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L. Hayes
Zucker School of Medicine at Hofstra/Northwell

P. Malhotra
Zucker School of Medicine at Hofstra/Northwell

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Case Report

Central nervous system infections masquerading as cerebrovascular accidents: Case series and review of literature

Lisa Hayes, Prashant Malhotra *

Department of Medicine, Division of Infectious Diseases, Hofstra North Shore-LIJ School of Medicine, 400 Community Drive, Manhasset, NY 11030, USA

ABSTRACT

Introduction: Central nervous system (CNS) infections can have various presentations including Cerebrovascular accidents (CVA) which may go unrecognized as a presentation of infection. We describe three cases of different CNS infections complicated by CVA.
Presentation: Case 1 describes a 27-year-old man, presenting with symptoms consistent with a transient ischemic attack found to have racemose neurocysticercosis. Case 2 describes a 55-year-old man with low grade fevers for 4 weeks accompanied by visual and gait disturbances and delayed speech diagnosed with multiple small left thalamocapsular and superior cerebellar infarcts secondary to cryptococcal meningitis. The third case describes a man with pneumococcal meningitis complicated by cerebellar infarcts.
Discussion: CNS vascular compromise secondary to infections may be due to vasculitis, an immune-mediated parainfectious process causing vasospasm or thrombosis, or a hypercoagulable state with endothelial dysfunction. Patients with CVAs are at risk for aspiration pneumonia, urinary tract infections (especially catheter related) and other nosocomial infections and their clinical presentation may be very similar to CNS infections.
Conclusion: The cases described demonstrate that CNS infections need to be considered in the differential diagnosis of CVAs presenting with fevers. The signs and symptoms of non-CNS infections associated with CVAs may be clinically indistinguishable from those of CNS infections. The outcomes of untreated CNS infections are extremely poor. It is thus imperative to have a high index of suspicion for CNS infection when evaluating CVAs with fevers or other signs of infection.

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Introduction

Central nervous system (CNS) infections can have various presentations including Cerebrovascular accidents (CVA) which may go unrecognized as a presentation of infection. We describe three cases of different CNS infections complicated by CVA.

Case series

Case 1

A 27-year-old Gautemalan man, with no past medical history presented after noticing dizziness and dysarthria, lasting for 2 min. He also described transient right-sided facial paralysis. On arrival his vital signs were stable, except blood pressure of 143/89. Physical exam revealed no neurological deficits. Laboratory results

were normal. His symptoms were thought to be consistent with a transient ischemic attack.

A CT scan of the head revealed moderate hydrocephalus with prominent cerebrospinal fluid in the left perimesencephalic cistern and the suprasellar cisterns. Magnetic resonance imaging and angiogram revealed multiple septated cystic lesions in the suprasellar and prepontine cisterns consistent with racemose neurocysticercosis (Fig. 1). There was mild narrowing of the middle cerebral artery branches, but no large vessel occlusions (Fig. 2).

Further testing revealed a positive serum cysticercosis antibody. He was treated with dilantin intravenous steroids and albendazole and subsequently discharged on albendazole 400 mg Po bid and prednisone taper. The patient had no recurrences and follow-up MRIs showed decreased size of the cystic lesions.

Case 2

A 55-year-old man with recently diagnosed renal cell carcinoma and partial nephrectomy 6 weeks prior to admission presented

* Corresponding author. Tel.: +1 516 562 4280; fax: +1 516 562 2626.
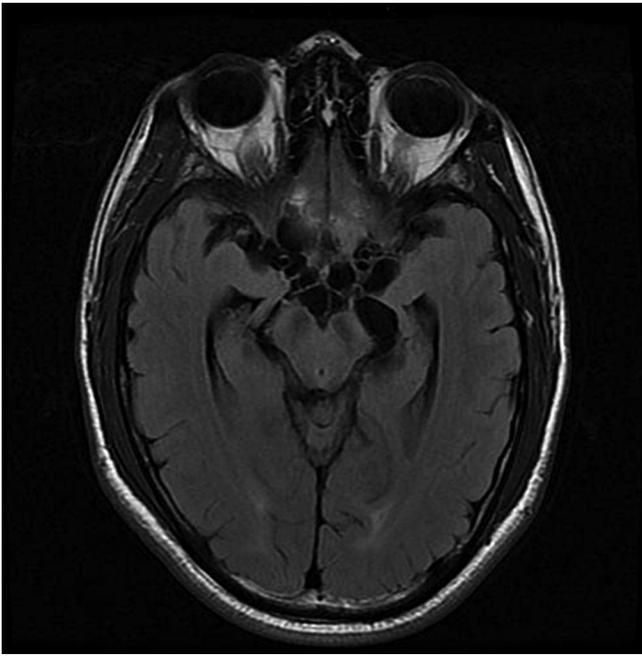E-mail address: pmalhotr@nshs.edu (P. Malhotra).

Fig. 1. T2 axial flair MRI demonstrating suprasellar and prepontine cistern multiple septated cystic lesions with slight enhancement consistent with racemose neurocysticercosis.

with low grade fevers for 4 weeks accompanied by visual and gait disturbances and delayed speech. Periods of altered mental status were also reported. Outpatient fever workup including echocardiogram, blood cultures, and HIV testing were negative.

