

Chikungunya virus infection

A retrospective study of 107 cases

S. W. BRIGHTON, O. W. PROZESKY, A. L. DE LA HARPE

Summary

A retrospective study of 107 cases of serologically proven chikungunya (CHIK) virus infection was undertaken. All respondents had contracted the disease at least 3 years previously; 87.9% had fully recovered, 3.7% experienced only occasional stiffness or mild discomfort, 2.8% had persistent residual joint stiffness but no pain, while 5.6% had persistent joint pain and stiffness and frequent effusions. Synovial fluid from 3 patients was analysed. All the patients with persistent joint pain and stiffness had very high antibody titres against CHIK virus.

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The name chikungunya is derived from the Swahili, meaning 'he who walks bent up'. The severe crippling pains encountered in the acute stages of the disease make this name particularly apt. The chikungunya (CHIK) virus is an alphavirus of the family *Togaviridae* of the arbovirus epidemiological group. The alphavirus group includes among others the Sindbis and CHIK viruses.

The virus is transmitted by a mosquito reported to be *Aedes aegypti*, but in the southern African epidemics of 1975, 1976 and 1977 *A. furcifer-taylori* appeared to be the main vector.¹

Departments of Physical Medicine, Rheumatology and Microbiology, H. F. Verwoerd Hospital and University of Pretoria

S. W. BRIGHTON, M.B. CH.B., F.F. PHYS. MED., M.MED. (PHYS. MED.),
Head, Department of Physical Medicine and Rheumatology
O. W. PROZESKY, M.D., *Department of Medical Microbiology*
A. L. DE LA HARPE, M.B. CH.B., *Medical Officer, Department of Rheumatology*

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The disease was first described in 1955 by Robinson² and Lumsden³ from Tanzania, where it occurred in epidemic form. Other outbreaks have been described in the Transvaal,⁴ Zambia,⁵ south-eastern Rhodesia,⁶ and Zaire.⁷ Antibody studies on human sera have indicated human infection in Mozambique, Caprivi, Botswana and Angola,⁶ and epidemics have been described in Thailand,⁸ Vietnam⁹ and India.¹⁰

The early clinical course of the disease has previously been described.^{11,12} It is characterized by severe conjunctivitis, a macular rash, fever, low back pain and a symmetrical polyarthritis of varying severity, the most commonly involved joints being the metacarpophalangeal joints, wrists, elbows, shoulders, knees, ankles and metatarsal joints.

Stiffness is a prominent feature. To date follow-up studies seem to have been limited to 18 months and no long-term studies have been reported. Cases of longer duration are the subject of this report.

Patients and methods

A list of all patients who had had serologically proven CHIK virus infections during epidemics in the northern Transvaal during 1975, 1976 and 1977 was obtained from Dr B. M. McIntosh, National Institute of Virology, Johannesburg. From this list 107 patients were traced either by telephone or personally. All were contacted after August 1980, the duration from the time of contracting the disease thus being 3-5 years.

Results

The 107 cases were divided into 4 groups.

Group 1

Group 1 consisted of 94 patients fully recovered from the infection. They were now free of any joint pain or stiffness, but all could still vividly describe the severe pain of the acute attack.

Although many could only vaguely recall how long their joints had taken to recover fully, 38 apparently recovered within a matter of weeks of the acute attack; 41 stated that they had recovered slowly over a period of up to a year and 15 said that the recovery period was 2-3 years. It is of possible significance that of these 94 patients now recovered, 42 were under the age of 17, the mean age of all patients being 37. It has previously been reported that the disease has a milder course in children.^{8,13,14}

Group 2

Group 2 consisted of 4 patients retaining only occasional stiffness or mild discomfort. The youngest was 45 and the oldest 60 years (mean age 54). Occasional stiffness or mild discomfort in the proximal interphalangeal (PIP) joints was experienced by all 4 patients, in the metacarpophalangeal (MP) joints (3 patients), in the wrists (3 patients) and in the knees (3 patients). The stiffness appeared to be very intermittent, but 3 of the 4 patients said the stiffness was noticeably aggravated by exercise. All 4 patients claimed to have had no joint pains or stiffness before the CHIK virus infection. None of the 4 cases showed objective abnormality of the joints, such as joint deformity, palpable synovitis or joint effusion.

Of the 4 patients, 2 were examined during a period when they were free of discomfort; no joint tenderness could be elicited. Of the other 2, both with joint discomfort and stiffness at the time of examination, one had very mild tenderness of the MP joints of both hands, while the other had none. On radiographs the involved joints appeared normal, as were results of special investigations and the ESR. The CHIK antibody titres were 1:40 and 1:80.

