CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL



# Case 5-2012: A 39-Year-Old Man with a Recent Diagnosis of HIV Infection and Acute Psychosis

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N Engl J Med 2012;366:648-57.


## PRESENTATION OF CASE

*Dr. Carlos Fernandez-Robles:* A 39-year-old man with a recent diagnosis of human immunodeficiency virus (HIV) infection was transferred to this hospital from another hospital because of fever, sweats, and psychosis.

The patient had been well until 4 months before admission, when fevers with temperatures up to 40.6°C, night sweats, and chills developed. During the next 3 months, anorexia, nonproductive cough, and unintentional weight loss (7 to 14 kg) occurred, associated with early satiety, epigastric burning that improved with eating, and abdominal pain that was intermittent, mild, and crampy. Two courses of antibiotics were reportedly administered, without improvement.

Six days before admission, the patient was seen in the emergency department at the other hospital. The evaluation was reportedly negative; a skin test for tuberculosis was administered, and he was discharged. The next day, he saw his internist. Computed tomography (CT) of the abdomen, after the administration of contrast material, revealed a thick-walled mass near the duodenum (7 cm by 2.2 cm, with air in its center), scattered lymph nodes near the porta hepatis, a thickened gallbladder wall, and mild splenomegaly (13.5 cm). The patient was admitted to the other hospital.

On examination, the patient was alert, oriented, cooperative, and thin, with shaking chills. The temperature was 38.5°C, the blood pressure 135/76 mm Hg, the pulse 106 beats per minute, the respiratory rate 20 breaths per minute, and the oxygen saturation 93% while he was breathing ambient air. There was mild epigastric and right-upper-quadrant tenderness, with no induration at the site of the skin test for tuberculosis. The hematocrit was reportedly 31.9%, the white-cell count 4600 per cubic millimeter (with 75% neutrophils and 14% lymphocytes), the blood level of alkaline phosphatase 233 U per liter, and the level of aspartate aminotransferase 47 U per liter. Broad-spectrum antibiotics and intravenous pantoprazole were administered.

During the next 2 days, the temperature rose to 39.4°C and the stools became black and tarry; the hematocrit was 28.3%. Magnetic resonance imaging (MRI) of the abdomen, after the administration of contrast material, revealed a thick-walled

lesion that was contiguous with the posteromedial wall of the duodenum, mild distention of the gallbladder, and a small amount of fluid adjacent to the gallbladder wall. A unit of red cells was transfused. On the fourth day, esophagogastroduodenoscopy revealed a duodenal ulcer and gastritis. Testing for antibody to HIV was positive. During that night, the patient became agitated, reporting a nightmare in which he was dying. On the fifth day, he appeared tense, speaking with his teeth and fists clenched and his eyes staring ahead; religious delusions developed. Psychiatric consultation was obtained, and olanzapine was prescribed. The patient was transferred to this hospital.

The patient had had herpes zoster of the thoracic dermatome 4 years before admission and again 3 months before admission. He had no known allergies. He had immigrated to the United States from a Caribbean country more than a decade earlier. Testing for HIV and syphilis had reportedly been negative 11 years before admission. He had a history of alcohol abuse and did not smoke or use intravenous drugs. He lived with his partner and her children. He had biologic children who lived in his native country. A bird and a turtle were in the home. His parents and siblings were healthy, with no family history of psychiatric illness.

On admission, the patient was awake but initially unresponsive. The temperature was 37.6°C and the blood pressure 148/81 mm Hg; other vital signs and the remainder of the physical examination were normal. He became agitated and continued to have bizarre delusions. Olanzapine and haloperidol were administered. On psychiatric examination later that day, the agitation had resolved. He was not oriented to date and was found not to have the capacity to sign out against medical advice. Twenty-four-hour accompaniment was begun. Blood levels of platelets, bilirubin, amylase, lipase, calcium, phosphorus, magnesium, vitamin $B_{12}$, folic acid, thyrotropin, and ammonia were normal, as were the results of tests of renal function and urinalysis; tests for toxic drugs and hepatitis B and C viruses were negative. Other test results are shown in Table 1.