On admission vital signs were normal except a blood pressure of 145/95. Physical and neurologic exam revealed an awake male who was slow to answer questions, able to name some objects, and repeat words. Motor and sensation were intact. No dysmetria was noted. CT of the head revealed a new focal hypodensity involving the posterior limb of the left internal capsule and medial aspect of the left globus pallidus concerning for infarct. Given the concern

for a CNS infection a lumbar puncture (LP) was obtained. Treatment with ceftriaxone and acyclovir was initiated. Admission blood and urine cultures were eventually negative. LP revealed a total nucleated cell (TNC) count of 350 cells/μL, with a lymphocytic pleocytosis (84%), protein 169 mg/dL, glucose 15 mg/dL. MRI of the brain revealed a basilar leptomeningeal process and multiple small left thalamocapsular (Fig. 3) and superior cerebellar infarcts concerning for an arterial vasculitis secondary to the leptomeningitic process. Bacterial culture, fungal culture, acid fast bacilli, herpes simplex virus, enterovirus, and VDRL were all negative from the CSF.

CSF cryptococcal antigen was positive with a titer of 1:16. Treatment with amphotericin and flucytosine was initiated on hospital day 3, other antimicrobials were discontinued. Repeat HIV testing was negative. Amphotericin and flucytosine were later discontinued and IV fluconazole was started on day 11 due to elevated creatinine. On hospital day 13 the patient was discharged on IV fluconazole to finish a 3 week course. Repeat serum cryptococcal antigen was negative and repeat MRI showed evolution of the original infarcts. After 3 months of treatment, the fluconazole was discontinued.

Case 3

A 48-year-old man with a past medical history of multiple sclerosis presents with a few hour history of confusion, rigors, and headache. The patient was in his usual state of health until 3 days ago when his wife noted the patient to have some nasal congestion, attributed to seasonal allergies. Family history and social history were noncontributory and there was no recent travel.

On presentation, he had temperature of 101.3°F. Blood pressure was 240/108, heart rate 112, and respiratory rate 26 breaths per minute. Physical exam revealed an obtunded male, sluggish pupillary light reflexes bilaterally, nuchal rigidity, and left ear otitis media. CT head was negative for infarct, hemorrhage, or mass effect but was positive for a left mastoiditis and acute sinusitis of the left maxillary and ethmoid sinuses. Lumbar puncture revealed TNC 94 cells/μL, 96% neutrophil, protein 119 mg/dL, and glucose 60 mg/dL. Serum glucose was 126 mg/dL and WBC 10,700 cells/μL. Gram stain from the CSF had numerous gram positive cocci in

Fig. 2. 3D volume rendered MRA revealing narrowing of several branches of the middle cerebral arteries within the sylvian fissure.
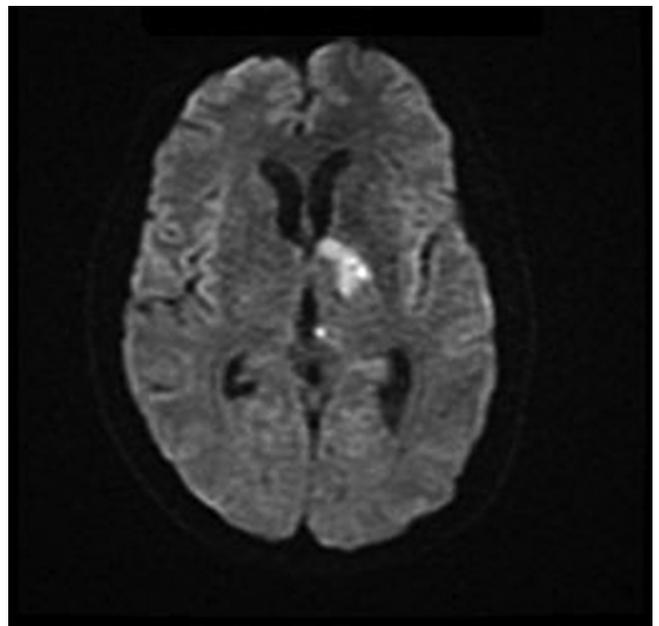

Fig. 3. Diffusion weighted MRI revealing small left thalamocapsular acute infarct.

pairs. The patient was treated with intravenous ceftriaxone, vancomycin, and dexamethasone. The patient required intubation due to poor control of secretions and worsening neurological status and was admitted to the medical intensive care unit. CSF culture and blood cultures grew *Streptococcus pneumoniae* sensitive to ceftriaxone, (with a penicillin MIC of 0.047) and vancomycin was discontinued on hospital day 3.

Repeat LP on day 5 revealed glucose 60 mg/dL, protein 57 mg/dL, TNC 21 cells/μL, 88% lymphocytes with a negative gram stain and culture. MRI revealed stable demyelinating disease but, multiple new infarcts involving the right cerebellar hemisphere.

