Acute Bilateral Carpal Tunnel Syndrome Associated with Human Parvovirus B19 Infection

Kaveh Samii, Pascal Cassinotti, Jean de Freudenreich, Yves Gallopin, Dominique Le Fort, and Hans Stalder

From the Policlinique de Médecine, Department of Community Medicine, Hôpitaux Universitaires de Genève, Geneva; the Institute for Clinical Microbiology and Immunology, St. Gall; and private practice, Geneva, Switzerland

Human parvovirus B19 has been described as a causative agent of erythema infectiosum (a disease common in children), aplastic crisis in patients with hemolytic disorders, and arthralgias and arthritis. Joint involvement may be a prominent clinical feature of parvovirus B19 infection and may last for several weeks. We describe three cases of acute bilateral carpal tunnel syndrome associated with parvovirus B19 infection as evidenced by serological data and, in one case, by detection of parvovirus B19 DNA in blood with use of PCR.

Human parvovirus B19 was first discovered in asymptomatic blood donors [1]. Since then it has been identified as the causal agent of erythema infectiosum (fifth disease), a childhood febrile illness associated with exanthema [2]. Parvovirus B19 infection may trigger aplastic crisis in patients who have hemolytic disorders [3, 4]. The most common features of parvovirus B19 infection in adults are symmetrical peripheral polyarthralgias of sudden onset. Less than one-half of patients with this infection have prodromal symptoms (e.g., myalgia and fever), and the typical rash (slapped cheek) is rarely seen in adults. The number of females with parvovirus B19 infection is four times higher than the number of males with this infection. In general, the joint symptoms associated with parvovirus B19 infection resolve within 2 to 8 weeks, but an infected patient may occasionally present with chronic arthritis [5, 6]. We report three cases of acute bilateral carpal tunnel syndrome associated with parvovirus B19 infection.

Case Reports

Case 1. A previously healthy 49-year-old woman presented to her private physician in December 1992 with transient fever and myalgias. Two days later, swelling of the distal extremities associated with painful paresthesia of the first three digits of both hands was noted. The patient was hospitalized. On examination, the pharynx was hyperemic, and suboccipital lymph nodes were found. Hypoesthesia was noted in the sensory region of the right median nerve, and a positive Tinel's sign was noted on the left. Muscle power was preserved. The wrist was infiltrated with steroids, which led to immediate and definitive amelioration of the symptoms.

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Reprints or correspondence: Professor Hans Stalder, Policlinique de Médecine, Hôpitaux Universitaires de Genève, 1211 Geneva 14, Switzerland.

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Case 2. A 38-year-old woman presented to her private physician at the end of January 1993 with sudden onset of nocturnal arthralgias involving the joints of her elbows, wrists, hands, and feet. She had noted stiffness and numbness of these joints in the morning. Her condition did not improve after she received therapy with antiinflammatory drugs. Her 7-year-old daughter had presented earlier in the month with a rubella-like skin rash. The patient's physical examination revealed mild swelling of the metacarpophalangeal and proximal interphalangeal joints. It was difficult and painful to close her hand and especially to open it. She had decreased sensitivity to a pinprick in the sensory regions of both median nerves. Muscle power was preserved. The acute symptoms gradually subsided after 3 days, and only mild hypoesthesia of the distal phalanx of the third right digit remained 8 weeks later.

Case 3. A 49-year-old woman presented to her private physician with headaches, fever (temperature to 39°C), chills, and nausea. The symptoms, which appeared in the middle of July 1993, spontaneously decreased, and the patient presented 1 week later with high fever, a maculopapular rash involving the face, and painful swelling of the extremities. Physical examination showed bilateral hypoesthesia in the sensory regions of the right and left median nerve associated with swelling of the hands and feet. The symptoms rapidly decreased within a few days, but numbness of the second and third digits persisted for 2 months.

Laboratory Findings

Patients 1 and 3 underwent electromyography 1 week after the onset of acute illness, and patient 2 underwent electromyography 5 weeks after the onset of illness (patient 2 refused to have her right side examined). In all cases, median nerve sensory-motor conduction velocity at the wrist was slow and there were no denervation potentials; in contrast, the other tested nerves did not have any conduction anomalies (table 1).

Various blood samples were analyzed by nested PCR for the presence of parvovirus B19 DNA as previously described

Table 1. Clinical features of and serological findings for three patients with parvovirus B19 infection and acute carpal tunnel syndrome.

