Clinical and Laboratory Study of a Newly Observed Viral Infection in the Philippines: A Preliminary Report*

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ABSTRACT

Eighteen (18) cases of Chikungunya (or a very close related virus) infection, a newly observed clinical entity in the Philippines, are presented. Diagnosis was established by serological studies consisting of hemagglutination-inhibition (HI) and complement fixation (CF) tests.

The clinical picture is characterized by a symptom-complex consisting essentially of fever, severe, incapacitating, recurrent joint pains and a rash. There is no involvement of the respiratory system and no bleeding tendencies were observed. The erythrocyte sedimentation rate was elevated, more so towards the later part of the illness. The platelet counts were normal. No residual joint deformity morbidity or mortality was encountered.

Key Words: Chikungunya virus, Philippines, arthritis

INTRODUCTION

In October to December 1967, several patients were seen at the Philippine General Hospital Out-Patient Department presenting with a clinical trial of fever, joint pains and a rash, a symptom-complex attributed to influenza, German measles and dengue fever. Similar outbreaks were noted in South Africa,[2] Thailand,[3] India,[4,6] and Singapore wherein the Chikungunya virus was implicated as the etiologic agent.

No outbreak of Chikungunya or a closely related virus has been reported in our country aside from a similar article which is currently in press.[1] The authors, therefore, decided to investigate the clinical aspects, laboratory manifestations, serologic studies and viral isolation of the possible etiologic agent of this newly observed clinical entity.

MATERIALS AND METHODS

Fourteen adult females and four adult males were seen at the Out-Patient Department of the Philippine General Hospital, in the months of October to December, 1967, complaining of fever, severe joint pains and a rash. Hemagglutination inhibition and complement fixation tests were done against Dengue 2, 3 & 4, Japanese B, Chikungunya, Semliki Forest and Sindbis viruses on the day of consultation and 10 days after. Results were considered positive for a particular viral antigen when there was a demonstrable rise in the antibody titer of at least four-fold between acute and convalescent serum samples, when a titer of 1:640 or greater was present in the absence of a four-fold

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rise in samples collected later than the 5th day of illness and when a significant decrease was recorded after an initially high titer of 1:640 or greater in samples collected later than the 10th day of illness. Ten patients were seen during the first week of illness, 4 during the 7th-14th day and 4 during the 4th week of illness.

A complete blood count including erythrocyte sedimentation rate was done on 17 patients, urinalysis in 12, serum uric acid in 11, fasting sugar, urea nitrogen and creatinine in 8, electrocardiogram in 6 and test for rheumatoid factor in 2. All of the above studies were done within the first 3 days of consultation.

RESULTS AND DISCUSSION

Clinical Aspects

In most cases, the patients were seen because of severe, excruciating joint pains which were aggravated by movement and weight bearing. The arthralgia was not accompanied by any significant inflammation. The clinical manifestations are recorded in Tables 1 and 2.

Fever

1. Onset: usually sudden and high-grade (38.5 – 39°C)
2. Prodrome: chills or chilliness in some
3. Duration: 1-4 days; recurrent in 3 patients in whom it was associated with an exacerbation of joint pains.

Rash

1. Onset: 1st to 4th day of illness, more frequently on the 2nd and 3rd day, within a few hours to 72 hours after the temperature spike.
2. Description: macular, popular, maculo-papular, punctate, rose to light-red
3. Distribution: external surfaces of forearms, arms, legs, and thighs, usually; at times, face, trunk and nape
4. Duration: 1-3 days
5. Other associated symptoms:
   a. Itching: present in 3 patients so that the rash was attributed to "allergy"
   b. Desquamation was not seen in any of these patients

Joint pains

1. Onset: sudden, excruciating and incapacitating; ushered in the illness in 5 patients
2. Distribution:
   a. Any joint, including the spine, could be involved and involvement was usually multiple but asymmetrical
   b. Joints of the lower extremities were more commonly affected
3. Aggravating factors:
   a. Movement
   b. Weight bearing
4. Accompanying signs:
   a. No definite signs of inflammation
   b. Swelling of involved joint; minimal in most cases, fusiform in 2
   c. No effusion into the joints
5. Duration and recovery:
   a. Varied from 1 week to as long as 4 months; on the average, 2-3 weeks
   b. Slow clearing of arthralgia
   c. Exacerbation of arthralgia was observed in some and was associated with a rise in temperature in 3 patients (37.8°C, 38°C, 39°C).
   d. No residual deformity observed

Table 1. Presenting signs and symptoms

		No. of Patients
1.	Fever	2
2.	Rash	2
3.	Joint Pains	13
4.	Pedal Edema	1

Table 2. Clinical manifestations during the course of the illness

		No. of Patients
1.	Fever	18
2.	Rash	18
3.	Joint Pains	18
4.	Malaise	11
5.	Myalgia	11
6.	Anorexia	8
7.	Chills, Chilliness	6
8.	Pedal Edema	6
9.	Headaches	3
10.	Lymphadenopathy	3
11.	Numbness	2
12.	Oral Eruptions	2
13.	Flushing	1
14.	Constipation	1

Table 3. Distribution of joint involvement

		No. of Patients
Upper Extremity		
1.	Shoulder	2
2.	Elbow	1
3.	Wrist	4
4.	Metacarpal	3
5.	Proximal Interphalangeal	3
6.	Distal Interphalangeal	1
Spine		1
Lower Extremity		
1.	Hip	2
2.	Knee	5
3.	Ankle	11
4.	Metatarsal	6
5.	Proximal Interphalangeal	3
6.	Distal Interphalangeal	1

