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POGOSTA DISEASE: CLINICAL OBSERVATIONS DURING AN OUTBREAK IN THE PROVINCE OF NORTH KARELIA, FINLAND

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SUMMARY

Objective. To characterize the clinical picture of Pogosta disease.

Methods. The data of 73 patients who had had Pogosta disease in 1981 and who then had been seen by a local physician in North Karelia were analysed.

Results. The main manifestations were fever (23%), rash (88%) and joint symptoms (93%). The joint symptoms in some patients lasted for several months and were severe enough to cause immobilization. The clinical picture was identical in those patients who had a definite serological diagnosis and those who did not have a detectable antibody response.

Conclusion. The symptoms of Sindbis virus-induced Pogosta disease consist of fever, rash and joint symptoms, which may be severe and prolonged.

KEY WORDS: Pogosta disease, Sindbis virus, Reactive arthritis, Ockelbo disease, Karelian fever.

POGOSTA disease was first described and named in the 1970s in Ilomantsi, in the Eastern part of Finland, by Kuusisto [1]. He has been collecting data from patients with typical symptoms of Pogosta disease in Ilomantsi health centre for over 20 yr. The word *pogosta* means a village centre in Northern Karelia. A disease with similar symptoms was described earlier in Sweden and named Ockelbo disease [2]. Further, in Karelian regions of Russia, the so-called Karelian fever strongly resembles Pogosta disease [3].

Viruses that cause these three diseases are very closely related to Sindbis virus, which belongs to the genus alphaviruses [4, 5]. Ockelbo virus was isolated in 1982 in Sweden from a pool of female *Culiseta* mosquitos [6]. The sequence differences between Sindbis virus prototype (AR339) and Ockelbo virus are very small. There is evidence that Ockelbo and Karelian virus genomes are the same, and it has also been assumed that the same strain of Sindbis virus causes both Ockelbo and Pogosta disease [7, 8]. All attempts to isolate Pogosta or Ockelbo virus from human subjects have been unsuccessful so far. The Ockelbo virus RNA was detected from skin biopsies by means of the polymerase chain reaction (PCR) method [9]. For the serological diagnosis, haemagglutination inhibition or immunofluorescence have been used earlier [10, 11], and the current method is an enzyme immunoassay (EIA) [12–14].

Although it is known that the typical and most common symptoms of Pogosta disease are rash, arthralgia and fever, the complete clinical picture has not been accurately described [1, 2]. Interestingly, Pogosta disease has a tendency to cause outbreaks every 7 yr, and the same pattern has been claimed for Ockelbo disease and Karelian fever [2, 3]. In 1981, such an epidemic occurred in Northern Karelia. The clinical data of patients were collected and an analysis of them has now been carried out.

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MATERIALS AND METHODS

Seventy-three patients had a clinical picture strongly suggesting Pogosta disease, and were given a questionnaire which contained specific questions concerning the duration of joint symptoms and the presence of any other symptoms at the time of their first visit. They were examined at onset of disease and 2–3 months later. Serology was performed in the department of virology at the University of Helsinki, and some of the results have been presented earlier [1, 10]. Of the 73 patients, only 60 showed a diagnostic increase to Sindbis virus in the haemagglutination inhibition test. The clinical features of those serologically positive ($\geq$4-fold antibody rise to Sindbis virus antigen) and serologically negative patients are presented separately in Table I, but are discussed together in the text.

RESULTS

Clinical results

The majority of cases occurred in August 1981 (74%) and the rest in September and October. Of the 73 patients, 41 were women and 32 men. The average age at the onset of the disease was 40 yr for both sexes (range 5–68 yr). All patients presented with arthralgia or rash at their first visit.

General symptoms

The clinical symptoms among the 73 patients are given in Table I. Almost all had skin and/or joint symptoms. Only 23% of the patients had fever over 37.5°C. Sixty-four had skin symptoms and in 49 of them the rash was the first sign of disease. The rash was normally small papulous, all the papules being in the same phase (Fig. 1). None of the patients had exanthema on the face, but some had it on the oral mucosa. In some cases, the rash was morbilliform.

