</td>
<td>--/--</td>
<td>Face to trunk, limbs</td>
<td>--</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>3</td>
<td>10 M</td>
<td>++/++</td>
<td>--/--</td>
<td>Face to trunk to limbs</td>
<td>+</td>
<td>Croup, diarrhea, hepatitis</td>
</tr>
<tr>
<td>4</td>
<td>9 M</td>
<td>++/++</td>
<td>+/−</td>
<td>Trunk to face to limbs</td>
<td>+</td>
<td>Croup, diarrhea</td>
</tr>
<tr>
<td>5</td>
<td>11 M</td>
<td>++/++</td>
<td>+/−</td>
<td>Face to trunk, limbs</td>
<td>+</td>
<td>AOM, pneumonia</td>
</tr>
<tr>
<td>6</td>
<td>29 F</td>
<td>++/−</td>
<td>+/−</td>
<td>Face to limbs to trunk</td>
<td>−</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>7</td>
<td>10 M</td>
<td>++/++</td>
<td>+/−</td>
<td>Limbs to face to trunk</td>
<td>−</td>
<td>Bronchiolitis, croup</td>
</tr>
<tr>
<td>8</td>
<td>25 F</td>
<td>++/++</td>
<td>++/−</td>
<td>Face to trunk to limbs</td>
<td>+</td>
<td>Croup, hepatitis</td>
</tr>
</tbody>
</table>

AOM = acute otitis media.

Figure 1 Exanthem of measles. (A) Conjunctivitis. Note the crusting on eyelash. (B) Tongue mucositis may be mistaken for thrush. (C,D) Koplik’s spots.
ages ranged from 9 months to 5 years and 5 months old; four were 11 months old or younger. None of the children had received measles vaccinations except for the index case.

Fever lasting for 2–12 days was the presenting symptom in all eight patients. The classic “3Cs”, cough, coryza and conjunctivitis developed in eight, seven, and eight patients, respectively, either at the same time as fever onset, or several days after. Koplik’s spots were observed in six patients (75%) (Figure 1). After a prodrome of 0–6 days (mean 2.9 days), all patients developed a generalized exanthem involving the face (Figure 2), trunk, and extremities (Figure 3). The early exanthem consisted of non-scaly, blanchable, erythematous macules and papules. The lesions were either sparse or rapidly coalesced into wheal-like plaques covering most of the body. The characteristic cephalocaudal spreading of the rash occurred in half of the patients, while the rash first appeared on the trunk or extremities in three of the other patients. Pruritus was observed in five patients (62.5%). The exanthem began to fade, usually after defervescence, after 3–6 days, leaving brown pigmentation and desquamation (Figure 4).

Atypical lymphocytes or immature blood cells were present in six patients (75%). Five patients (62.5%) had elevated transaminase levels, mostly within three times the upper limit of normal values. IgM antibodies against measles were detected in the blood of all patients, while all patients were negative for IgG measles antibodies. Measles virus was isolated from the urine and throat swabs in four out of six and four out of seven of the patients tested, respectively.

All of the patients had at least one complication after measles, including hepatitis (5 patients, 62.5%), croup (4 patients, 50%), diarrhea (2 patients, 25%), pneumonia (1 patient, 12.5%), bronchiolitis (1 patient, 12.5%), and acute otitis media (1 patient, 12.5%). There was no mortality and no cases of encephalitis.

Discussion

The World Health Organization/United Nations International Children’s Fund comprehensive strategy for reducing measles mortality reduced global mortality from measles by 74% between 2000 and 2007. However, there were still 197 000 estimated measles deaths worldwide in 2007, with southeast Asia accounting for 70% of the mortality. Measles is highly contagious through contact with infectious droplets, and delayed diagnosis may therefore result in rapid spreading among susceptible individuals. Dermatologists play an important role in the evaluation of febrile exanthem during routine practice, and must be proficient in the diagnosis of measles.

The cutaneous presentations in our patients were non-specific in terms of their morphology, distribution, sequence of appearance, and symptoms. Similar rashes can
Figure 3  Trunk and limbs exanthem. (A) The rash may be urticaria-like, profuse and confluent. (B) The rash may be non-specific maculopapules. (C) The rash may be sparse. (D) Reticulated erythematous maculopapules on limbs.

Figure 4  Resolution of the exanthem. (A,B) Resolving exanthem and desquamation on the face. (C) Post-inflammatory hyperpigmentation and fine desquamation on the back.
be associated with many other infections, cutaneous adverse drug reactions, and autoimmune diseases. Contrary to the “non-pruritic” rash described in the textbooks, pruritus was observed in over half of our patients. The notable cephalo-caudal spread of the rash from forehead and behind the ears, down the neck and trunk, and finally to the extremities, was recorded in only half of our patients.

Koplik’s spots are 1–2-mm white papules on the buccal mucosa near the second molars. Although a search for this pathognomonic sign can be worthwhile, it can easily be overlooked during physical examination of agitated, ill children. Cough and coryza are present in most viral syndromes and their presence is of limited use in differential diagnosis. Routine laboratory studies frequently reveal abnormalities in blood cell counts and transaminases, which are also non-specific.

In our experience, the combination of exudative conjunctivitis with febrile exanthem is the most distinguishable feature of measles. Conjunctivitis usually developed several days after the onset of fever and before the exanthem had peaked. Patients presented with photophobia, violaceous erythema and swelling of the eyelids, and injected bulbar as well as palpebral conjunctivae. Increased ocular discharge and crusting on the eyelids are valuable for the differentiation of Kawasaki disease, in which the conjunctivitis is non-exudative.

When the clinical presentation is suspicious for measles, serologic studies and virus isolation from the blood, nasopharyngeal swabs and urine should be performed immediately. IgM antibodies against measles virus increase with the onset of the rash and last for about 1 month. This is the most useful diagnostic tool, and the result can be obtained within a few hours. After establishing the diagnosis, the patient should be admitted to a high-efficiency particulate air isolation ward, or be advised to stay at home to avoid secondary spread of the virus. Exposed susceptible individuals should receive immunoglobulin prophylaxis within 6 days of exposure, and should be given measles vaccine 5 months later to confer long-term immunity. The majority of patients require only supportive treatment. Younger children and adults have higher complication rates and should therefore be monitored carefully.

Until 2006, the measles vaccination schedule in Taiwan consisted of a single dose of measles vaccine at the age of 9 months, and two doses of measles-mumps-rubella vaccine at 15 months and 5–6 years old, respectively. The overall vaccine coverage exceeded 95%, and the measles incidence rate in Taiwan remained low (0–0.14 per 100 000) during the past decade. The first dose of measles vaccine scheduled at 9 months of age was cancelled in 2006. The long-term effect of this change remains to be determined, although it could lead to an accumulation of susceptible individuals, especially among children younger than 15 months old. Increased international travel, immigration of foreign workers, and overseas marriages increase the risk of a measles resurgence in Taiwan. Dermatologists bear the responsibility of identifying measles patients to prevent the potential morbidity and mortality associated with possible outbreaks in the near future.

References