Pneumocystis carinii Infection Presenting as an Intra-Abdominal Cystic Mass in a Child with Acquired Immunodeficiency Syndrome

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We describe the case of a pediatric patient with acquired immunodeficiency syndrome (AIDS) with an unusual large, fluid-filled intra-abdominal cystic lesion in which Pneumocystis carinii trophozoites were identified. Extrapulmonary P. carinii infection should be considered in the differential diagnosis of an intra-abdominal cystic mass in a child with AIDS.

A 14-year-old girl with perinatally acquired HIV type 1 (HIV-1) infection presented at Bellevue Hospital in New York with a 3-day history of worsening diffuse abdominal pain and fever. She had experienced an 11.4-kg weight loss over the course of a 1-month period, during which time she had complained intermittently of vague abdominal discomfort, persistent anorexia, and early satiety. One episode of esophageal candidiasis was noted as the only opportunistic infection in her medical history. She had been treated unsuccessfully with various antiretroviral regimens, including several protease inhibitors. The latest regimen, which included efavirenz, lamivudine, and didanosine, had failed because of poor adherence. Trimethoprim-sulfamethoxazole (TMP-SMX) had been prescribed for this patient as Pneumocystis carinii prophylaxis for many years, but she was compliant only intermittently. The patient later admitted that she had not taken TMP-SMX at all for at least 8 weeks before the onset of the presenting symptoms. On the day of admission, the patient appeared mildly cachectic and was in moderate distress. She had a temperature of 38.5°C. The physical examination was remarkable for abdominal tenderness in the periumbilical region. The abdominal wall was not distended and did not show rebound tenderness or guarding, and bowel sounds were present. Neither abdominal masses nor hepatosplenomegaly were appreciated. Laboratory tests showed a hemoglobin level of 8.5 g/dL, a platelet count of 307,000 platelets/mm³, and a WBC count of 1900 cells/mm³, with 54% polymorphonuclear neutrophils, 15% band forms, 25% lymphocytes, and 6% monocytes. The serum electrolytes, blood urea nitrogen, calcium, amylase, lipase, liver enzymes, and serum bilirubin levels were within normal limits. The T lymphocyte profile revealed an absolute lymphocyte count of 475 lymphocytes/μL, a CD4⁺ count of 1 cell/μL (0.3%), and a CD8⁺ count of 123 cells/μL (26%). Her HIV RNA level was 25,000 copies/mL of plasma. CT of the abdomen was notable for a large (13-cm), fluid-filled complex cystic mass in the left upper quadrant and areas of focal low attenuation in the spleen (figure 1). A cannula was percutaneously placed into this cystic lesion, and ~800 mL of brown fluid was drained. Initial diagnostic analysis showed a hematocrit of 7%, a WBC count of 1000 cells/mm³, an amylase level of 1000 U/mL, a lactate dehydrogenase level of 2093 U/mL, and a protein level of 3.1 g/dL. Cytologic examination, which included Gomori’s methenamine silver stain,

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Figure 1. CT of the abdomen of a 14-year-old HIV-infected girl, at time of presentation with abdominal pain and fever. CT demonstrated a 13-cm complex cystic, predominantly homogeneous, low-attenuation mass, with Hounsfield measurements consistent with fluid in the left upper quadrant, compressing the stomach. The mass was adjacent to the medial aspect of the spleen, and there were areas of low attenuation in the spleen.
revealed no unusual findings. Gram and acid-fast stains—as well as bacterial, mycobacterial, and fungal cultures—failed to reveal any pathogen. Subsequent ultrasound-guided biopsy of the spleen in an area of decreased echogenicity revealed spindle-cell proliferation and focal necrosis. Gomori’s stain of the biopsy material was negative. Because of persistent remittent abdominal pain and daily intermittent fever (temperature of 39.5°C–40.0°C), an exploratory laparotomy was performed. Numerous abscess cavities located superior to the spleen and extending medially were found and drained. The spleen itself was described as unremarkable. Histopathologic examination of a biopsy specimen from one of the abscess walls demonstrated necrotizing granulomas and collapsed cavitary lesions surrounded by extensive fibrosis and granulation tissue, with signs of acute and chronic inflammation as well as calcifications.