On formal psychiatric examination on the second day, the patient had disorganized and guarded behavior, flat affect, thought blocking, and bizarre nihilistic delusions, including statements that he had died and was dead. Although the cognitive examination was limited in scope because of the patient's lack of cooperation, it revealed deficits in attention (inability to name months of the year backward), anterograde memory (inability to orally recall three objects), and the performance of visuospatial tasks (Fig. 1) in the absence of fluctuations in the level of consciousness.

On the third day, the patient appeared lucid and somber and had appropriate speech content. The maximum temperature was 40.3°C. There were white plaques on the tongue, scars from zoster on the right thorax, and small, rubbery lymphadenopathy in the left axilla. Blood tests for IgG antibodies to toxoplasma and cytomegalovirus (CMV) was positive, and testing for syphilis, CMV antigen, strongyloides antibody, cryptococcal antigen, and urine histoplasma antigen was negative. The aspartate aminotransferase level increased to 155 U per liter. Broad-spectrum antibiotics were stopped, and nystatin was begun orally. Respiratory-isolation measures were instituted. A portable chest radiograph was normal; CT of the abdomen and pelvis obtained after the administration of contrast material showed upper abdominal, retroperitoneal, and pelvic lymphadenopathy; splenomegaly; a duodenal diverticulum; and gallbladder-wall thickening.

During the next 9 days, psychiatric symptoms persisted. Fevers occurred daily, with temperatures up to 40.1°C, and extrapyramidal side effects developed. CT of the brain showed no clinically significant abnormality. CT of the chest without contrast material revealed a few nonspecific nodules and multiple supraclavicular, mediastinal, and upper abdominal lymph nodes, up to 12 mm in diameter. MRI scans of the brain obtained before and after the administration of contrast material showed multiple punctate foci of enhancement, up to 4 mm in diameter, in the right and left cerebral hemispheres, with mild surrounding hyperintensity on fluid-attenuated inversion recovery (FLAIR) images. The distribution of the lesions was predominantly intraaxial and involved white matter and the junction of the gray and white matter, although one lesion appeared extraaxial and another lesion appeared to involve cortical gray matter. The results of portable electroencephalography were normal, with overlying beta activity and no evidence of epileptiform activity. Three induced-sputum specimens showed hyphae on fungal wet preparation and were negative for acid-fast bacilli. Cultures of sputum grew *Candida*

**Table 1. Laboratory Data.***

| Variable | Reference Range, Adults† | On Admission, This Hospital |
|---|---|---|
| Hematocrit (%) | 41.0–53.0 (men) | 32.2 |
| Hemoglobin (g/dl) | 13.5–17.5 (men) | 11.0 |
| White-cell count (per mm$^3$) | 4500–11,000 | 6700 |
| Differential count (%) | | |
| Neutrophils | 40–70 | 86 |
| Lymphocytes | 22–44 | 9 |
| Monocytes | 4–11 | 5 |
| Mean corpuscular volume ($\mu$m$^3$) | 80–100 | 78 |
| Smear description | | 1+ Microcytes |
| T-cell subsets | | |
| Absolute lymphocyte count (per mm$^3$) | 950–2967 | 463 |
| CD4 T-cell count (per mm$^3$) | 348–1456 | 30 |
| CD8 T-cell count (per mm$^3$) | 148–1173 | 322 |
| Activated partial-thromboplastin time (sec) | 21.0–33.0 | 25.9 |
| Prothrombin time (sec) | 10.8–13.4 | 15.1 |
| International normalized ratio | | 1.3 |
| Sodium (mmol/liter) | 135–145 | 136 |
| Potassium (mmol/liter) | 3.4–4.8 | 3.2 |
| Chloride (mmol/liter) | 100–108 | 103 |
| Carbon dioxide (mmol/liter) | 23.0–31.9 | 24.9 |
| Glucose (mg/dl) | 70–110 | 123 |
| Protein (g/dl) | | |
| Total | 6.0–8.3 | 7.7 |
| Albumin | 3.3–5.0 | 3.5 |
| Globulin | 2.6–4.1 | 4.2 |
| Alkaline phosphatase (U/liter) | 45–115 | 266 |
| Aspartate aminotransferase (U/liter) | 10–40 | 61 |
| Alanine aminotransferase (U/liter) | 10–55 | 27 |
| Lactate dehydrogenase (U/liter) | 110–210 | 443 |
| IgG (mg/dl) | 614–1295 | 1759 |
| HIV antibodies (by enzyme-linked immunosorbent assay) | Negative | Positive, confirmed by Western blot analysis |
| HIV nucleic acid (copies per ml of plasma, by RT-PCR) | | 893,000 |