Group 3

Group 3 consisted of 3 patients with persistent residual stiffness but no pain. Their ages were 65, 60 and 55 years. The 65-year-old patient stated that the joint pains had settled rapidly after the acute attack, but stiffness remained in the wrists, MP joints, PIP joints, knees and ankles. This gradually improved but she retained some stiffness in the ankles and knees, this being present in the morning for over an hour and aggravated by exercise. No abnormalities were noted on examination of the involved joints or on radiographs. The other 2 patients had residual morning stiffness in the wrists, MP joints and knees, lasting for 15-30 minutes. There was also no objective evidence of joint damage on physical examination or radiography. Special investigations were negative and CHIK antibody titres were 1:160, 1:80 and 1:40 in the 3 cases.

Group 4

Group 4 consisted of 6 patients with persistent joint pain and

stiffness with or without swelling (Table I). Pain was graded on a scale of 4: 0 = no pain; 1 = pain, but no tenderness on palpation of the involved joint; 2 = pain and tenderness on palpation of the joint; 3 = pain and tenderness on palpation sufficient to cause wincing from pain; 4 = pain on palpation causing withdrawal of the limb. These 6 cases are reported in detail below.

Case 1

In a 60-year-old woman the duration of the disease was 3 years and 2 months. The pain was always present but tended to fluctuate in severity over fairly lengthy periods. She was examined during a painful period. Wrists, MP joints, PIP joints, shoulder, neck, knees, ankles and subtalar joints were all involved. A mild synovitis was present in the ankles and wrists, but the patient would not consent to synovial biopsy. Aspiration of the knee yielded synovial fluid of reduced viscosity, with poor mucin clot formation, slight turbidity and 5 000 leucocytes/ μ l. Insufficient fluid was obtained for complement function tests. Morning stiffness persisted for 30 minutes and exercise, particularly climbing stairs, aggravated the pain and stiffness on the following day.

The blood count was normal on four occasions, and on four occasions the ESR was between 20 and 25 mm/h (Westergren). The antinuclear factor test was negative, normal serum complement levels were found, the Heller test was negative, investigations of kidney and liver function gave normal results and immunoglobulin (IgG, IgA, IgM) levels were all normal. Markedly raised antibody titres against CHIK virus were encountered on three occasions: 1:2 560, 1:640 and 1:640. Investigations for other arbovirus infections were negative.

Case 2

A 16-year-old girl had complained of persistent pain since contracting CHIK infection in 1976. She apparently had had severe pain during the acute stage for several weeks; this settled down into a steady pain and tenderness (grade 1-2) of the knees, wrists, ankles and small joints (MPs and PIPs) of the hands. She had morning stiffness for 20 minutes each day. The joint symptoms were markedly aggravated by exercise.

Special investigations showed a normal full blood count, an ESR of 18 mm/h (Westergren), a negative rheumatoid factor test, and a C-reactive protein level of 13,2 μ g/ml. Liver and kidney function tests were all negative, the urine was microscopically and biochemically normal, and the serum complement and immunoglobulin levels were within normal limits. Synovial fluid analysis revealed straw-coloured fluid of reduced viscosity and with poor mucin clot formation. Complement levels were normal and the white cell count was 2 000/ μ l. Radiographs of the joints were normal. Arthroscopy was performed on the right knee by an orthopaedic surgeon experienced in this technique. A very thin, pale, atrophic-looking synovium was found but a specimen taken was reported as being normal.

TABLE I. GRADING OF JOINT PAIN IN 6 PATIENTS WITH PERSISTENT PAIN AND STIFFNESS

Case	Wrists		MP		PIP		DIP		Elbow		Shoulder		Neck	Hip		Knee		Ankle		Subtalar		Toes	
	L	R	L	R	L	R	L	R	L	R	L	R		L	R	L	R	L	R	L	R	L	R
1	2	2	1	1	1	1	0	0	0	0	1	1	1	0	0	2	2	2	1	1	1	0	0
2	2	2	1	1	1	1	0	0	0	0	0	0	0	0	0	2	2	2	2	0	0	0	0
3	1	1	0	0	1	1	1	1	0	0	1	1	0	0	0	0	0	2	2	0	0	0	0
4	2	2	2	2	1	1	1	1	1	1	0	0	1	0	0	1	1	1	1	1	1	0	0
5	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
6	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	2	2	1	1	0	0	0	0

DIP = distal interphalangeal joints.

