The condition was self-limited. Cultures for streptococci were not performed for the partners, who were not described as having systemic complaints, in this study.

Carlino and Calzavara [2] described a case of "chronic urethritis" with recurrent attacks of cellulitis. Chlamydiae were isolated at the onset, and group G streptococci were isolated each time the cellulitis recurred. No cultures were performed for the female partner.

We believe that the two cases of penile cellulitis described herein were due to each female partner's vaginal streptococcus. In both cases, the women were asymptomatic. Both men were symptomatic, with penile swelling and erythema and marked tender inguinal adenitis. Both were febrile and responded to treatment with amoxicillin. The patient in case 1 had a recurrence of his infection, and he and his partner were retreated. Both patients claimed to be monogamous.

We believe that this report represents the first description of streptococcal penile cellulitis that occurred following vaginal intercourse. The recurrent nature of the first case underlines the need to counsel such patients when the diagnosis is first made. Perhaps some cases previously described as idiopathic penile edema represent a mild form of streptococcal cellulitis. In situations where penile edema associated with inguinal adenitis and a systemic illness are encountered, cultures of the female partner's vaginal secretions may help elucidate the etiology of the condition, and appropriate therapy may be instituted for both individuals.

Jack Mendelson and Mark Miller
Department of Microbiology, The Sir Mortimer B. Davis—Jewish General Hospital, and Division of Infectious Diseases, McGill University, Montreal, Canada

Figure 1. Penile edema with erythema of the skin due to the Streptococcus pyogenes that occurred following sexual intercourse.

and his wife were treated with amoxicillin, and the patient's condition improved within 1 week.

In previous reports of penile edema, the causes were largely unclear. In an early report [4], the "coexisting penile disease" included urethritis and/or an infected skin lesion, scabies, and trauma. In 52% of cases, inguinal adenopathy was present, and his wife were treated with amoxicillin, and the patient's condition improved within 1 week.

In previous reports of penile edema, the causes were largely unclear. In an early report [4], the "coexisting penile disease" included urethritis and/or an infected skin lesion, scabies, and trauma. In 52% of cases, inguinal adenopathy was present, and his wife were treated with amoxicillin, and the patient's condition improved within 1 week.

Systemic Paradoxical Response to Antituberculous Drugs: Resolution with Corticosteroid Therapy

The term paradoxical expansion of tuberculosis (TB) refers to an infrequent syndrome characterized by the development of previously nonexistent TB lesions or worsening of preexistent lesions during antituberculous treatment [1]. To our knowledge, systemic paradoxical responses to therapy have not been previously reported. We describe an immunocompetent patient who developed a severe, life-threatening systemic syndrome while receiving treatment for miliary tuberculosis.

A 28-year-old man who had previously been in good health was admitted to our hospital because of a 2-week history of fever (temperature, 38.5°C–39°C), cough, and constitutional symptoms. He had also had lumbar pain for the last 2 months. Findings on physical examination were unremarkable except for the presence of fever (temperature, 39°C).

The initial results of laboratory studies are presented in table 1. Radiographs of the chest showed a miliary pattern. A Ziehl-
Neelsen stain of sputum disclosed numerous acid-fast bacilli, and 2 weeks later, an isolate of Mycobacterium tuberculosis that was susceptible to isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin was recovered. A Mantoux skin test was not performed. A CT scan of the lumbar spine revealed spondylitis at L2—L3 and a right psoas muscle abscess. Bed rest and standard therapy with isoniazid, rifampin, and pyrazinamide were prescribed. The patient’s fever resolved 3 days later, with general improvement in his condition.

Two weeks later, the fever (temperature, 40°C) reappeared; during the following 8 weeks the patient lost 15 kg in body weight and developed multiple cervical, axillary, and inguinal lymphadenopathies (some of which spontaneously drained); massive enlargement of the liver and spleen, which were palpable 5 cm and 4 cm, respectively, below the costal margin; and anemia requiring transfusion of RBCs. He also developed pleural and pericardial effusions in association with clinical and echocardiographic signs of cardiac tamponade.

Stains and cultures of the pericardial fluid (protein level, 3.8 g/dL; lactate dehydrogenase level, 215 U/L; and WBC count, 700/mm³ with 90% lymphocytes) were negative. Examination of a lymph node biopsy specimen revealed necrotizing granulomas with numerous acid-fast bacilli, and M. tuberculosis with the same susceptibility pattern as the previous isolate was recovered from the specimen. A repeated CT scan showed resolution of the psoas abscess. A Mantoux skin test was positive (induration, 25 mm, with central necrosis). A test for antibodies to HIV, which was repeated 6 months later, was negative. No other immunodeficiency was found.