* To convert the values for glucose to millimoles per liter, multiply by 0.05551. HIV denotes human immunodeficiency virus, and RT-PCR reverse-transcriptase polymerase chain reaction.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

*albicans* and normal respiratory flora. Cultures of sputum, urine, and blood for mycobacteria and fungi remained negative. Lumbar puncture was performed, and analysis of the cerebrospinal fluid (CSF) was normal. The HIV RNA level was 3010 copies per milliliter of CSF, with no malignant cells on cytologic examination.

On the ninth day, fine-needle aspiration of the peripancreatic lymph node showed no malignant cells, and flow cytometry revealed T lymphocytes

with an inverted ratio of CD4 T cells to CD8 T cells and no monoclonal B cells. Ophthalmologic examination showed retinal lesions, including superficial whitening and fluffy white infiltrate, findings consistent with retinopathy from CMV or HIV. Transthoracic echocardiography was normal.

Haloperidol was stopped, and olanzapine and lorazepam were administered as needed for agitation. Treatment with antiretroviral medications (emtricitabine, tenofovir, atazanavir, and ritonavir) and prophylactic trimethoprim–sulfamethoxazole was begun.

On the 12th day, a diagnostic procedure was performed.

## DIFFERENTIAL DIAGNOSIS

*Dr. Oliver Freudenreich:* I am aware of the diagnosis in this case. May we review the imaging studies?

*Dr. Mykol Larvie:* The abdominal CT scan (Fig. 2A) shows a structure posterior to the second part of the duodenum that is typical in appearance for a duodenal diverticulum, although it initially raised concern for a mass, either inflammatory or malignant. There are enlarged, low-density lymph nodes, including aortocaval and periaortic nodes (Fig. 2B), some of which were originally worrisome for a parapancreatic mass. The gallbladder wall is thickened with a small amount of pericholecystic fluid.

CT of the brain revealed no clinically significant abnormality. A tiny punctate intraaxial calcification was a nonspecific and nonacute finding. MRI of the brain (Fig. 3) revealed multiple predominantly punctate, enhancing, hyperintense foci on $T_2$-weighted images, including one focus in the right medial temporal lobe and another in the inferior left frontal lobe, with no evidence of mass effect. Although the images are degraded by motion artifact, there is no gross evidence of hemorrhage or abscess.

*Dr. Freudenreich:* This patient has new-onset psychosis. He also made repeated statements about having died and being dead that are consistent with nihilistic delusions (termed the Cotard syndrome), which occur when the self becomes unfamiliar, leading to a delusion of being dead.[1,2] Psychosis is a symptom, not a diagnosis, and can be organized into primary and secondary (organic) psychoses. Unfortunately, there is no easy way to reliably differentiate primary from secondary psychoses on the basis of the characteristics of the psychosis itself,[3,4] and assessment of the overall clinical situation is very important in narrowing the differential diagnosis and determining the degree of urgency.

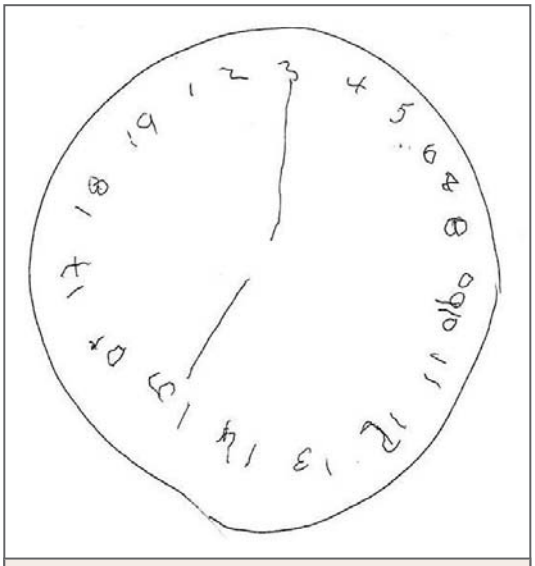

**Figure 1. Clock Drawing.**

On the second hospital day, visuospatial skills were assessed by having the patient draw a clock. Severe visuospatial disorganization is evidenced by the poor spacing between the numbers, omission and repetition of numbers, numbers written inaccurately, and numbers continued past the number 12. Also, although there are two distinguishable hands, the time is not identified correctly, evidencing deficits in abstract thinking and in the ability to translate the concept of time into a drawing.