	Patient no.		
	1	2	3
Feature			
Age (y)/sex	49/F	38/F	49/F
Known exposures	None	Daughter with rubella-like rash	None
Clinical features			
Fever	+	−	+
Peripheral arthralgia	−	+	+
Myalgia	+	−	−
Swelling of the extremities	+	+	+
Hypoesthesia in the median nerve territory	+	+	+
Rash	−	−	+
Results of EMG (no. of days after onset of symptoms)	+(7)	+(7)	+(35)

	No. of days after onset of symptoms						
Serological data	1	7	18	18	39	4	67
IgM to parvovirus B19	+	+	+	+	+	+	+
IgG to parvovirus B19	−	+	+	+	+	+	+
IgM to rubella	−	NT	NT	−	NT	−	NT
IgG to rubella	+	NT	NT	+	NT	−	NT
IgG to *Borrelia* species	−	NT	−	−	−	−	−
Rheumatoid factor	−	NT	NT	−	NT	−	NT
Antinuclear factor (titer)	<1:80	NT	NT	<1:40	NT	<1:40	NT
Detection of parvovirus B19 in serum by PCR	+	+	+	−	−	−	NT

NOTE. + = present; − = absent; EMG = electromyogram; NT = not tested.

[7]. In brief, a fragment of the gene coding for VP2, the major capsid protein, was amplified after DNA was recovered from the serum by heating. The first amplification consisted of 35 cycles with use of 0.2 m*M* each of the outer primers TJI (direct primer, nucleotide 3775 to 3792), and TJII (reverse primer, nucleotide 3956 to 3975) numbered according to Shade et al. [8]. An aliquot of the reaction product was used as substrate for the second round of amplification, which consisted of 35 cycles with use of 0.2 m*M* each of the inner primers 968 (direct primer, nucleotide 3818 to 3837) and 967b (reverse primer, nucleotide 3920 to 3928). The presence of a 120-bp diagnostic amplicon was detected by agarose gel electrophoresis. Several negative and positive controls were included in each PCR.

The presence of IgM and IgG antibody to parvovirus B19 was tested with a commercial enzyme immunoassay on the basis of the use of recombinant surface proteins of parvovirus B19 (IBL, Parvovirus IgM/IgG ELISA; Gesellschaft für Immunchemie und Immunbiologie MBH, Hamburg, Germany). Rheumatoid factors were eliminated by treating the blood with a rheumatoid factor absorbent.

In each case, IgM antibody to parvovirus B19 was detected in the first serum sample collected after the onset of acute illness. IgG antibody to parvovirus B19 was also detected in the first serum sample collected from patients 2 and 3, whereas it appeared only in a second blood sample from patient 1. Parvovirus B19 DNA was detected in the blood of patient 1 by PCR.

Discussion

The three women described in our report presented with acute bilateral carpal tunnel syndrome that was confirmed by electromyographic studies that showed involvement of the median nerves at the wrist. All patients had joint pains, two had fever, one presented with a maculopapular rash, and one had

been in contact with a child who had an exanthematous illness. All symptoms resolved after a few weeks.

Carpal tunnel syndrome has several causes. *Rubella* virus, *Borrelia* species, *M. tuberculosis,* and other *Mycobacterium* species are the most frequent of these rare infectious causes [9]. We searched for these etiologies and ruled them out either clinically or with use of laboratory tests.

The course of a parvovirus B19 infection is characterized by viremia that lasts ~1 week. The titer of IgM antibody to parvovirus B19 rises at the end of the viremic period and is followed a few days later by the IgG response to parvovirus B19. The appearance of specific symptoms coincides with the appearance of IgG antibody to parvovirus B19. These symptoms may be due to the cytopathogenic effect of the virus since it has been isolated in synovial fluid [10]. An immune-mediated mechanism is also a possible cause of these symptoms. IgM antibody to parvovirus B19 remains detectable for 1–3 months, whereas IgG antibody to parvovirus B19 persists and is considered to confer lifelong immunity. Thus, the level of viremia may be over or below the detection limit of PCR when antibodies to parvovirus B19 are present in the blood. This would explain why the results of PCR were negative for patients 2 and 3.

In the case of patient 1, the positive results obtained by PCR and the seroconversion that occurred are compelling evidence that parvovirus B19 infection was the cause of her symptoms. In the case of the other two patients, the clinical symptoms and the presence of specific IgM antibodies to parvovirus B19 are highly suggestive of parvovirus B19 infection.

To our knowledge, this is the first time that parvovirus B19 infection has been suggested as the causal agent of acute bilateral carpal tunnel syndrome. Faden et al. reported paresthesias in patients with parvovirus B19 infection but attributed them to peripheral neuropathy [11]. The neurological symptoms reported in our paper are most likely due to mechanical entrapment of the median nerves in relation to the acute arthritis, as has been described for carpal tunnel syndrome associated with rubella [12]. The rapid decrease in our patients' symptoms, either spontaneously or after injection with steroids, tends to support this hypothesis. In summary, we believe that parvovirus B19 infection should be considered among the possible etiologies of acute carpal tunnel syndrome.

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