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Acute Meningoencephalitis as the Sole Manifestation of Q Fever

M. Guerrero[1], J. Gutierrez[2]*, C. Carnero[1], R. Gonzalez-Maldonado[1], C. Maroto[2]

The case of a 25-year old man who presented with meningoencephalitis as the sole clinical manifestation of Q fever is described. Serological studies revealed the presence of IgM and IgG antibodies to *Coxiella burnetii*. The patient responded favourably to a ten-day course of i.v. ceftriaxone and was discharged without any neurological sequelae.

Coxiella burnetii, the causative agent of Q fever, is a rickettsia distributed worldwide that can produce an acute or chronic infection. Q fever is a febrile illness that frequently affects the lungs, endocardium or liver. Severe headache is the most common neurological manifestation, although there is little evidence of serious brain involvement, a very rare complication of this disease (1).

We present a case of acute meningoencephalitis with IgM and IgG antibody titres for *Coxiella burnetii* in serum as the sole clinical manifestation of Q fever with a subsequent excellent recovery.

Case Report. A 25-year-old man who had been suffering from fever, headache and vomiting for ten days was admitted to our hospital. He was treated with erythromycin without improvement. The patient was a university student whose medi-

[1]Servicio de Neurología and [2]Departamento de Microbiología, Hospital Universitario San Cecilio, Universidad de Granada, Avd. Doctor Oloriz s/n, 18012 Granada, Spain.

cal history did not reveal any relevant antecedent events.

On examination the patient was febrile (38.4 °C) and had tachycardia; his blood pressure was normal. The subject's mental state was slightly clouded, and he was amnesic and partially disoriented. A stiff neck and Kernig's and Brudzinski's signs were present. Funduscopy revealed mild papilledema. The patient's gait was ataxic. The rest of the neurological examination was normal. Further tests indicated a hematocrit of 37.4 %, leukocyte count of 14,800/mm^3 (83 % neutrophils, 9 % lymphocytes, 4 % monocytes) and platelet count of 345,000/mm^3. The prothrombin time was 67 %, the partial thromboplastin time 35 seconds, and fibrinogen degradation products were normal. The erythrocyte sedimentation rate was 79 mm in the first hour. ALT was mildly elevated at 0.77 ukat/l (46 U/l), likewise GGT at 3.3 ukat/l (198 U/l); AST and alkaline phosphatase were normal, as was bilirubin. Other biochemical tests were either normal or not relevant. Radiographs of the chest were normal.

A lumbar puncture was performed; the cerebrospinal fluid (CSF) was clear and colourless, with a raised pressure (400 mm of water), and contained 1,600–1,625 leukocytes/mm^3 (80–90 % lymphocytes, 10–20 % neutrophils). The glucose level was normal. Table 1 indicates the CSF/serum albumin ratio (an index of 0.0075 is considered the normal upper limit value; index A), and the CSF antibody titre/serum antibody titre to CSF albumin/serum albumin ratio (a ratio above 0.8 is suggestive of inthrathecal synthesis; index B).

The standard blood culture and CSF cultures to detect bacteria, fungi or mycobacteria were negative. Blood and CSF serological tests were normal for syphilis, *Rickettsia conorii, Cryptococcus neoformans, Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia psitacci,* herpes simplex viruses, varicella-zoster, mumps, measles, rubella, hepatitis A, B, C viruses and HIV.

Table 1 also shows the results of the indirect immunofluorescence test for *Coxiella burnetii* (bioMérieux, Spain) to detect IgG in blood and CSF (Phase II) and IgM in CSF. IgM was detected in blood with the Absorbent RF test (Behring Institute, Spain). Serial electroencephalographic readings revealed paroxysms of bilateral high voltage delta waves in the frontal lobes, with theta waves in the left frontotemporal hemisphere. Contrast-enhanced computerized tomography showed normal.

A ten-day treatment with ceftriaxone i.v. was initiated after admission because meningitis was suspected. The clinical, CSF and electroencephalographic findings of the patient returned to normal, and he was discharged without any neurological sequelae. The patient continued his university studies with no further problems.

