

First European Pediatric Case of Human Granulocytic Ehrlichiosis

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Herein we report on the first confirmed pediatric case of acute human granulocytic ehrlichiosis in Europe. Presentation in this 11-year-old girl was comparable to clinical findings seen in adult European patients with human granulocytic ehrlichiosis; i.e., she had self-limited febrile illness with leukopenia, thrombocytopenia, and elevated serum C-reactive protein concentration. It is of interest that the patient not only had a fourfold change in antibody titer to *Ehrlichia phagocytophila* but also developed antibodies to *Ehrlichia chaffeensis* and that her PCR test result was positive on the third as well as on the 22nd day after the onset of illness, that is, 16 days after spontaneous defervescence.

CASE REPORT

On February 21, 2001, an 11-year-old girl was admitted to the Department of Infectious Diseases, University Medical Center Ljubljana, Ljubljana, Slovenia, with a 3-day history of high fever, fatigue, headache, nausea, and abdominal pain. She had no known chronic illnesses, had not been vaccinated against tick-borne encephalitis (TBE), and had not traveled outside Slovenia. The patient had received a tick bite on her neck 9 days before the onset of the illness, during a trip to the southwestern part of Slovenia. The region is known to be an area of endemicity for TBE and Lyme borreliosis; an adult patient diagnosed recently with proven human granulocytic ehrlichiosis (HGE) had received tick bites in this area. Tick bites in February are highly unusual in this part of Central Europe; however, the winter of 2001 was exceptionally mild. The patient's physical examination was notable for fever (38.8°C), conjunctivitis, erythematous throat, and right upper quadrant abdominal tenderness. Meningeal signs were absent. Initial laboratory findings revealed normal erythrocyte sedimentation rate, serum electrolyte concentrations, and transaminase and alkaline phosphatase activities. The serum C-reactive protein value was 39 mg/liter (normal value, <5 mg/liter), the total leukocyte count was 2.3×10^9 /liter (16% band forms, 28% segmented, 41% lymphocytes, 15% monocytes), and the platelet count was 90×10^9 /liter, while red cell counts were normal. The girl was treated symptomatically. On the third day of hospitalization (sixth day of illness) fever and all other signs and symptoms disappeared. The child remained well during the whole observational period of 2 months; the results of control laboratory examinations were in the normal range.

Indirect fluorescent-antibody assays for immunoglobulin M (IgM) and IgG antibodies to *Borrelia burgdorferi* sensu lato (whole cells of a local isolate of *Borrelia afzelii* were used as an antigen) as well as enzyme-linked immunosorbent assays (Dade Behring) for the presence of TBE IgM and IgG anti-

bodies in acute- and convalescent-phase serum samples were negative. PCR testing of DNA extracted from the leukocyte fraction of blood yielded positive results. Subsequent sequence analysis of the amplified portion (1,256 bp) of the GroESL gene of *Ehrlichia phagocytophila* revealed complete identity to those previously amplified from HGE patients in Slovenia (6). PCR results and serum antibody titers to *E. phagocytophila* (the causative agent of HGE) and *Ehrlichia chaffeensis* (the etiologic agent of human monocytic ehrlichiosis) at the time of acute illness and during convalescence are presented in Table 1. It is of interest that our patient developed a fourfold increase of antibody titer to *E. phagocytophila* but also developed low-titer antibodies to *E. chaffeensis*. The significance of this finding is still unclear, but it probably represents only a low level of cross-reactivity as previously reported from the United States and Europe (1, 6).

Three tick-transmitted ehrlichial diseases were discovered during the last 15 years in the United States: human monocytic ehrlichiosis, caused by *E. chaffeensis*, was reported for the first time in 1987 (7); HGE was first reported in 1994 (3); and the disease caused by *Ehrlichia ewingii* was first reported in 1999 (2). The first confirmed European HGE case was discovered in 1996 in Slovenia (8). More than 600 patients with HGE were reported until 2000, the large majority being from the United States (1). Clinically, HGE is manifested by fever, headache, myalgias, and arthralgias, and it is often accompanied by lab-

TABLE 1. Serum antibody titers to *E. chaffeensis* and *E. phagocytophila* and *E. phagocytophila* PCR findings in an 11-year-old girl from Slovenia

Days from onset of fever (days from tick bite)	Serum antibody titer or PCR result for:			
	<i>E. chaffeensis</i>		<i>E. phagocytophila</i>	
	IgM	IgG	IgG	PCR
3 (12)	Negative	Negative	1:256	Positive
22 (31)	Negative	1:256	>1:4,096	Positive
33 (42)	Negative	1:256	>1:4,096	Negative

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oratory findings such as thrombocytopenia, leukopenia, mildly elevated liver transaminases, and/or elevated serum C-reactive protein concentrations (1). The clinical characteristics in children are assumed to be similar to those in adults (5). However, the clinical information on HGE in children is limited to individual case reports and is completely restricted to data from the United States (4, 5).

Our patient represents the first European child with confirmed HGE. Her presentation was comparable to clinical findings seen in our adult patients with HGE (6), with the exception of abdominal pain, which is probably not specific for HGE in childhood because it is seen quite often also in several other infectious diseases in children but only exceptionally in adults.

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