TABLE I
Clinical symptoms and findings in 73 patients with Pogosta disease

	Group 1	Group 2
Number of patients	13	60 (serologically confirmed)
Female/male	9/4	32/28
Mean age (yr)	42.3 (range 13–67)	39.6 (range 5–68)
General symptoms		
Rash	10 (77%)	54 (90%)
Mean duration of rash (days)	4	4
Rash as first symptom	7 (54%)	42 (70%)
Fever $>37.5^{\circ}C$	3 (23%)	14 (23%)
Muscle pains	1 (8%)	11 (18%)
Malaise/headache/nausea	6 (46%)	28 (47%)
Retro-orbital ache	1 (8%)	6 (10%)
Joint symptoms		
None	0 (0%)	5 (8%)
Arthralgia	4 (31%)	28 (47%)
Definitive arthritis	8 (62%)	22 (37%)
Severe and prolonged arthritis	1 (8%)	5 (8%)
Number of joints affected		
<2	1 (8%)	7 (12%)
2–5	8 (62%)	30 (50%)
>5	4 (31%)	23 (38%)
Median duration of joint symptoms (months)	1.5 (range 0.1–12)	0.5 (range 0–8)

FIG. 1.—Maculopapular rash on the legs of a female patient with Pogosta disease.

Forty patients reported itching when asked about it. The average duration of the skin symptoms was 4 days.

Other general symptoms were muscle pains in 12 patients. Thirty-four patients suffered from malaise, headache and/or nausea, and seven patients from retro-orbital pain. The main clinical symptoms of the 60 serologically confirmed Pogosta disease patients are shown separately in Table I. Overall, the clinical features in the two groups were almost the same, and a statistical analysis (χ^2) confirmed this impression.

Joint symptoms

The main clinical symptoms were related to the joints. The most common manifestations were swelling and tenderness of the ankle, knee, wrist or fingers, especially the metacarpophalangeal joints.

Thirty patients had definitive swelling and tenderness of the affected joints, and 32 experienced arthralgia severe enough to affect their daily activities. For some of them, the discomfort was severe enough to necessitate the use of non-steroidal anti-inflammatory drugs. Only five patients had no joint symptoms, four of them being under 15 yr of age. Thirty-eight patients (52% of the entire group) had symptoms in 2–5 joints and 27 patients in >5 joints at the same time. The duration of these symptoms varied from 0 to 12 months (mean 1.8 months). Six patients had severe and prolonged joint discomfort in many joints affected with definitive swelling, and active inflammation in the joint and general symptoms that restricted their daily activities. The erythrocyte sedimentation rate (ESR) varied from 1 to 91 mm/h and the C-reactive protein (CRP) was normal in $>90\%$ of all patients. Four patients were positive for rheumatoid factor, one of them being serologically uncertain regarding Pogosta disease. One of the samples positive for rheumatoid factor came from a patient with persisting arthritis, and a diagnosis of rheumatoid arthritis was made later. It must be pointed out, however, that she had already had arthritis a few months before contracting the Pogosta infection. Other serology was not routinely carried out, and results are available for half of the patients. It included tests for antistreptolysin-O (AST), antinuclear, anti-cardiolipin and anti-*Yersinia* antibodies. In two patients, AST was slightly elevated, but in these the serology for Pogosta disease was strongly positive. Antinuclear antibodies were weakly positive in four cases. The joints most affected were the same in both patient groups. The duration of arthritic symptoms in the two groups differs because of the one patient included in Table I who had persisting arthritis for the whole follow-up period of 12 months.

Typical case history

A 55-yr-old previously healthy farmer's wife had been bitten by mosquitoes. A few days later, she developed maculopapular and itchy rash all over her body, except the face. The rash lasted for 4 days and at the same time she had fever up to 37.5°C for 3 days. A few days later, she started to have pains in her joints, especially in the knees. The knee joints were found to be tender, but not swollen or red. Joint symptoms lasted for 2 weeks. She used antihistamine for itching and non-steroidal anti-inflammatory drugs for joint pains. In November, she was seen on a control visit for Pogosta disease and for evaluation. At this time, she had no more symptoms.

DISCUSSION

The present study was carried out in order to characterize in detail the clinical picture of Pogosta disease. The study was made possible since two of the authors have been working in the highly endemic area for over 20 years, during which at least four Pogosta disease outbreaks have been recognized, in 1974, 1981, 1988, 1995. There were only a few cases of Pogosta disease in the years between; the outbreaks of Pogosta disease seem to occur every 7 yr. We had data from Ilomantsi health centre collected from the 1981 outbreak by one of the authors (PK). We also wanted to compare the clinical picture of Pogosta disease with that of Ockelbo disease and Karelian fever [3, 15–17].

