Short Communication

Severe dengue outbreak in Yunnan, China, 2013

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ARTICLE INFO

Article history:
Received 21 January 2014
Received in revised form 21 March 2014
Accepted 27 March 2014
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Dengue
Severe dengue
Dengue virus serotype 3 China

SUMMARY

In recent decades, the impact of dengue has increased both geographically and in intensity, and this disease is now a threat to approximately half of the world's population. An unexpected large outbreak of dengue fever was reported in Xishuangbanna Dai Autonomous Prefecture, Yunnan Province, China, in 2013. This was the first autochthonous outbreak with a significant proportion of severe dengue cases in mainland China in a decade. According to the 2009 World Health Organization guidelines, half of the 136 laboratory confirmed cases during the epidemic were severe dengue. The clinical presentation included severe haemorrhage (such as massive vaginal and gastrointestinal bleeding), severe plasma leakage (such as pleural effusion, ascites, or hypoproteinaemia), and organ involvement (such as myocarditis and lung impairment); 21 cases eventually deteriorated to shock. During this outbreak, all severe cases occurred in adults, among whom about 43% had co-morbid conditions. Nucleic acid detection and virus isolation confirmed dengue virus serotype 3 (DENV-3) to be the pathogenic strain of this outbreak. Phylogenetic analyses of envelope gene sequences showed that these DENV-3 isolates belonged to genotype II. This finding is of great importance to understand the circulation of DENV and predict the risk of severe disease in mainland China. Here, we provide a brief report of the epidemiology, clinical manifestations, and aetiology of this dengue fever outbreak, and characterize DENV strains isolated from clinical specimens.

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1. Introduction

In mainland China, dengue is listed as a notifiable infectious disease by the Ministry of Health of China, and sporadic dengue epidemics have been reported in several provinces of Southeast China, including Guangdong, Fujian, and Zhejiang. An autochthonous dengue outbreak has not been recorded in Yunnan Province in the last decade. From August to October 2013, an unexpected large outbreak of dengue with a significant proportion of severe cases was reported in Xishuangbanna Dai Autonomous Prefecture, Yunnan Province, China. In this study, we investigated the aetiology of this severe dengue outbreak and analyzed the dengue virus (DENV) genotype isolated from clinical specimens.

2. Methods

Clinical information and samples were collected from patients at Xishuangbanna Dai Autonomous Prefecture People's Hospital (XDAPPH). Serum samples obtained from suspected cases were originally tested for the NS1 antigen and DENV serotype-specific genome fragments were detected by in-house real-time RT-PCR assays. A random subset of positive samples was sent to Beijing Institute of Microbiology and Epidemiology for virus isolation and full genome sequencing.1,2 The study was approved by the Ethics Review Committee of Guangzhou 8th People's Hospital (GPH).

3. Results

During the epidemic, a total of 1245 cases were identified in Jinhong City, Mengla and Menghai counties of Xishuangbanna, of which 19 were classified as imported cases returned from Myanmar, Laos, and Thailand. Xishuangbanna is located at the...
lower altitude of Yunnan and has a typical tropical climate; it neighbours Myanmar, Laos, Bangladesh, Vietnam, and Thailand (Figure 1A), where dengue is endemic. In this outbreak, 861 patients ranged in age from 15 to 45 years, 375 patients were aged over 45 years and only nine patients were aged <15 years. Using real-time RT-PCR assays, the cause of the epidemic was identified to be DENV serotype 3 (DENV-3).

Among the 136 hospitalized cases, 70 were diagnosed as severe dengue according to the 2009 World Health Organization (WHO) guidelines, and their mean age was 44.17 years. Severe haemorrhage was seen in 28 patients, severe plasma leakage in 27 patients, and 35 patients developed organ impairment. A total of 21 cases finally deteriorated to shock; their mean age was 29.6 years. In addition, 30 severe cases had underlying diseases such as fatty liver, emphysema, and coronary heart disease. All patients received case management by the collaborative team of doctors from XDAPPH and GPH in accordance with the 2009 WHO guidelines. All patients eventually recovered and were discharged from hospital.

Two DENV-3 strains from 17 patient acute-phase serum samples were isolated in mosquito C6/36 cells and named YN01 and YN02, respectively. The complete genome sequences of the two isolates were determined as described previously1–3 and were submitted to GenBank (KF824902 and KF824903). Phylogenetic analyses based on the complete envelop gene of these new isolates were carried out by neighbour-joining method. The results showed that YN01 and YN02 fell into genotype II together with most Southeast Asian strains isolated in recent years (Figure 1B). YN01 and YN02 have the highest amino acid homology (98.8%) to the Bangladesh strain BDH02-7 isolated in 2002, suggesting that the Yunnan isolates may have originated from neighbouring countries.

4. Discussion

This is the first large severe dengue outbreak in Yunnan Province during recent decades. In this epidemic, all the severe cases were adults, which is quite different to the situation in other Asian dengue hyperendemic countries, in which most severe cases have been children. This explosive epidemic of severe dengue was probably associated with immune status and the introduction of a novel virus. This situation is similar to that of Taiwan in 1998 and in Brazil in 2003, when DENV-3 was newly introduced. DENV-3 genotype II strains are now active and have been isolated from dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) cases in Southeast Asia7 (Figure 1B). Virological characterization and an analysis of viraemia in patients are currently underway to clarify the potential association of virus virulence and disease severity. Among the five DENV-3 genotypes, genotypes III and V were recently isolated from patients in mild dengue fever epidemics in China11,12. Thus, at least three genotypes of DENV-3 have been introduced into mainland China in recent years.

The invasion and spread of *Aedes aegypti* is also believed to have played a critical role in the explosive nature of this outbreak.
Previously, *Aedes albopictus* was predominant in Yunnan Province, which is a less efficient vector of DENV than *A. aegypti*. Generally, dengue epidemics caused by *A. albopictus* tend to be mild and short-lived, and this probably explains the dengue-free status of Yunnan Province. However, during this outbreak, *A. aegypti* was detected for the first time in Xishuangbanna. The spread of *A. aegypti* in this area has aroused special attention. The coinstantaneous introduction of a new DENV strain and an effective vector into Xishuangbanna, a dengue-free region, carries a high risk for a severe epidemic and endemicity. Strict vector control measures, extensive field surveillance, and laboratory investigations are needed in the near future.

**Acknowledgements**

We thank Xinlou Li and Dr Liqun Fang for drawing the map and Shun-Ya Zhu for technical assistance. This study was supported by the Key Research Project of Guangzhou Health Bureau (No. 201102A212020), the Special Program of National Science and Technology of China (No. 2013ZX10004-805), and the National Natural Science Foundation of China (No. 81301491 and No. 31270974).

**Conflict of interest:** There are no conflicts of interest to declare.

**References**