Discussion. Neurological manifestations related to Q fever are very uncommon. Severe headache with aseptic meningitis and encephalitis occur in some cases, and a variety of other manifestations, including extrapyramidal disease, dementia, abducens paralysis and optic neuritis, have been reported (1–8). Our patient had a febrile illness with acute meningoencephalitis and abnormal liver and coagulation tests. The serological test confirmed the etiology of *Coxiella burnetii.*

The entry of an infectious agent into the central nervous system generally results in a local antibody response, which may be detected by sensitive test methods. However, infection may also originate from passive transfer of serum proteins through a damaged blood-brain barrier, as is frequently seen in the initial phase of meningitis, or as a result of the process of CSF extraction itself. Therefore, in order to determine whether the antibodies have been synthesized inside the central nervous system, it is necessary to previously confirm the correct functioning of the blood-brain barrier and the time of CSF extraction. Using indexes A and B, we were able to ascertain that infection was due to a reactive affec-

Table 1: Titres of antibodies to *Coxiella burnetii* in serum and CSF and indexes (see text).

	At admission	Day 10	Day 40	Month 5
IgM serum	+	+	+	–
IgG serum	–	1/320	1/320	1/640
IgM CSF	–	–		
IgG CSF	–	1/80		
Index A	0.99	0.90		
Index B	0	0.3		

tion of the central nervous system (immunomediated leucoencephalitis). The IgM titre in CSF was negative and the two different indexes showed the blood-brain barrier to be damaged, findings that support this hypothesis. Other authors have suspected central nervous system infection (7, 9, 10), although little evidence exists of serious brain involvement in Q fever. However, the clinical course of the infection in our patient, as well as in other cases reported (3, 6), was favourable regardless of treatment with ineffective antibiotics. These cases illustrate that meningoencephalitis is a possible clinical manifestation of *Coxiella burnetii* infection.

We conclude that acute meningoencephalitis due to *Coxiella burnetii* should be suspected and its presence or absence confirmed with appropriate serological studies in all cases of uncertain neurologic infections.

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Invasive Infection with *Mycobacterium genavense* in Three Children with the Acquired Immunodeficiency Syndrome

D. Nadal[1]*, R. Caduff[2], R. Kraft[4], M. Salfinger[3], T. Bodmer[5], P. Kirschner[7], E.C. Böttger[7], U.B. Schaad[6]

Three children with human immunodeficiency virus infection and invasive infection with *Mycobacterium genavense* are reported. Fever spikes, abdominal cramps and distension, diarrhea or ileus, and anemia were the predominant symptoms in the severely immunodeficient patients (CD_4 lymphocytes < 0.04 x 10^9/l). Numerous acid-fast bacilli were readily detectable by microscopy in stool samples and in lymph node biopsies, but cultures for mycobacteria remained negative. *Mycobacterium genavense* should be sought when invasive non-tuberculous mycobacteriosis is suspected and mycobacterial cultures from blood or other sites show limited growth. Multiple-drug regimens including amikacin, ethambutol, rifampin, and clarithromycin may be of benefit in controlling the infection, as observed in two patients.

Nontuberculous mycobacteria are infrequent pathogens in the immunocompetent host (1) but contribute substantially to increased morbidity and mortality in patients with advanced acquired immunodeficiency syndrome (AIDS) (2–4). Organisms of the *Mycobacterium avium* complex (MAC) have been identified in most cases as the causative agent of disseminated nontuberculous mycobacterial infection in AIDS patients (2–4).

We report here on the first three cases of pediatric AIDS with invasive infection due to *Mycobac-*

[1]Department of Pediatrics, Division of Immunology/Hematology, [2]Department of Pathology, Institute of Clinical Pathology, and [3]Department of Medical Microbiology, University of Zurich, Steinwiesstrasse 75, CH-8032 Zurich, Switzerland.
[4]Department of Pathology, [5]Institute of Medical Microbiology, and [6]Department of Pediatrics, University of Berne, Berne, Switzerland.
[7]Institute of Medical Microbiology, Medical School Hannover, Hannover, Germany.