### DELIRIUM

The first question we must ask is whether this patient's new-onset psychosis is caused by an underlying, life-threatening medical condition, such as delirium. Psychosis is common in patients with delirium.[5] The clinical diagnosis of delirium hinges on the presence of two cardinal features: disruption of attention and disruption of the sleep–wake cycle, which leads to fluctuation in symptoms over the course of a day.[5] A delirium can be easily missed if ancillary features such as psychosis overshadow the core problem of inattention. An electroencephalogram (EEG) that shows diffuse slowing is suggestive of a delirium, but as in this patient, a normal EEG is not sensitive enough to reliably rule out a delirium.[6]

The sudden onset of psychosis in a patient with fluctuating mental status and fevers is a delirium

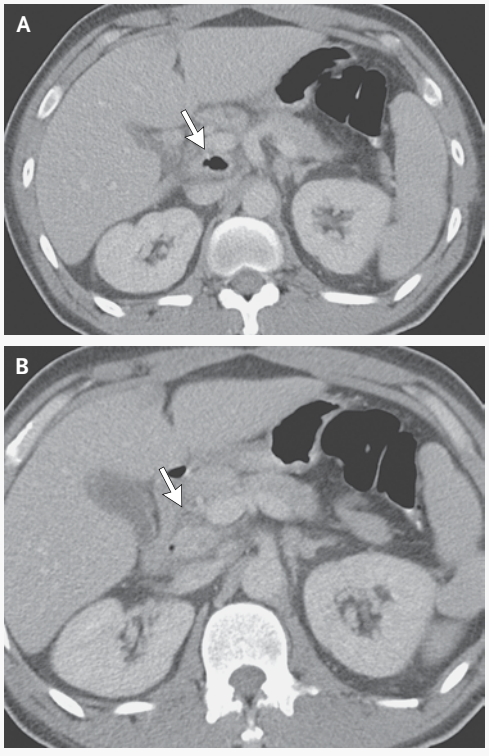


**Figure 2. Abdominal CT Scan.**

A structure posterior to the second part of the duodenum (Panel A) has an appearance typical of a duodenal diverticulum (arrow). There are enlarged, low-density lymph nodes, including aortocaval and periaortic nodes (Panel B, arrow).

until proved otherwise. In this patient, our differential diagnosis and evaluation must focus on his advanced HIV infection. Therefore, a thorough evaluation involving CSF analysis and MRI is warranted for ruling out infection and a malignant condition of the central nervous system.

### HIV-ASSOCIATED DEMENTIA

Delirium often occurs in patients with cognitive impairment and dementia. Since this patient has advanced HIV infection, he is at risk for HIV-associated dementia, which was a common problem before the introduction of highly active antiretroviral therapy (HAART).[7] The typical presentation is a progressive dementia with subcortical features (apathy, inattention, and loss of retentive memory) and abnormalities of motor function, such as psychomotor slowing. When psychosis occurs in patients with HIV-associated dementia, it is characterized by prominent agitation, irritability, and delusions[8] (all of which were present in this patient) and is often part of a manic syndrome that has been called "AIDS mania."

HIV-associated dementia is a diagnosis of exclusion, supported by findings on CSF analysis and MRI. This patient almost certainly has some degree of brain involvement by HIV infection, as suggested by the severe immunosuppression and presence of HIV RNA in the CSF. The extent of his cognitive impairment will require reexamination with a full battery of neuropsychological tests after his acute illness has resolved. Most likely, he is in an early stage of HIV-associated dementia, since he did not have focal findings and his history showed no cognitive decline.