Gomori’s methenamine silver stain revealed \( P. \text{carinii} \) organisms within the necrotizing granulomas. Postoperative treatment with iv TMP-SMX (20 mg/kg/day) was initiated. The patient’s fever subsided after 2 days. After 8 weeks of iv therapy, the patient was discharged home with an oral regimen of TMP-SMX (5 mg/kg/day), which was subsequently complicated by the development of a hypersensitivity skin reaction. A repeat CT scan at the time of discharge revealed the residual cyst, with its wall calcified and punctate high-attenuation densities in the postero medial aspect of the spleen, possibly representing focal calcifications (figure 2). A “mega highly active antiretroviral therapy”–like regimen that included 7 antiretroviral drugs was begun, which resulted in an undetectable HIV plasma RNA level and a significant increase in CD4\(^+\) cells (211 cells/mm\(^3\); 26%). As of the writing of this report, the patient is well and free of relapse, 14 months after initial presentation, and is maintained on a prophylactic regimen with atovaquone.

At the time the diagnosis was made, a sample of the fluid originally drained from the intra-abdominal cyst, which had been stored at \(-70°C\), was submitted to the parasitology research laboratory at New York University School of Medicine for further investigation. By use of a highly sensitive isolation and purification method, described elsewhere [1], \( P. \text{carinii} \) was identified. In brief, 5 mL of drained fluid was mechanically homogenized with a Dounce homogenizer. Large debris was removed by centrifugation at 32 \( g \) for 5 min. The cell pellet was isolated from the supernatant by centrifugation at 5000 \( g \) for 10 min. Host DNA was removed by resuspension of the pellet in 10 mL of homogenizing buffer containing 0.10% DNase I type IV and incubation at 37°C for 10 min. The purified cells were washed 3 times in a buffer (containing 2.68 mM KCl, 1.47 mM \( \text{KH}_2\text{PO}_4 \), 51.1 mM \( \text{Na}_2\text{HPO}_4 \), 7.43 mM \( \text{NaH}_2\text{PO}_4 \), 62 mM \( \text{NaCl} \), 0.05 mM \( \text{CaCl}_2 \), and 0.05 mM \( \text{MgCl}_2 \)) to remove the digestion products. Citrate and dithiothreitol were included to help dissociate clumps of \( P. \text{carinii} \), thus facilitating identification on Giemsa-stained smears [2]. The isolated \( P. \text{carinii} \) was subsequently cultured for 2 weeks, using a culture system that was recently described elsewhere [2]. \( P. \text{carinii} \) was confirmed in originally drained cyst fluid and in culture by PCR, using primers that amplify the mitochondrial rRNA locus [3]. Sequencing of the amplified product identified \( P. \text{carinii} \) forma specialis \( \text{hominis} \).

 Whereas intra-abdominal cystic lesions located within the retroperitoneum in children and adolescents usually are of renal origin, intraperitoneal cystic masses can originate from various organs, including the ovaries, liver, biliary tract, omentum, mesentery, intestines, and pancreas. Such masses most commonly represent anomalies of development or neoplasms [4]. In patients with HIV-1 infection who develop AIDS, however, the differential diagnosis of intra-abdominal masses includes mainly mycobacterial or fungal infection, lymphoproliferative disease, Kaposi’s sarcoma, smooth-muscle tumors, and \( P. \text{carinii} \) infection. On abdominal CT, such lesions present as lymph node enlargement, hepatop- or splenomegaly, gastrointestinal mass or wall thickening, and low-attenuation lesions in the liver or spleen [5]. Extrapulmonary \( P. \text{carinii} \) infection (EPC) presenting as a large intra-abdominal cystic lesion has not, to our knowledge, been described elsewhere. Hence, the current case is a unique clinical presentation of a \( P. \text{carinii} \) infection.

