Occurrence and management of leprosy reaction in China in 2005

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Summary

Background Leprosy reactions are a major cause of disability before, during and after anti-bacterial treatment. Prompt diagnosis and correct management of reaction is a crucial matter for improving the quality of leprosy health services.

Objectives To describe the pattern of leprosy reaction and its management in China during 2005.

Methods A retrospective survey using a questionnaire was carried out in all the provinces of China at the beginning of 2006. Patients included were those presenting with leprosy reaction between 1 January and 31 December 2005.

Results 452 questionnaires from 25 provinces were analysed. There were 313 male and 139 female patients who had 159 Type I reactions, 273 Type II reactions and 20 Type I and II mixed reaction. 72.4% of reactions occurred in the first year of MDT and 27.6% of patients during the second year of MDT. The highest frequency of reaction was during the first 6 months of MDT; 57.3% of patients developed new nerve impairment during and after MDT.

Conclusions New nerve function impairment and disability still occurs among patients during and after MDT. The early detection and management of leprosy reaction remains important.

Introduction

Leprosy reaction is a major cause of disability in patients with leprosy in China. It can occur before, during and after the multidrug therapy (MDT) and can be difficult to manage patients with severe reaction, especially in field conditions. It has been reported that nerve function impairment (NFI) and reaction after registration are common. A study in India showed that 39.8% of patients had reactions during and after MDT, and 23.3% of patients with Type I
reaction and 28% of patients with Type 2 reaction developed deformity. In China in 2005, 89.1% of all newly detected patients had multibacillary leprosy (MB) and the proportion of Grade 2 disability among newly detected patients was 21.3%. Leprosy patients in China have a higher risk of developing new nerve function impairment and reaction. Currently the leprosy control programme is only partly integrated with the general health services in case finding; all patients with leprosy reactions are diagnosed and treated by doctors with a special training in leprosy at or above county level. Medical records are maintained at county level. We conducted a retrospective survey of all reported leprosy reactions in China during 2005 to describe the pattern of leprosy reactions, its management and problems in management in the country.

**Patients and Methods**

Patients developing any type of reaction between 1 January and 31 December 2005 were included in the study. According to the national policy, multibacillary (MB) leprosy patients are treated with the WHO/MB drug regimen for 24 months and paucibacillary leprosy patients (PB) are treated with WHO/PB drug regimen for 6 months. A detailed questionnaire was developed to collect relevant data for the study which included: the patient’s demographic details, clinical type of leprosy, initial bacteriological index, the date beginning MDT, regimen, time of stopping MDT, type of leprosy reaction, time of developing reaction, episodes of reaction within one year, duration of the reaction(s), method of detecting reaction, time from onset of reaction to treatment, nerve signs and symptoms including nerve tenderness, pain, thickness, new disability, change of previous status of disability and sensory loss on the skin during MDT and following up, frequencies of consultation during reaction.

The questionnaires were sent to each province with a formal government document to request each provincial manager to carry out this survey based on the original patient medical history record kept at the county units responsible for leprosy control. The questionnaires were filled in for all patients who developed leprosy reaction in 2005 by doctors at or above the county level and were submitted to provincial unit responsible for leprosy control.

**Definition of Leprosy Reaction**

Type I reaction was diagnosed if existing skin lesions became inflamed or if the patients developed nerve tenderness or new nerve function impairment (sensory or motor). Type II reaction was diagnosed if the patient developed crops of erythematous tender nodules (erythema nodosum leprosum, ENL) with the presence of any of the following: malaise, fever, peripheral nerve damage, lymphadenitis, iridocyclitis, orchitis and arthralgia. Mixed leprosy reaction was diagnosed if patients had typical ENL and at the same time had severe peripheral nerve pain which could not be relieved by a routine dose of prednisone. If patients had nerve tenderness, nerve pain, nerve thickness, they were diagnosed as neuritis during reaction. Type 1 reaction, including neuritis, was treated mainly with a standard 12 week course of steroids as recommended by WHO with a starting dose of 40 mg/day. Type 2 reaction was mainly treated with the same dose of 40 mg/day of prednisone in a reducing regime. thalidomide at a starting dosage of 300 mg/day was used only in a small number of patients with Type II reaction who had no contraindications to the drug. Since thalidomide is costly, this was used in a few economically well-developed provinces in the east of China.
Availability of loose clofazamine tablets is limited in China and therefore patients with Type 2 reactions were rarely treated with clofazamine. During the survey, we emphasised the need to distinguish leprosy reactions from leprosy relapse by supportive information such as clinical course, treatment status, bacterial test and biopsy if necessary.