### PSYCHOSIS DUE TO GENERAL MEDICAL CONDITIONS

Psychosis can occur in patients with delirium and in those with dementia. It may also occur as a direct manifestation of an underlying medical condition, such as HIV infection. The common clinical features of HIV-associated psychosis include sudden onset without prodrome, delusions (87% of patients), hallucinations (61%), and mood symptoms (81%).[9] In HIV-associated psychosis, neurologic findings are typically limited and CT findings are nonspecific; however, EEGs are abnormal in 50% of cases.[9] Cognitive impairment has consistently been described as a feature of HIV-associated psychosis,[9,10] although it cannot be distinguished from a first episode of schizophrenia.[11,12] Since substance abuse is a common coexisting disorder in HIV-infected patients and can further impair cognition, it is important to rule out the use of alcohol or other drugs as a contributing cause.[13] I would not diagnose HIV-associated psychosis in a patient with a delirium, which some of the patients cited in the literature might have had.

### PRIMARY PSYCHIATRIC DISORDERS

A primary psychiatric disorder such as schizophrenia, without HIV as a causative factor, develops in some patients who have established HIV infection. In this patient, a first episode of schizophrenia is unlikely, since the onset of schizophrenia is typically not sudden but instead involves a prodromal period of several years, with gradual loss of function and social competence.[14] This patient was married, had children, and at the age of 39 years would be unusually old to be having a first episode of schizophrenia, since men typically

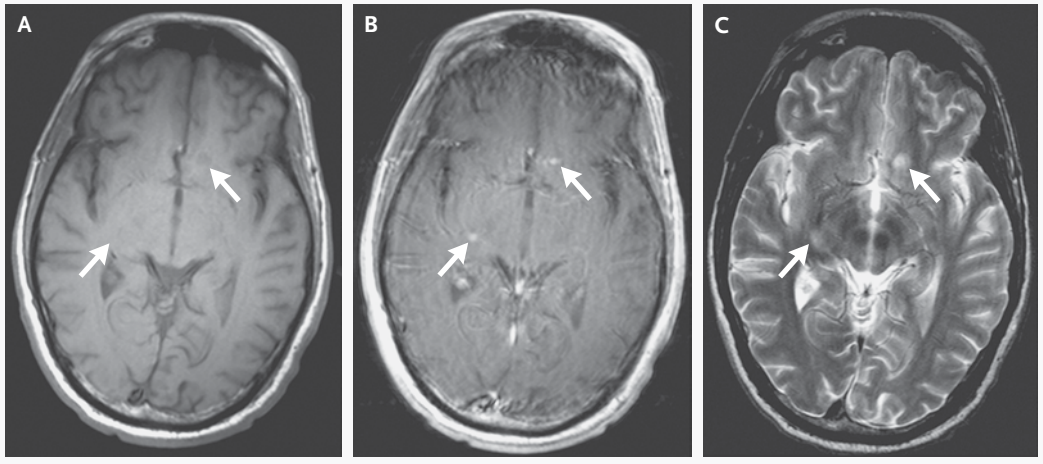


**Figure 3. MRI Scans of the Brain.**

Shown are corresponding axial images — $T_1$-weighted (Panel A), $T_1$-weighted after the administration of contrast material (Panel B), and $T_2$-weighted (Panel C). There are scattered hyperintense, enhancing foci throughout the brain on $T_2$-weighted imaging. Arrows identify lesions in the left inferior frontal lobe and in the junction of the right temporal lobe and insula.

become ill in their 20s. However, psychosis is a feature of other psychiatric disorders besides schizophrenia. For example, the very sudden onset of psychosis during the course of a day or so has been called "reactive psychosis," in response to stressors, and may occur in patients with HIV infection.[15] This patient's delirium is a sufficient explanation for his psychosis, and psychiatric causation does not need to be invoked.

To summarize, the clinical history (sudden onset of psychosis in a patient with constitutional symptoms and fevers) and results of the serial mental status examination (characterized by delusions, attentional problems, and disorientation at times) suggest a delirium in this patient with AIDS and severe immune suppression. The nonspecific MRI findings and the lumbar puncture that showed HIV viral replication but no other infection suggest one of the HIV-associated neurocognitive disorders as a vulnerability factor for the delirium. The small lesions seen on MRI are not sufficient to explain this patient's psychosis, particularly given the clear evidence that he had a delirium, most likely from systemic infection.