Pogosta disease is caused by a virus antigenically related to Sindbis virus [13]. Several studies have demonstrated that Pogosta disease and Ockelbo disease have the same or very closely related aetiological agents, and that these viruses are members of the group A arboviruses [2, 4, 5, 7, 13]. Other mosquito-borne alphavirus infections have been reported from Europe, Africa, Asia and Australia [18]. So far, all attempts to isolate Pogosta virus from whole blood, serum or synovial fluid have been unsuccessful.

The clinical patient data have now been analysed. We found that there is a group of patients who had negative serological findings but a surprisingly clear clinical picture of Pogosta disease. In this study, we divided the patients into two groups: one with positive serological and clinical findings, and the other with uncertain serological findings but positive clinical findings. For antibody determination, haemagglutination inhibition or immunofluorescence had been used [10, 11]. Currently, serology is based on the EIA technique [12–14]. This study was carried out in a remote area by a local physician in 1981 and at that time the serology was carried out by methodology which is no longer appropriate. Another study currently under way will hopefully elucidate the value of the present serology in the diagnosis of Pogosta disease. The main symptoms observed were arthralgia, rash and in some patients fever. Forty-seven per cent of all patients had nausea, malaise or headache. Two clinical features deserve special attention, namely skin and joint symptoms.

The rash of Pogosta disease is described as small papulous and non-itchy [19]. In most cases, the lesions exhibit a vesicle-like formation in the centre. Papules appear equally distributed over the body, except the face. All papules are of the same size and alike, with a diameter from 1 to 3 mm. Thus, the rash is similar to the one reported in Ockelbo disease [2, 19]. In this study group, a suprisingly high number of patients (40; 55%) complained of itching. This can partly be explained by the fact that it was specifically asked about. According to the results of this study, the skin symptoms in Pogosta disease are somewhat different from those described in Ockelbo disease. There is evidence suggesting that these two diseases are closely related, but not the same [7, 14]. For a comparison, the clinical features of our patients and those with Ockelbo disease, as described by Espmark and Niklasson [15], are given in Table II. Future research will clarify whether these conditions are actually identical regarding their aetiopathogenesis and clinical features.

Almost all patients (93%) had joint symptoms. It should be noticed that although it was mostly arthralgia (44%), 8% of the patients had very severe joint symptoms and almost 40% of all patients had polyarthritis. Patients experienced symptoms severe enough to affect their daily routines and some were immobilized for weeks. In one case, a possible rheumatoid arthritis was eventually diagnosed. Pogosta disease is considered to be a benign disease, but in some cases joint symptoms can be severe enough to cause immobilization. We have also tried to contact patients who had chronic arthritis after the control visit, now 15 yr later, but unfortunately it turned out to be impossible. Altogether, our findings regarding the joint symptoms are similar to those in Ockelbo disease and Karelian fever [15–17, 20]. The comparison in Table II suggests, however, that in Pogosta disease joint symptoms last longer.

The question about the value of serological findings in the diagnosis of Pogosta disease is very important. In our study, we found patients with uncertain sero-

TABLE II
Comparison of clinical symptoms in 60 patients with Pogosta disease and 50 patients with Ockelbo disease

	Pogosta disease*	Ockelbo disease†
General symptoms		
Rash	90%	96%
Itchy rash	55%	6%
Mean duration of rash (days)	4	5–7
Fever >38°C	15%	34%
Joint symptoms		
None	8%	6%
Arthralgia	47%	36%
Arthritis	45%	58%
Duration of joint symptoms		
≤1 month	45%	77%
>1 month	55%	23%

*The present material.
†According to Espmark and Niklasson [15].

logical findings, but with a clear clinical picture of Pogosta disease. We feel strongly that serology is, indeed, an important diagnostic criterion, but not an absolute one. Rather, we feel that the diagnosis of Pogosta disease is a clinical one. These observations resemble the results regarding Lyme disease: patients with clinical symptoms and positive PCR results have still been described to have negative serological findings [21]. On the other hand, it is well known that in Pogosta disease, Ockelbo disease and borreliosis, there are positive serological findings in people who have no clinical symptoms or findings at all [22]. It is obvious that the development of clinical symptoms and seroconversion may occur at a different pace. Thus, at the time of the first clinical signs, serology can still be negative.

In conclusion, our study demonstrates that Pogosta disease can cause serious symptoms for a long period. It seems to be closely related to Ockelbo disease, but is not necessarily identical. In order to solve this, further research, including studies of the causative virus, are necessary. We also conclude that although serology is of great importance, the diagnosis of Pogosta disease is a clinical one.

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