Management of leprosy reaction is difficult for doctors at general clinical settings because leprosy is a relatively rare disease in China. Patients with reaction are still treated by doctors with special training in leprosy at or above the county level.

**Results**

In 2005, there were 6393 registered leprosy patients who might have leprosy reaction. There were 1658 newly diagnosed patients, 69·2% classified as MB according to their positive skin smear. During the survey, 457 questionnaires were collected from 25 provinces endemic for leprosy in China. Among them, two questionnaires were duplicated and three were incomplete forms so only 452 questionnaires qualified for analysis. There may be some under-reporting of mild leprosy reactions due to many factors in the field situation. The data of the survey data basically reflected the frequency of leprosy reaction in China in a single year, 2005.

Four hundred and fifty-two patients having leprosy reaction represents a 7·1% of prevalence of reaction among all registered patients. The prevalence of Type I reaction was 2·5% (159), and Type II reaction was 4·3% (273), and mixed reaction was 0·3% (20) among registered patients. There were 313 male and 139 female patients with a sex ratio of 2·38. The mean ages of patients with Type 1, Type 2 and mixed reactions were 42·4, 43·7, and 40·6 years respectively, and the sex ratios 2·38, 2·17, and 2·33, respectively. The time of initial onset of reaction shown in Table 1, it is important to note that 72% of reactions occurred during the first year of MDT and 22% of reactions occurred before MDT.

It was noted that 37·5% of PB patients developed Type 1 reaction before MDT which was higher than that for MB patients. However, about 17·3% of MB patients developed Type 1 reaction 6 months after completion of MDT which was higher than that of PB patients (Table 2).

During the period of the study, each patient with reaction had 2·4 episodes of reaction on average, 1·55 episodes on Type I and 2·92 episodes on Type II reaction on average respectively. The last episode of reaction persisted for 8·5 weeks on average, 7·5 weeks for Type I and 9·2 weeks for Type II reaction. The methods of detecting patients with reaction are shown in Table 3. 65·1% of patients reported to doctors by themselves and 21·5% of patients

<table>
<thead>
<tr>
<th>Type of reaction</th>
<th>No of cases</th>
<th>Pre MDT (%)</th>
<th>MDT 1–6 (%)</th>
<th>MDT 7–12 (%)</th>
<th>MDT 13–24 (%)</th>
<th>1–12 after MDT (%)</th>
<th>&gt;12 after MDT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>159</td>
<td>34 (21·4)</td>
<td>66 (41·5)</td>
<td>18 (11·3)</td>
<td>17 (10·7)</td>
<td>9 (5·7)</td>
<td>15 (9·4)</td>
</tr>
<tr>
<td>II</td>
<td>273</td>
<td>62 (22·7)</td>
<td>82 (30·0)</td>
<td>46 (16·8)</td>
<td>41 (15·0)</td>
<td>21 (7·7)</td>
<td>21 (7·7)</td>
</tr>
<tr>
<td>Mixed</td>
<td>20</td>
<td>3 (15·0)</td>
<td>10 (50·0)</td>
<td>5 (25·0)</td>
<td>1 (5·0)</td>
<td>0 (0·0)</td>
<td>1 (5·0)</td>
</tr>
<tr>
<td>Total</td>
<td>452</td>
<td>99 (21·9)</td>
<td>158 (35·0)</td>
<td>69 (15·3)</td>
<td>59 (13·1)</td>
<td>30 (6·7)</td>
<td>37 (8·1)</td>
</tr>
</tbody>
</table>

| Time of first developing reaction (months) |

Availability of loose clofazamine tablets is limited in China and therefore patients with Type 2 reactions were rarely treated with clofazamine. During the survey, we emphasised the need to distinguish leprosy reactions from leprosy relapse by supportive information such as clinical course, treatment status, bacterial test and biopsy if necessary.

Management of leprosy reaction is difficult for doctors at general clinical settings because leprosy is a relatively rare disease in China. Patients with reaction are still treated by doctors with special training in leprosy at or above the county level.
with reaction were detected by doctors when they visited the patient’s home. The average delay time from reaction onset to being detected was 16·2 days.

A substantial proportion of patients (57%) developed new nerve damage during or after leprosy reaction as evidenced by the appearance of new or worsening nerve function impairment or new sensory loss of skin. Only 44·7% of patients did not change as compared to their previous status of nerve functions although they are at the risk of developing reaction/neuritis.

Discussion

This is a retrospective study on the occurrence and management of leprosy reaction in China during the course of one year. As it has been reported that leprosy reaction can occur even several years after stopping MDT,5,6 our study was focusing on the current situation of occurrence and management of leprosy reaction and relation between study results in China.