### LATE DIAGNOSIS OF HIV INFECTION

*Dr. Nesli Basgoz:* I am aware of the diagnosis in this case. In any patient with fever and sudden changes in mental status, infection or a malignant condition of the central nervous system must be considered. In this patient with HIV infection and a low CD4 T-cell count, our differential diagnosis has to include processes that cause central nervous system disease in immunosuppressed hosts. Cerebral toxoplasmosis is possible, since the patient has serologic evidence of past infection. However, no brain abscess was identified on MRI, making this diagnosis unlikely. Cryptococcal meningitis is another possibility. Results of CSF analysis are often bland in cryptococcal meningitis, since the organism may not elicit a robust inflammatory response. The absence of cryptococcal antigen in the CSF of this patient makes this diagnosis unlikely. Infection with *Mycobacterium tuberculosis* may cause chronic central nervous system disease. This patient does not have evidence of tuberculous meningitis or a tuberculoma. Although MRI may reveal gross disease, it is not particularly sensitive for the detection of invasion of the central nervous system; therefore, tuberculosis affecting the central nervous system cannot be ruled out. CMV infection should also be considered, especially given the abnormalities seen on retinal examination. Testing for CMV in the blood and CSF was negative, and this makes CMV encephalitis unlikely although not impossible. This patient is also at risk for progressive multifocal leukoencephalopathy or lymphoma associated with

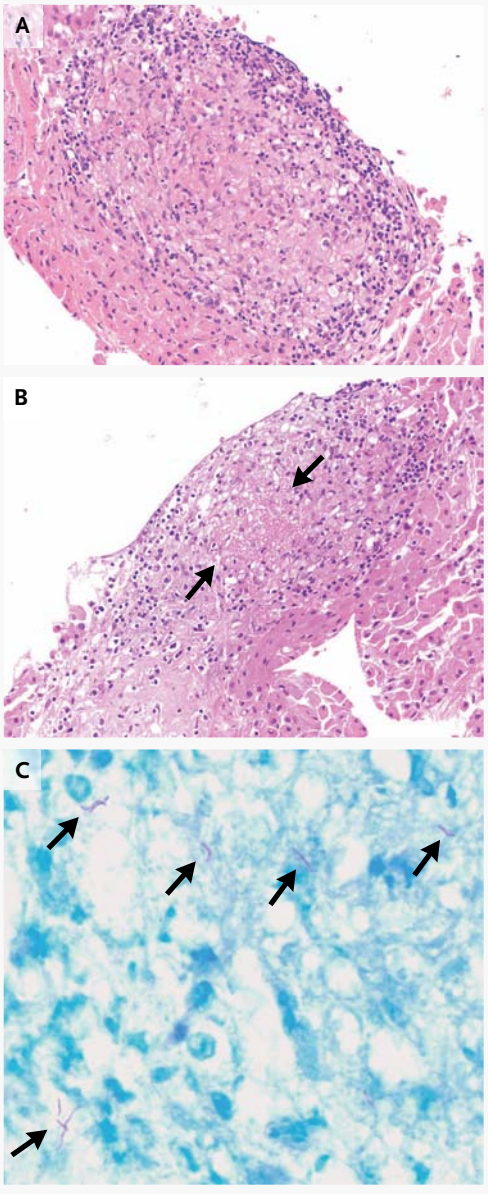


**Figure 4. Liver-Biopsy Specimen.**
Panel A (hematoxylin and eosin) shows an epithelioid granuloma with a cuff of lymphocytes. Some of the granulomas show central amorphous necrotic debris (Panel B, area between the arrows; hematoxylin and eosin). Numerous acid-fast bacilli are present (Panel C, arrows; Ziehl–Neelsen stain).

Epstein–Barr virus, but there is no imaging evidence to support these diagnoses.

In this profoundly immunosuppressed patient, multiple opportunistic infections may be involved, since the laws of medical parsimony do not apply to patients with low CD4 T-cell counts. The range of possible opportunistic infections is vast, but most disease is caused by a relatively small number of organisms. The two most important predictive factors in this case are the CD4 T-cell count of 30 per cubic millimeter and the fact that the patient comes from an island in the Caribbean where tuberculosis is endemic. His fever, chills, sweats, cough, and lymphadenopathy are all consistent with disseminated tuberculosis. Although he had a negative purified protein derivative skin test for tuberculosis, this test lacks sensitivity in normal hosts and is likely to be uninformative in this patient with a low CD4 T-cell count. We also need to consider fungal infections that behave like tuberculosis, including histoplasmosis.