Intravenous methylprednisolone (40 mg b.i.d.) was added to the antituberculous regimen, which remained unchanged. The patient’s fever resolved 2 days later, and the rest of the signs and symptoms progressively subsided. After this initial improvement in his condition, prednisone was administered orally, and therapy with this agent was tapered during the next 2 months. Therapy with isoniazid and rifampin was continued for 16 months (treatment with pyrazinamide was continued for the first 4 months). Thirty-six months later, the patient remained asymptomatic.

Paradoxical responses to antituberculous treatment have classically been described in patients with TB that is localized to the lymph nodes and in those with intracranial tuberculomas, adult respiratory distress syndrome, or worsening lung lesions. The cases share some intriguing features that include appearance or worsening of the TB lesions during chemotherapy and when the patient’s condition is otherwise improving, and frequent association with conversion or enhanced skin test reactivity. Our patient’s condition initially improved after he received therapy for miliary TB; however, severe, life-threatening systemic illness developed 2 weeks later. The addition of high-dose steroid therapy resulted in resolution of his lesions. Poor compliance with therapy can be ruled out as a cause of this paradoxical response because the patient took his medication under direct supervision in the hospital. The antituberculous treatment remained unchanged, so drug resistance, malabsorption, or adverse effects are highly improbable.

It is difficult to explain why our patient had a systemic response instead of the usual localized response. These responses are believed to be immune mediated; a diminished immune cellular response is common in miliary TB. It has been hypothesized that a predominance of type 2 T helper cell (Th2) activity is the basis of such diminished cellular response [2]. Effective therapy that drastically reduces bacterial load would stimulate an intense Th1-mediated hypersensitivity reaction, leading to a mixed Th1 and Th2 response that would cause tissue damage.

Corticosteroids, which are known to inhibit Th1 activity and TNF-α production and stimulate Th2 cell activity [3], could contribute to regulation of the immune response in paradoxical expansions of TB. Corticosteroid therapy is currently recommended in cases of TB, such as tuberculous meningitis or tuberculous pericarditis, in which some of the damage is thought to be immune mediated. We believe that steroid therapy might also be beneficial in cases of systemic paradoxical expansion of TB.

### References

Extreme Hyperferritinemia in Patients Infected with Human Immunodeficiency Virus Is Not a Highly Specific Marker for Disseminated Histoplasmosis

Patients infected with HIV constitute 16%–36% of individuals with serum ferritin (SF) levels of >1,000 ng/mL [1, 2]. Kim et al. [3] have suggested that a serum ferritin level of >10,000 ng/mL in an HIV-infected patient is a highly specific marker for disseminated histoplasmosis and is an indication for empirical amphotericin therapy. We reviewed our institutional experience with patients who were infected with HIV and had extreme hyperferritinemia.

Table 1. Summary of data for HIV-infected patients with serum ferritin levels of >10,000 ng/mL.

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Age (y)/gender</th>
<th>Race</th>
<th>Level of serum ferritin (ng/mL)</th>
<th>Concurrent infection*</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCMC</td>
<td>40/F</td>
<td>African American</td>
<td>13,006</td>
<td>Clostridium difficile colitis</td>
</tr>
<tr>
<td>UCMC</td>
<td>29/M</td>
<td>African American</td>
<td>&gt;30,000</td>
<td>Histoplasma capsulatum</td>
</tr>
<tr>
<td>UCMC</td>
<td>36/M</td>
<td>African American</td>
<td>13,030</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>UCMC</td>
<td>30/M</td>
<td>African American</td>
<td>&gt;30,000</td>
<td>H. capsulatum</td>
</tr>
<tr>
<td>UCMC</td>
<td>39/M</td>
<td>Caucasian</td>
<td>16,123</td>
<td>H. capsulatum</td>
</tr>
<tr>
<td>UCMC</td>
<td>39/M</td>
<td>Caucasian</td>
<td>20,046</td>
<td>C. difficile colitis, cytomegalovirus colitis</td>
</tr>
<tr>
<td>UCMC</td>
<td>34/M</td>
<td>African American</td>
<td>16,363</td>
<td>Mycobacterium avium–Mycobacterium intracellulare</td>
</tr>
<tr>
<td>CVAMC</td>
<td>44/M</td>
<td>African American</td>
<td>10,282</td>
<td>M. tuberculosis</td>
</tr>
</tbody>
</table>

* All infections were disseminated unless otherwise indicated.