Other Symptoms

1. Headache:
   a. Onset: occurred in the 1st 3 days of illness
   b. Intensity: mild 2, severe in 1
   c. Location: frontal; no relation to eye movements
2. Pedal edema:
   a. Onset: occurred in 1st 7 days of illness
   b. Duration: few days to weeks
   c. Character: pitting
   d. Severity: minimal
3. Lymphadenopathy:
   a. Onset: 3rd to 5th day of illness
   b. Distribution: posterior cervical, posterior auricular, inguinal.
   c. Size large, especially in the inguinal group
   d. Tenderness: moderate to severe
   e. Duration: 3-4 days
4. Numbness of fingers and hyperesthesia of the soles
   a. Occurred in 1 patient only
   b. No neurologic deficit elicited
5. Flushing
   a. Observed on the 1st day of illness
   b. Lasted for 1 day
6. Oral Eruptions
   a. Onset: 3rd-4th day
   b. Duration: 3 days

This was present in only 2 patients with inguinal adenopathy who had a more prolonged course and more incapacitating joint pains than most. It would be interesting to find out whether or not the presence of these 2 findings may help in detecting the more severe form of illness.

There were no bleeding tendencies or signs of respiratory involvement. No residual joint deformity, morbidity or mortality was encountered.

Laboratory Manifestations

Viral Studies

Hemagglutination inhibition and complement fixation studies are indicated in Tables 4A-C. Among the 18 paired sera submitted for serologic studies, 10 showed a rise of at least 4-fold from the acute to the convalescent phase, 2 showed a significant decrease after an initially high titer in a late 1st sample and in 6 whose initial samples were collected after the 1st 10 days of illness, the titer remained persistently high to Chikungunya virus.

Hematologic Studies

In 15 of the 18 cases, the white cell count was within normal limits, mild leukocytosis being encountered in only one patient and leukopenia in 2. An initial neutrophilia in the 1st 3-4 days of illness, followed by a return to normal and a secondary rise in the 2nd-3rd week of illness, was observed. The platelet counts were normal.

The erythrocyte sedimentation rate, which was high even in the early phase of the illness, was more significantly increased toward the later part of the illness.

Others

The various values for blood urea nitrogen creatinine, uric, acid, urinalysis, and rheumatoid factor are shown in Table 5. Essentially, there were no abnormalities noted in any of the above parameters except for traces of albumin in 2.

Electrocardiogram

This was done only in 5 patients during the 1st 4 days of illness. No evidence of myocarditis was noted, supporting the absence of clinical myocardial involvement.

Table 4A. Serologic Studies of Patients Showing Four-fold Rise in Titer

Patient		Hemagglutination Inhibition		Complement Fixation	
		1st sample	2nd sample	1st sample	2nd sample
1.	N.V-L.	160	640	<4	64
2.	G.R.	160	2560	<4	64
3.	C.R.	320	2560	<4	128
4.	Z.D.	<20	320	<4	128
5.	A.E.	640	2560	<4	32
6.	E.C.	<20	80	<4	128
7.	C.S.	<20	160	<4	128
8.	A.C.	<20	80	<4	32
9.	S.D.	20	640	<4	128
10.	A.V.I.	<20	160	<4	128

Table 4B. Serologic Studies of Patients With Persistently Elevated Titers

Patient		Hemagglutination Inhibition		Complement Fixation	
		1st sample	2nd sample	1st sample	2nd sample
11.	A.P.	2560	2560	128	128
12.	E.T.	1280	1280	128	128
13.	L.S.G.	640	640	128	128
14.	L.R.	320	320	128	128
15.	L.M.	640	640	128	128
16.	V.L.	640	640	128	128

Table 4C. Serologic Studies of Patients with Initially Elevated and Subsequently Low Titers

Patient		Hemagglutination Inhibition		Complement Fixation	
		1st sample	2nd sample	1st sample	2nd sample
17.	M.V.	640	80	128	32
18.	P.V.	2560	640	2128	16

Table 5. Initial Laboratory Examinations

Patient		Urinalysis	B U N (mg %)	Creatinine (mg %)	Uric Acid (mg %)	Rheumatoid Factor
1.	A.E.	Normal	12.3	1.72	—	—
2.	P.V.	Normal	13.9	1.5	3.5	—
3.	C.S.	Normal	—	—	4.0	—
4.	E.C.	Normal	12.5	1.72	—	—
5.	A.P.	—	—	—	3.75	—
6.	C.M.	Normal	11.0	1.2	4.2	—
7.	E.T.	—	—	—	4.62	—
8.	N.V.L.	Normal	—	—	3.0	—
9.	G.R.	Normal	—	—	3.8	—
10.	A.I.	Traces, Albumin	—	—	—	Negative
11.	L.S.G.	Traces, Albumin	8.0	1.8	5.8	Negative
12.	M.V.	Normal	12.5	1.9	—	—
13.	L.R.	Normal	14.0	1.6	4.0	—
14.	L.M.	Normal	12.0	1.7	4.4	—

THERAPY

Treatment was directed more towards the alleviation of distressing arthralgia. There was considerable relief of the pain in 5 patients placed on dexamethasone at a dose of 1.5 mg for 5-7 days. Exacerbation of the pain was noted in one while the steroids were being withdrawn. All these patients, however, were treated late in the 2nd week of illness. It is entirely possible that the arthralgia could have been minimized if the therapy was started during the initial stages of the illness.

In 4 patients in whom joint pains were moderate, indomethacin was given at a dose of 75 mg daily in 3 divided doses, which was followed by symptomatic relief.

Although steroids and indomethacin apparently relieved the arthralgia of the patients, the possibility exists that these patients would have been relieved anyhow, without the benefit of these medications, as a natural course of the illness. It will be important to get the control cases treated during the early part of the illness.

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