During the patient's hospital course, he had a persistently high aspartate aminotransferase level. Since the initial review of the lymph-node aspirate did not show acid-fast bacilli or fungi, the next step was a liver biopsy.

## DR. OLIVER FREUDENREICH AND DR. NESLI BASGOZ'S DIAGNOSES

Acute psychosis with Cotard's delusion, most likely superimposed on a mild HIV-associated neurocognitive disorder.

Delirium due to the systemic effects of an opportunistic infection or malignant condition, most likely *M. tuberculosis*.

## PATHOLOGICAL DISCUSSION

*Dr. Joseph Misdraji:* Examination of the liver-biopsy specimen revealed several epithelioid granulomas, some of them necrotizing (Fig. 4A and 4B). Histochemical staining for acid-fast organisms revealed numerous acid-fast bacilli (Fig. 4C). The diagnosis was mycobacterial infection of the liver with necrotizing granulomatous inflammation. Shortly after the diagnosis was made, various cultures were reported as positive for *M. tuberculosis* complex, including the liver biopsy, peripancreatic lymph-node aspirate, sputum, blood, and urine. Therefore, the final anatomical diagnosis is disseminated *M. tuberculosis* infection. The large number of bacilli and the somewhat looser arrangement of the histiocytes are features consistent with the immunodeficient status of the patient.

After the diagnosis of *M. tuberculosis* was confirmed, we took another look at the peripancre-

atic lymph-node aspirate to see whether we could find acid-fast bacilli. Review of the aspirate revealed lymphocytes and small amounts of amorphous granular debris in which acid-fast bacilli were identified. This case underscores the fact that the identification of acid-fast bacilli is challenging, and organisms can be overlooked. Therefore, when there is a high clinical suspicion of mycobacterial disease, it is important to notify the pathologist so that extra time can be spent reviewing the slide stained for acid-fast bacilli.

## DISCUSSION OF MANAGEMENT

### MANAGEMENT OF HIV-ASSOCIATED PSYCHOSIS

*Dr. Fernandez-Robles:* Reversal of organic psychosis involves treatment of the underlying disorder and symptomatic treatment with antipsychotic agents. This patient had markedly less agitation after 2 days of treatment with olanzapine, an antipsychotic agent. This drug was initially chosen because of its proven efficacy and relatively low risk of causing extrapyramidal symptoms and tardive dyskinesia, which are highly prevalent among patients with HIV.[16-19] This sensitivity is thought to be related to HIV-associated damage to the dopaminergic basal ganglia system and to increased plasma levels of antipsychotic agents because of interactions with antiretroviral drugs.[20,21] Dysfunction of the basal ganglia also heightens the risk for neuroleptic malignant syndrome, which has been well documented to occur in patients with HIV.[22]

On day 5, extrapyramidal symptoms developed, requiring the administration of lorazepam and a reduction in the dose of olanzapine. Because of the development of extrapyramidal symptoms, persistent high fever, and changes in mental status, we became concerned about the possibility of neuroleptic malignant syndrome. We closely followed the creatine kinase levels, which remained normal. On discharge, most of the patient's psychotic symptoms had resolved, except for a persistently flat affect and mildly monotonous speech.

### MANAGEMENT OF TUBERCULOSIS AND HIV INFECTION

*Dr. Basgoz:* This patient has at least two life-threatening infections, HIV and tuberculosis, both of which require complex treatment regimens. His subsequent clinical course highlights an unresolved clinical question regarding the timing of the initiation of antiretroviral therapy in patients with a low CD4 T-cell count and concurrent opportunistic infection.[23-29]

This patient was initially started on a standard four-drug antiretroviral regimen, and approximately 1 week later, therapy directed against tuberculosis was initiated. Within 6 days after the initiation of antituberculous therapy, high temperature, cough, and tachypnea developed, with worsening malaise. Severe scrotal pain also developed, with swelling, tenderness, and induration. Ultrasound examination of the scrotum showed a complex testicular mass with epididymal enlargement that was thought to be consistent with involvement by disseminated tuberculosis. During this time, there was also an increase in the alkaline phosphatase level, from 185 U per liter to 722 U per liter, suggesting worsening of the patient's liver disease. This constellation of findings is consistent with the immune reconstitution inflammatory syndrome (IRIS), a paradoxical worsening of inflammation caused by the reconstitution of immune function while on antiretroviral therapy. As his immune function started to recover, the patient mounted an exuberant inflammatory response, probably directed against antigens liberated from dead or dying mycobacteria.