Before the HIV-1 epidemic, EPC was observed infrequently; only 16 cases of non–HIV-related EPC in adults and children were reported from 1954 through 1996 [6]. Four of the children in that group had congenital hypogammaglobulinemia, 1 child had thymic alymphoplasia, and underlying conditions were unknown in 2 children [6–8].
The HIV-1 epidemic was accompanied by a dramatic increase in cases of *P. carinii* pneumonia (PCP), and reports of a total of 90 cases of EPC in HIV-1–infected adults and 1 case in an HIV-1–infected child have been published subsequently [6, 9]. The overall incidence of EPC among HIV-1–infected individuals was estimated to be 0.06%–2.5% by a number of studies [6]. EPC has been described in almost every organ as part of a disseminated infection, with or without involvement of the respiratory tract. Lymph nodes, spleen, liver, and bone marrow are most commonly involved [6–8]. In patients who are not infected with HIV-1, EPC is infrequently recognized preterm, unless it was associated with disseminated disease with concurrent PCP [7]. In contrast, HIV-infected patients with EPC often present with symptoms that are referable only to the affected organ or tissue, without concurrent or prior PCP [6]. Similarly, our patient presented with clinically apparent tissue involvement and either absent or clinically insignificant pulmonary involvement.

Autopsy findings indicate that dissemination of the infection most likely occurs by direct spread or by hematogenous or lymphatic routes [6, 7]. Studies in animal models in which PCR assays were used have shown that extrapulmonary dissemination of *P. carinii* during the course of pneumocystosis is a common phenomenon [10]. Hence, the intra-abdominal focus in our patient may have developed as part of a disseminated *P. carinii* infection, with seeding to the peritoneal cavity coincident with or extending from a splenic focus. Even though we were unable to identify *P. carinii* in biopsy material from the spleen, CT findings in our patient of focal hypodense splenic lesions, which eventually calcified in a punctate fashion, correspond well with CT findings in cases of EPC reported elsewhere [11].

In the current case, the diagnosis was established only after exploratory laparotomy, by demonstration of *P. carinii* cysts in the abscess wall using Gomori’s methenamine silver stain. The initial routine examination of the cyst fluid did not find *P. carinii*. The preparation of the sample, including concentration of the material by centrifugation and preparation of a cell block, followed by staining with Gomori’s stain, was not sufficient to isolate the rare *P. carinii* organisms. Only the application of a more intensive purification method allowed identification of *P. carinii* by Giemsa stain in the originally drained cyst fluid. 

*P. carinii* infection was subsequently confirmed by the successful cultivation of *P. carinii*, as well as by PCR and sequence analysis identifying *P. carinii hominis*. Thus, contamination with the rat strain of *P. carinii* that is commonly used in this laboratory was excluded. The capability to multiply *P. carinii* by an axenic cultivation system was only recently achieved; its potential clinical application may be the detection and characterization of drug resistance in clinical isolates [2]. Questions about *P. carinii* strains that are resistant to TMP-SMX have been raised repeatedly in other reports of patients with EPC who responded suboptimally to TMP-SMX [9]. Because our patient promptly showed clinical improvement with TMP-SMX, drug susceptibility testing was not done. In reports published elsewhere, splenectomy has been described as a treatment modality for patients with EPC and splenic involvement [12]. Our experience suggests that this is not always necessary and that a trial of medical treatment with effective antipneumocystis agents should be first attempted.

In summary, this is the first reported case of EPC presenting as a large intra-abdominal cystic lesion and the second reported case of EPC in a child with AIDS. *P. carinii* infection should be considered in the differential diagnosis of an intra-abdominal cystic mass in an HIV-infected child with severe immune dysfunction. In patients who are at risk for *P. carinii* infection and who have undiagnosed extrapulmonary lesions, more-sensitive methods of isolation and detection of *P. carinii* in extrapulmonary samples may be useful and may lead to a more rapid diagnosis and obviate the need for more-invasive procedures.

References