Their SF levels were >10,000 ng/mL. Three patients had disseminated histoplasmosis, two had disseminated tuberculosis, two had Clostridium difficile colitis (one had concurrent cytomegalovirus colitis and intestinal Kaposi’s sarcoma), and one had disseminated Mycobacterium avium–Mycobacterium intracellulare infection. All but two of the patients were African-American. The mean SF level was higher for patients with disseminated histoplasmosis than for the other patients (>25,374 ng/mL vs. 14,545 ng/mL, respectively), but this difference was not statistically significant (P = .10; Mann-Whitney test). Although the proportion of African Americans in this cohort of patients (75%) was greater than it is in the overall HIV-infected population observed at the University of Cincinnati Medical Center (22%), this difference is also not statistically significant (P = .13; Fisher’s exact test).

Our results suggest that SF levels of >10,000 ng/mL in HIV-infected patients are a nonspecific indicator of significant superimposed infection, rather than a specific marker for a specific clinical syndrome. Elevated SF levels in general appear to be a marker for relatively advanced HIV disease with low CD4 cell counts, the presence of opportunistic infections, and limited survival [4, 5], so the finding that high SF levels are nonspecific markers is not unexpected. Our results suggest that an SF level of >10,000 ng/mL in an HIV-infected patient should prompt an aggressive search for a specific infection; however, since we observed this finding only in hospitalized, febrile HIV-infected patients, it is unclear whether this laboratory test result would add anything to the evaluation already indicated by the patient’s clinical circumstances.

Stacey W. McKenzie and Robert T. Means, Jr. AIDS Clinical Trials Unit and Diagnostic Hematology Laboratory, Divisions of Infectious Diseases and Hematology/Oncology, University of Cincinnati College of Medicine, and Department of Veterans Affairs Medical Center, Cincinnati, Ohio

During the period 1 July 1992–30 June 1996, 7,392 SF determinations were performed by the Diagnostic Hematology Laboratory, University of Cincinnati College of Medicine (Cincinnati). On one or more occasions, 26 patients were found to have SF levels of >10,000 ng/mL. Seven of these patients were infected with HIV. An eighth HIV-infected individual with SF levels of >10,000 ng/mL was identified from the records of the Hematology/Oncology Section of the Cincinnati Veterans Affairs Medical Center.

The records of these patients were reviewed at the time that SF levels were determined, and the data are summarized in table 1. All patients were hospitalized with febrile illnesses at the time that of Cincinnati Medical Center (22%), this difference is also not statistically significant (P = .13; Fisher’s exact test).

Our results suggest that SF levels of >10,000 ng/mL in HIV-infected patients are a nonspecific indicator of significant superimposed infection, rather than a specific marker for a specific clinical syndrome. Elevated SF levels in general appear to be a marker for relatively advanced HIV disease with low CD4 cell counts, the presence of opportunistic infections, and limited survival [4, 5], so the finding that high SF levels are nonspecific markers is not unexpected. Our results suggest that an SF level of >10,000 ng/mL in an HIV-infected patient should prompt an aggressive search for a specific infection; however, since we observed this finding only in hospitalized, febrile HIV-infected patients, it is unclear whether this laboratory test result would add anything to the evaluation already indicated by the patient’s clinical circumstances.

Stacey W. McKenzie and Robert T. Means, Jr. AIDS Clinical Trials Unit and Diagnostic Hematology Laboratory, Divisions of Infectious Diseases and Hematology/Oncology, University of Cincinnati College of Medicine, and Department of Veterans Affairs Medical Center, Cincinnati, Ohio
References


Diagnosis of Cytomegalovirus Meningoencephalitis by Polymerase Chain Reaction in an Immunocompetent Infant Who Recovered After Treatment with Ganciclovir

Cytomegalovirus (CMV) infection of the CNS is rarely observed in immunocompetent infants after the first month of life [1]. Until recent molecular techniques became available, this infection was diagnosed exclusively on the basis of the results of CSF culture and of immunohistochemical studies of a brain biopsy specimen. The outcome of this infection was poor in most instances but improved when ganciclovir became available. We describe a patient with CMV encephalitis who recovered after receiving treatment with ganciclovir.

A 6-week-old boy was born in the city hospital of Sint Nicolas after a normal term delivery. His mother had been treated with amoxicillin/clavulanic acid for postpartum endometritis; her bacterial cultures were negative. The infant was breast-fed during the first week of life. From the age of 5 weeks, convulsions of the right arm and leg were noted; these convulsions evolved to generalized convulsions.