For treatment of IRIS, we added prednisone to the patient's regimen. He had a rapid clinical response, with a decrease in alkaline phosphatase levels and an improvement in fever. However, he had reactivation of a latent CMV infection and required treatment with ganciclovir. As we tapered the dose of prednisone, fever recurred, but the pattern of fever was relatively constant, lacking the normal diurnal variation that is typical of infection. The patient looked and felt well, which suggested that the fever might be medication-related. We discontinued rifabutin, which was part of his antimycobacterial regimen, and the fever resolved.

After discontinuation of prednisone, asymptomatic hypercalcemia developed, with calcium levels measured as high as 13.5 mg per deciliter (3.4 mmol per liter). We assumed that this was caused by a parathyroid-hormone–independent mechanism related to the production of 1,25-dihydroxyvitamin D by the macrophages in reaction to the tuberculosis infection. Hypercalcemia is much more commonly seen in other granulomatous diseases, such as sarcoidosis, than in tuberculosis. We restarted low-dose prednisone,

and the hypercalcemia rapidly resolved with ketoconazole, which inhibits a step in the production of 1,25-dihydroxyvitamin D. The patient was discharged after 4 weeks in the hospital, at which time he was medically stable and had a markedly improved mental status. He continued therapy for tuberculosis and HIV.

On examination by the retina service, the patient was noted to have bilateral retinopathy, which was considered to be due to CMV or HIV. However, there was a focal area of chorioretinitis in the left eye that was not considered typical of CMV retinitis and was thought to possibly be a granulomatous lesion from tuberculosis. Approximately 14 months after discharge, at the time of his last eye examination, the eye lesions were quiescent and there was no evidence of active retinitis.

Thirty months after discharge, the patient is doing exceptionally well medically, feels strong, and exercises frequently. His last CD4 T-cell count was 231 per cubic millimeter, and plasma HIV RNA was not detected.

*Dr. Freudenreich:* I saw the patient in outpatient psychiatry for follow-up 6 months after his acute illnesses had resolved. He had made a remarkable recovery but had residual cognitive problems, particularly in processing speed, recall memory, and frontal-lobe functions, all of which might have functional ramifications. His clock drawing was intact. Of note, he scored 7 out of 16 on the HIV Dementia Scale (with scores of 10 or less indicating HIV-associated dementia).[30]

This case exemplifies the effect that HIV infection may have on the brain, particularly late in the course of infection. Early diagnosis and treatment of HIV infection may help to limit brain disease. Therefore, I consider HIV testing in any patient presenting with psychosis[14] or with cognitive problems.[31]

*Dr. Theodore A. Stern* (Psychiatry): In light of the patient's episodic belief that he was dead, should we consider the possibility that this thought or feeling was derived from a complex partial seizure in the temporal lobe? The theme of death in complex partial seizures has been described in the literature.[32]

*Dr. Freudenreich:* An EEG was obtained to rule out seizures and was normal in this patient. I do not think it is possible to establish causality between this patient's lesion in the temporal lobe and his psychosis.

## FINAL DIAGNOSES

Disseminated infection with *Mycobacterium tuberculosis*, including the liver, peripancreatic lymph node, sputum, blood, and urine, with delirium and acute psychosis with Cotard's delusion.

Mild HIV-associated neurocognitive disorder.

Presented at the Psychiatry Grand Rounds.

Dr. Freudenreich reports receiving consulting fees from Beacon Health Strategies and Transcept Pharmaceuticals, grant money from Pfizer, and honoraria from Reed Medical Education. Dr. Basgoz reports receiving stock options and income for board membership from Forest Laboratories. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Dr. Joshua Roffman (Psychiatry) for assistance with organizing the conference.

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