Case 3

A 54-year-old man had developed CHIK infection in 1977, with fever, severe joint and muscle pains and a mild rash. The severe pain slowly receded and 4 years after infection he was left with involvement of the wrists, PIP joints, distal interphalangeal (DIP) joints, shoulders and ankles and morning stiffness for 15 minutes. The blood count was normal, and the ESR 20 mm/h (Westergren). The rheumatoid factor and antinuclear factor tests were negative. Liver and kidney function and serum complement levels were all within normal limits. The serum antibody titre against CHIK virus was 1:640.

Case 4

A 52-year-old woman had contracted the infection in 1975, and was completely bedridden for 4 weeks with severe joint pain. Thereafter the pain subsided but left her, 6 years after the infection, with residual symptoms in the wrists, MP joints, ankles and subtalar joints and morning stiffness of 15 minutes' duration. There was no soft-tissue swelling of the joints but mild effusions were present in both knees. The patient did not consent to joint aspiration. The full blood count, liver and kidney function and serum immunoglobulin levels were all normal, while rheumatoid factor and antinuclear factor tests were negative. The ESR was 20 mm/h (Westergren). The antibody titre against CHIK virus was 1:160. No erosions could be demonstrated on radiography.

Case 5

A 52-year-old man had contracted CHIK infection in 1976. The severe, acute pain gradually subsided over a period of several months, but left him with pain in the PIP, DIP and MP joints, including the thumbs, wrists and ankles, with morning stiffness of 30 minutes' duration. Mild synovial thickening of the wrists and MP joints was noted. The full blood count, rheumatoid factor and antinuclear factor tests, and tests of liver and kidney function gave results within normal limits. The ESR was 15 mm/h (Westergren) and the CHIK antibody titre 1:160.

Case 6

A 64-year-old man had contracted CHIK infection in 1976 and had been left with constant pain in the knees, ankles, wrists and MP joints and morning stiffness of 15 minutes' duration. Marked effusions were noted in both knees. On aspiration synovial fluid with a low viscosity, poor mucin clot formation, very low complement levels and a total white cell count of 4 000/ μ l was found.

The serum complement level, the full blood count, and liver and kidney function were all normal. The rheumatoid factor test was negative and the ESR 15 mm/h (Westergren).

Discussion

This study was conducted to investigate the incidence and nature of residual symptoms in patients who had contracted CHIK virus infection at least 3 years previously. Of the 107 patients investigated 94 (87,9%) had fully recovered and had no residual symptoms 3-5 years after the infection. Of the remainder, 4 (3,7%) had only occasional stiffness or mild discomfort, 3 (2,8%) had persistent stiffness but no pain, and 6 (5,6%) had persistent pain and stiffness with or without joint swelling.

The patients were a selected group of people, i.e. those who had sought medical help during the acute phase of the disease and whose infection had been proved serologically. The possibi-

lity that a larger group with milder disease had not consulted a doctor must be considered. Epidemiological studies to identify this group are in progress. Further investigations were only carried out on symptomatic patients. None had any abnormalities of the full blood count. Only in the 6 patients with persistent pain and stiffness was the ESR accelerated. All the symptomatic patients had serum antibodies against CHIK virus, as expected, but of particular interest were the high titres encountered in the patients with persistent joint symptoms (group 4). Whether this is indicative of persistent virus antigen or due to some other mechanism is not clear. Virus could not be cultured from the blood or synovial fluid of the patients with high titres. Serological investigations of the fully recovered, asymptomatic patients should be of interest. To date only 4 of the 94 patients in this group have been investigated for CHIK antibody titres. All 4 had levels of 1:40, which is indicative of their immune status.

None of the patients had any radiological evidence of bony destruction, although one report of possible bony erosions following CHIK infection has appeared in the literature.¹² Morning stiffness appears to be a major feature in those with residual symptoms. Stiffness persisted for a mean of 35 minutes in patients with no joint pain, and for 24 minutes in patients with joint pain.

Synovial fluid analysis was carried out in 3 patients, all with persistent joint symptoms; the fluid was of reduced viscosity and showed poor mucin clot formation. Total white cell counts in the three samples were between 2 000 and 5 000/ μ l. In one sample the complement levels were reduced but in the remaining two samples these were within normal limits.

The most commonly involved joints are the wrists and ankles, followed by the knees and the MP and PIP joints of the hands. Three patients had involvement of the DIP joints of the hands. No evidence of any destructive process could be found in the joints.

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