A case of Sindbis virus infection in Kuala Lumpur

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ANTIBODY SURVEYS ON SERA from persons resident in different parts of West Malaysia indicate that there was evidence of low activity for Group A arbovirus (Rudnick 1967). However, no case of human disease by Group A has yet been recorded in West Malaysia, although it was evident that there was infection occurring. The presence of these viruses had been observed as several Group A arboviruses, including Sindbis, have been isolated from mosquitoes before. This is probably due to mild disease produced as a result of infection with Group A and consequently the patients were not hospitalised and no laboratory investigations were carried out. It was thus fortuitous that this case was picked up routinely as it was being investigated for dengue infection.

This report describes briefly the clinical and serological findings in a patient seen at the Institute for Medical Research, Kuala Lumpur.

Case Report

A 20-year-old Malay male was seen at the outpatient clinic of the Institute for Medical Research suffering from fever, cough, headache, rash and generalised body aches for 1 day. There were no joint pains.

On examination, he had a temperature of

102°F, generalised erythematous rash all over the body and infected pharynx. There was no lymphadenopathy or hepatosplenomegaly or other positive findings. He was treated symptomatically with

Tetracycline 250 mgs —
6 hourly daily for 5 days.
Paracetamol lg —.
3 times daily for 4 days.
Chlorpheniramine maleate (Piriton) 4 mgs —
3 times daily for 4 days.

He came back after 4 days with the fever and generalised rash still persisting and was again treated symptomatically. A sample of blood was taken for viral studies as dengue was suspected clinically and he was asked to come back again after 2 weeks for a second specimen of blood to be taken. He made an uneventful recovery and was quite well when the 2nd specimen of blood was taken.

Methods and Materials

(1) **Sera** — The 2 samples of serum were taken from clotted blood after overnight storage at 4°C; they were then centrifuged and stored at -20°C before testing at a later date.

(2) **Viruses** —
- (a) Dengue 1. Hawaii strain; 131st mouse passage
- (b) Dengue 2. Trin. 1751 strain; 66th mouse passage
- (c) Dengue 3. H-87 strain; 23rd mouse passage
- (d) Dengue 4. H-241 strain; 31st mouse passage
- (e) Japanese Encephalitis (JE), Nakayama strain; 52nd mouse passage
- (f) Tembusu, AMM 1775 strain; 16th mouse passage
- (g) Zika, B 24982 strain; 155th mouse passage obtained from Dr. A. Rudnick, University of California.
- (h) Sindbis, P 886 strain; 29th mouse passage
- (i) Chikungunya, African strain; 180th mouse passage.

(3) **Haemagglutinin — inhibition test.** The test as described by Hammon and Sather (1969) was used. The antigens were prepared according to the sucrose-acetone method of Clarke and Casals. The sera were treated by the acetone-extraction method and the titration was carried out by the microtechnic using perspex plates with U-shaped cups. The results were expressed as a reciprocal of the highest serum dilution causing inhibition. The lowest serum dilution tested was 1/10.

(4) **Neutralisation test** — Sindbis seed virus was prepared from brains of suckling mice which had been inoculated intracerebrally. The constant serum-varying virus dilution method was used and the neutralisation index and log rise in titre calculated.

Laboratory Results

(a) **Virus Isolation**

An attempt at isolation of virus was made in this case but proved negative. The first blood specimen was taken on the 4th day of illness and it was passed in suckling mice. Failure to isolate the virus in this case was probably due to high antibody content in the blood or low concentration of free virus and not loss of viability during transportation as the patient was bled at the Institute where the virus investigation was carried out.

(b) **Serological Findings**

Haemagglutination-inhibition test

Virus antigen	Serum specimen	
	1st specimen 4th day of illness	2nd specimen 21st day of illness
Group A		
Sindbis	320	2560
Chikungunya	<10	<10
Group B		
Dengue 1	<10	<10
Dengue 2	<10	<10
Dengue 3	<10	<10
Dengue 4	<10	<10
Japanese Encephalitis	<10	<10
Tembusu	<10	<10
Zika	<10	<10

The haemagglutination-inhibition test against Group B antigens were all negative but when carried out against Group A, i.e. Sindbis, there was a significant rise in titre. Sindbis virus antigen is routinely used in the laboratory as a representative for Group A in the haemagglutination-inhibition test. To rule out the possibility that this reaction could be the result of a Chikungunya infection, the haemagglutination-inhibition test was carried out

Neutralisation test			
Serum Specimen	Virus antigen Sindbis; log LD_{50}	Neutralisation index	Log rise in titre
1st specimen	-4.1	3.6	—
2nd specimen	-4.2	3.5	-0.1
Control normal rabbit serum	-7.7	—	—
Positive control serum	-3.4	4.3	—

against Chikungunya virus antigen. This turned out to be completely negative on 2 separate occasions tested. Chikungunya and Sindbis virus antigens are the only 2 Group A antigens used in this laboratory.

The neutralisation test showed that neutralising antibodies were present to almost the same extent in both specimens of blood (Neutralisation index of 3.6 and 3.5) although there was no rise in titre. It would appear from these results that there was an accelerated response to haemagglutination-inhibition antibody but a poor response to neutralising antibody in the 2nd specimen of blood. Although there was no rise in titre of the neutralising antibody, there was, however, a large amount of antibody present. This is probably due to a secondary response as a result of a secondary infection with Sindbis virus or one that is antigenically closely related to it.

Discussion

There is little doubt that this is a case of Sindbis virus infection. The clinical findings, however, are minimal and the only signs and symptoms of any significance are fever, headache, rash and generalised body aches. These features are indicative of a mild form of the disease. In severe cases (Malherbe et al 1963), the rash proceeded to painful vesiculisation, and hands and feet were swollen. In addition, there were joint pains and soreness of tendons leading to prostration. A virus was isolated from these vesicles which was later characterised and identified as Sindbis virus. In our case, no vesicles were noted and attempts at virus isolation from blood was unsuccessful. Further, there was no swelling of the hands and feet and joint pains.

In the cases studied by McIntosh (McIntosh et al 1964), he described upper respiratory symptoms in 4 cases. There was mild sore throat with small ulcers irregularly distributed in the mouth and pharynx. In our case, no ulcers were seen in the mouth or pharynx although the latter was injected.

Finally, our patient made a complete and uneventful recovery in 2 weeks and there were no residual signs or symptoms.

On carrying out epidemiological investigations, it was found that this patient had come to Kuala Lumpur from Kedah (a state about 250 miles by road to the north of Kuala Lumpur) 21 days prior to the onset of fever. The purpose of coming to Kuala Lumpur was to join the Institute for Medical Research as a trainee laboratory assistant. On first arrival, he stayed with relatives at a military camp on the outskirts of Kuala Lumpur and was still staying there at the onset of illness. It would appear that he developed the disease whilst staying at the military camp. This camp is a sprawling complex of stores, offices and residential buildings. It is bounded on one side by large areas of currently used as well as disused tin mining pools. On first glance, it would appear that this would be an ideal breeding area for Culex mosquitoes from which species Sindbis virus have been isolated before in West Malaysia. Detailed entomological investigations are being planned and antibody surveys among the population there are being carried out. Preliminary results indicate that there is some evidence of low activity with Group A arbovirus.

No virus was isolated from this case and the diagnosis was based on clinical and serological evidence.

Summary

A case of Sindbis virus disease in man occurring in Kuala Lumpur is presented. This is the first time that it has been observed in Malaysia.

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