Kumar et al. reported5 that the incidence of reversal reaction (RR) was highest during 6–12 months after starting MDT, and ENL was noted to occur mostly during the second or third year after starting MDT. Vijakumaran et al.7 also reported that the majority of leprosy reactions occurred during the first 3 years of surveillance. Bernink reported about 81% of severe reactions occurred in the first year of the treatment.8 In our study, we found that our results were different from those reports. Both Type 1 or Type 2 reactions occurred mostly during the first 6 months of starting MDT (41% and 30% respectively). During the first year of MDT, 72% of patients developed reaction, and during the second and third year after starting MDT, only a total of 19·8% of patients developed reaction.

We found that although 65·1% of patients with reaction reported to doctors by themselves, there were still 21·5% of patients whose reactions were detected by doctors.

<table>
<thead>
<tr>
<th>Type of patients</th>
<th>No of cases</th>
<th>Time of first developing type 1 reaction (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB</td>
<td>32</td>
<td>Pre MDT</td>
</tr>
<tr>
<td>MB</td>
<td>127</td>
<td>12 (37-5)</td>
</tr>
<tr>
<td>Total</td>
<td>159</td>
<td>33</td>
</tr>
</tbody>
</table>

Table 2. Difference of the first episode of type 1 reaction between PB and MB patients

<table>
<thead>
<tr>
<th>Type of reaction</th>
<th>No. of cases</th>
<th>Patient seeing doctor (%)</th>
<th>Doctor visiting patient (%)</th>
<th>Family member reported (%)</th>
<th>Other person reported (%)</th>
<th>Unknown (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>159</td>
<td>98 (61-6)</td>
<td>33 (20-8)</td>
<td>14 (5-9)</td>
<td>8 (5-0)</td>
<td>6 (3-8)</td>
</tr>
<tr>
<td>II</td>
<td>273</td>
<td>176 (64-5)</td>
<td>56 (20-5)</td>
<td>22 (8-1)</td>
<td>8 (3-0)</td>
<td>11 (4-0)</td>
</tr>
<tr>
<td>Mixed</td>
<td>20</td>
<td>11 (55-0)</td>
<td>8 (40-0)</td>
<td>1 (5-0)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
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<td>Total</td>
<td>452</td>
<td>285 (65-1)</td>
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<td>17 (3-8)</td>
</tr>
</tbody>
</table>
Delays in patients with reaction reporting to doctors, was mainly due to economic reasons, such as it being a long distance to a clinic. The delay time from onset of reaction to being detected was 16-2 days on an average. Thus, it was reasonable to conclude that the frequency of contacts between the patients and the doctors should be strengthened during the chronic phase of the disease in order to detect leprosy reaction early. Improvement in health education for patients can encourage early self-reporting of reaction and the key to controlling severe leprosy reaction is individualised treatment according to the patient’s clinical condition with daily monitoring in a hospital, but this is not feasible now in China.

Recurrences in leprosy reactions are well documented. Pocaterra et al. reported multiple episodes of ENL among borderline lepromatous and lepromatous leprosy patients. Schreuder reported that chronic recurrent ENL especially had become a major problem. Based on data of 445 patients with leprosy reaction in our study, each patient had an average of 2-4 episodes of reaction, 1.55 for Type I and 2.92 for Type II reaction for each patient, respectively. When analysing the relation between episodes and disability, it showed no direct relationship between them. It seemed that early detection and proper management of reaction was a key factor in the prevention of NFI.

According to the current literature, a considerable proportion of patients develop NFI during and after MDT. Pimentel reported 34% of patients developed neuritis during MDT and 45% had neuritis episodes during the follow-up period. Schreuder reported that 11% of MB patients who already had impairment at the first examination developed new NFI during MDT treatment of MB patients, 18% got worse, 2.9% kept the same impairment. Sharma reported that 7.9% of patients developed claw hand during and after MDT. Richardus also reported that 7.9% of previously normal MB patients sustained NFI during MDT. In our study, 6.4% of patients had new disability, 9.5% patients had their previous disability increased and 41.4% of patients developed new sensory loss during and after MDT. Many authors have considered that regular surveillance of patients to detect NFI during and after MDT should be emphasised. However, we do not know why some patients treated with standard prednisone regimen in well organised programmes in the area still develop new NFI and new deformity. We found that the standard regime of prednisone was only effective and feasible for mild Type I and Type II leprosy reaction in the field. However, a routine regime of prednisone was not adequate for treatment of some severe leprosy reactions, especially for BL leprosy patients with Type I reaction. However, the etiology of neuropathy in some patients is still unclear. Silent neuritis among some patients may also be due to new NFI that was overlooked by patients and local health workers or neuritis may also be a result of stopping prednisone treatment early.

Acknowledgements

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References