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Case Reports

Psychosis Due to Disseminated Cryptococcal Infection and Delirium in an Immunocompetent Patient: A Case Report and Review of the Literature

Jungjin Kim, M.D., Georgina Hartzell, M.D., Neguine Rezaii, M.D., Lauren Gensler, M.D., Wendy Baer, M.D., F.A.P.M., Raymond Young, M.D., F.A.P.M., Ann C. Schwartz, M.D., F.A.P.M.

Introduction

Cryptococcus neoformans meningitis (CM) is an opportunistic neuroinfection acquired by inhalation, and usually latent in the lung lymph nodes before disseminating. CM commonly affects individuals with HIV or other forms of immunosuppression; cases of CM in otherwise healthy individuals are relatively rare in the United States with an incidence of 1/100,000/y.[1] Nevertheless, CM in immunocompetent individuals is associated with high mortality (27% at 90 d), which is likely in part due to a delay in diagnosis.[1,2] Therefore, it is clinically imperative to consider CM in cases of suspected meningitis. The indolent and varied presentation of CM in immunocompetent hosts makes diagnosis especially challenging. Typically, CM presents with headache, altered mental status, fever, nausea, and vomiting. However, immunocompetent hosts tend to present 6–12 weeks after infection, and often will not have fevers. Psychiatric symptoms can also be present, most commonly mania, and also depression, anxiety, and psychosis.[3] When psychiatric or behavioral symptoms predominate, clinicians may quickly overlook medical etiologies in favor of a primary psychiatric diagnosis. This is especially problematic in CM when the presentation can be subtle with a subacute onset of nonspecific physical symptoms. Given the high morbidity and mortality of untreated CM, timely and accurate diagnosis is critical.

Herein, we present the case of Ms. A, an immunocompetent woman presenting with psychosis originally attributed to newly diagnosed schizophrenia, later identified as being caused by disseminated cryptococcal infection. We next review the extant literature on cases of CM in immunocompetent hosts initially presenting with primarily psychiatric symptoms. This case reminds clinicians to consider infectious etiologies in cases of new-onset psychosis, even in the absence of expected clinical findings.

Case Presentation

Ms. A, a 50-year-old woman with no known psychiatric history and a medical history of lytic bone lesions, was brought to an emergency department of an outside hospital with delusions that someone was breaking into her house and stabbing her with a spider. Per family, she was at her baseline mental state until earlier that day when she was found in her room kicking imaginary spiders off the bed. Family reported that

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From the Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA (J.K., G.H., N.R., L.G., W. B., R.Y., A.C.S.). Send correspondence and reprint requests to Jungjin Kim, M.D., Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 12 Executive Park Drive, Suite 331, Atlanta, GA 30329; e-mail: jkim61@emory.edu

Ms. A was a retired nurse in the military and functioned independently and managed her own affairs. It was not known how long she had experienced these delusions before her initial presentation. Further history from Ms. A and her family was significant for a 4-month history of left-sided hip pain and difficulty with ambulation, which was thought to be due to lytic bone lesions on her proximal left femur, left ilium, and L4 spinous process seen on a radionuclide whole-body bone survey from an outside hospital 2 months before presentation. A follow-up whole-body positron emission tomography integrated with computed tomography (CT) had shown multiple hypermetabolic lesions in her axial and appendicular skeleton, subcutaneous nodules, and a single retroperitoneal lymph node, all concerning for malignancy. Her vital signs were within normal limits. The chemistry panel was unremarkable with the exception of an elevated globulin gap of 4.6 g/dL; her urine drug screen and urinalysis were unremarkable. A complete blood count was significant for mild normocytic anemia (hemoglobin = 10.2 g/dL), mild leukocytosis (white blood cells = 10,900 cells/mL; neutrophils = 73% and lymphocytes = 16%), and thrombocytosis (platelet = 465,000/mm^3). A CT of the head was also unremarkable. A formal cognitive assessment was not performed during this hospitalization. Given the presence of delusions, hallucinations, and disorganized speech and thought, Ms. A was diagnosed with schizophrenia and admitted to the psychiatric unit at the outside hospital. She continued to report left leg and hip pain on the psychiatric inpatient unit, and on hospital day 2, she was transferred to our facility, a large urban hospital, for further evaluation of her lytic bone lesions presumed to be due to malignancy.

On admission to our facility, she reported transient headaches, but denied fevers, chills, nausea, vomiting, or blurry vision. Her vital signs were stable, and her neurologic examination was nonfocal and without meningeal signs. The remainder of the physical examination was notable for multiple tender, pruritic, and hyperpigmented subcutaneous nodules scattered on her neck, chest, and back, which had not been observed during her initial hospitalization. Head CT on admission was unremarkable, like the previous scan from the referring hospital. Laboratory values at our hospital were remarkable for a normocytic anemia (hemoglobin = 8.4 g/dL), mild leukocytosis (white blood cells = 10,200 cells/mL) with elevated neutrophils (64%) and lymphocytes (23%), thrombocytosis (platelets = 423,000/mm^3), elevated globulin gap (4.5 g/dL), normal calcium, normal creatinine, and a negative HIV test. These findings were comparable to values at the referring institution, with the exception of a further decrease in hemoglobin. A psychiatry consultation was requested for management of her schizophrenia as the medical team continued workup of her lytic lesions.

On initial interview by the psychiatry consultation-liaison (C-L) service, Ms. A was poorly groomed, exhibited marked psychomotor retardation, and displayed inappropriately elevated affect. Her thought process was disorganized with loss of goal. She endorsed auditory hallucinations of her mother's voice and visual hallucinations of spiders. Her Montreal Cognitive Assessment score was 9 of 30 points, although she was oriented to self, partly to place (city and state), partly to time (month, year, and season), and to situation. The nursing report confirmed that she had a waxing and waning course of attention. She denied any significant travel history, and had no family history of psychiatric illness, further raising our suspicion of delirium rather than a primary psychotic process.

Low-dose haloperidol (1 mg/d) was started for presumed delirium with minimal effect in her disorganization and inattention. She underwent a bone marrow biopsy that was not consistent with multiple myeloma or another hematologic malignancy. On hospital day 5, she developed sudden-onset lower extremity weakness, which prompted a repeat head CT scan. The CT scan showed right sulcal effacement in the frontotemporal region, and magnetic resonance imaging (MRI) was recommended for further evaluation. The brain MRI demonstrated extensive areas of leptomeningeal enhancements, including in the right temporal lobe and cingulate gyrus, which was suggestive of a metastatic or infectious process. A lumbar puncture was performed with normal opening pressure, and intravenous acyclovir was empirically started given concern for herpes simplex virus encephalitis in light of the involvement of the right temporal region. Cerebrospinal fluid studies showed an elevated white blood cell count (98/mm^3) with neutrophilic pleocytosis (81%), low glucose (15 mg/dL) and an elevated level of total protein (86 mg/dL). The cerebrospinal fluid cryptococcal antigen was positive in a 1:40 titer. Cerebrospinal fluid