Laboratory investigations at the age of 5 weeks revealed a normal complete blood cell count and an increased level of C-reactive protein (25 mg/L). Examination of the CSF revealed a WBC count of 2/mm³, an increased protein level (472 mg/dL), and a low glucose level (3 mg/dL). No C-reactive protein was found in CSF, and bacterial cultures were sterile. The serum CMV IgM titer was 1.5 AU/mL (positive, >0.5 AU/mL), and the CMV IgG titer was 73.4 AU/mL (immune, >15 AU/mL).

The patient’s clinical condition did not improve after iv treatment with cefotaxime, dexamethasone, and phenobarbital was administered, and the infant was transferred to our hospital. A physical examination revealed fever (temperature, 38°C), generalized hypotonia, and frequent myoclonic convulsions of the right arm. The WBC count and serum C-reactive protein level were within normal limits. Examination of the CSF revealed a WBC count of 940/mm³ (47% monocytes, 27% lymphocytes, 24% neutrophils, and 4% Zolo plasma cells) and confirmed the high protein (708 mg/dL) and low glucose (2 mg/dL) concentrations. Antibiotic treatment consisted of cefotaxime (50 mg/kg every 6 hours), ampicillin (25 mg/kg every 6 hours), and a 4-day course of tuberculostatic drugs for possible bacterial meningitis.

A CT scan of the brain showed ventricular dilatation and a periventricular low-density lesion in the deep white matter of the right parieto-occipital region that was confirmed by an MRI scan. Bacterial and serial viral cultures (including those for CMV) of urine, saliva, and CSF as well as PCR for detection of herpes simplex in the CSF remained negative. An electroencephalogram showed bilateral high voltage paroxysmal discharges. The patient had progressive hydrocephaly and protracted convulsions. Nine days after admission, cultures of saliva yielded CMV. On day 11, CMV was detected in the CSF by PCR (this procedure was previously described by Bale et al. [2]).

Antibiotic treatment was stopped, and therapy with ganciclovir (5 mg/kg every 12 hours) was started. No side effects were observed during 31 days of treatment. During antiviral treatment, the convulsions disappeared, CSF values progressively normalized, and the epileptic discharges on the electroencephalogram disappeared. The child had no neurologic impairments at the age of 3 years. Serum CMV IgM antibodies were not detected 8 weeks postpartum, although CMV IgG antibodies were detected in the mother. The patient’s immunoglobulins, IgG subclasses, and T cell subsets were normal; antibodies to HIV were not detected.

In our patient’s case, the diagnosis of CMV meningoencephalitis was suggested by the periventricular lesion found on the CT and MRI scans, the CSF findings, and the positive specific serum IgM titers; however, this diagnosis was questioned because serial viral cultures of urine, saliva, and CSF remained negative and because CSF findings were compatible with bacterial meningitis. CSF findings in immunocompetent patients with CMV encephalitis are variable, and the absence of viruria does not rule out CNS infection [3]. Recently, identification of viral DNA in CSF by PCR, as was done in our case, has proved to be a reliable marker of CNS involvement [4] and has replaced more cumbersome and invasive methods [5].

Since no cultures were performed in the first 2 weeks of life, the etiology of our patient’s infection remains uncertain. The absence of periventricular calcifications suggests a postnatal infection or a congenital infection during late pregnancy. In the event of a congenital infection, the absence of viruria and generalized infection and the regression of the neurological symptoms would be unusual. It is unlikely that our patient acquired CMV infection postnatally through breast milk since he was nursed for a short period; like nosocomial infection, CMV infection acquired postnatally usually remains asymptomatic [1, 6]. Although ganciclovir therapy is not efficacious in AIDS patients, it has been shown to be efficacious in immunocompetent patients with CMV encephalitis [3, 5, 7].

The present case illustrates that CMV encephalitis should be considered in the differential diagnosis for patients with protracted convulsions even if CSF findings suggest bacterial infection and viral cultures remain negative. Our case highlights the value of PCR for establishing the diagnosis of CMV encephalitis and demonstrates that immunocompetent patients with this infection may be successfully treated with ganciclovir.

Reprints or correspondence: Dr. Ludo M. Mahieu, Department of Pediatrics, University Hospital of Antwerp, Wijnjekerstraat 10, B-2650 Antwerp, Belgium.

Clinical Infectious Diseases 1997;24:520–1
© 1997 by The University of Chicago. All rights reserved.
1058-4838/97/2403—0041$02.00