Patient subsequently improved on intravenous penicillin 24 million units a day and was eventually discharged to a rehabilitation facility on IV ceftriaxone to complete a 3 week course of antibiotics and had a slow recovery with some residual cerebellar defects.

Discussion

We describe three different CNS infections, parasitic, fungal, and bacterial, all presenting as CVAs. Numerous other infectious etiologies can present as CVAs. These include pyogenic meningitis, tuberculosis, syphilis, lyme disease, HIV, primary varicella zoster, reactivated herpes zoster, aspergillosis, mucormycosis, coccidiomycosis, and histoplasmosis [1]. The possible mechanisms in which CNS vascular compromise develops secondary to infections is independent of the type of infection and may include vasculitis, an immune-mediated parainfectious process causing vasospasm or thrombosis, or a hypercoagulable state with endothelial dysfunction [1]. Conversely, patients with CVAs are at risk for aspiration pneumonia, urinary tract infections (especially catheter related) and other nosocomial infections and their clinical presentation may be very similar to CNS infections.

Neurocysticercosis (NCC) has variable presentations, which are nonspecific and depend on the number of cysts, location, stage, and host immune response to the parasite [1–3]. Cerebrovascular complications occur in 3–12% of patients with NCC [1]. Common manifestations include seizure, altered sensorium, signs and symptoms of increased intracranial pressure, and focal neurologic deficits either secondary to the location of the cysticerci or from the result of a CVA [2]. Headache is also a more common finding in NCC associated CVA compared to traditional CVAs as reported in case reports from Ecuador and Mexico [4,5]. Cerebrovascular complications from NCC can present as lacunar infarcts, large infarcts, a progressive midbrain syndrome, and transient ischemic attacks (TIA) as in our case 1[1,4,6]. Lacunar infarcts, due to a mild arachnoiditis, are the most common complication and are typically situated in the lenticulostriate branches of the anterior or middle cerebral artery [2]. Less devastating complications of TIAs may be caused by positional cerebral ischemia from the rotation of the cysts [2]. On MRI, our patient had narrowing of the middle cerebral artery branches, possibly causing a TIA, which without immediate treatment may have progressed to a CVA. The infarcts result from an occlusive endarteritis caused by an inflammatory reaction within the subarachnoid space that is triggered by meningeal cysticerci [2]. Infarcts may also develop after the initiation of treatment with antiparasitic therapy secondary to an intense inflammatory response to the dying parasite, and for this reason, antiparasitic therapy should be preceded by anti-inflammatory treatment with steroids [1]. NCC must be considered in those patients presenting with stroke from endemic areas, such as India, China, sub-Saharan Africa, and Latin America, especially in younger patients [3].

Case 2 depicts a case of cryptococcal meningitis presenting in a subacute fashion similar to how most present with this disease [7]. Symptoms may include headache, fever, and periods of altered sensorium as in our patient. Common CSF studies include a pleocytosis (average of 50–200 WBCs/mm^3), elevated protein, and low to normal glucose; with a CSF pressure of greater than 200 mm H$_2$O. *Cryptococcus neoformans* is the most common cause of fungal meningitis and may present in an immunocompetent or immunocompromised host. Diagnosis is confirmed by the presence of yeast on India ink staining of CSF or with CSF cryptococcal antigen which has a sensitivity of about 90% [1].

Cerebral infarction is less common with cryptococcal meningitis compared to other meningitides with a wide range of incidence between 4% and 32%. Blood vessels that travel through the exudates of the basal meninges are compressed, become inflamed, and result in narrowing, necrosis, and thrombosis leading to infarcts. The Circle of Willis can be encased in heavy exudates and infarction commonly results in the basal ganglia, internal capsule, and thalamus, as seen in our patient. In addition, as in NCC, infarct may develop after initiation of appropriate antifungal treatment as a complication of persistent arachnoiditis or due to inflammation from the dying micro-organism [8]. Hydrocephalus may also lead to compression of vessels causing ischemia and stroke [1].

Vascular complications of bacterial meningitis are common, occurring in about 15–20% of all cases, with even higher rates of about 33% in cases of pneumococcal meningitis [9–12]. Mortality is high with these vascular complications and patients may have permanent deficits. Neurologic deficits found at the time of presentation may be associated with a worse outcome [9]. One series of 17 cases of pneumococcal meningitis reports a median time to onset of 4 days after initiation of treatment, with 10 of the cases presenting after 6 days of therapy [13].

Arterial complications are more common with bacterial meningitis, though both arterial and venous have been described in the literature. One retrospective study of 87 adults with pneumococcal meningitis had 21.8% of patients with arterial infarctions, 10.3% with venous complications, and 9.2% with intracranial hemorrhages [9]. Arterial stenosis in bacterial meningitis is thought to occur from encasement of the large vessels at the base of the brain by subarachnoid inflammatory exudates; invasion of the vessel wall by inflammatory cells, causing intimal thickening, focal narrowing, dilatation, and edema; and vasospasm without evidence of inflammation [10]. An activation of proinflammatory procoagulant cascades may also lead to intravascular thrombi from a hypercoagulable state leading to infarction [14,15]. As in the other infections described above, increased intracranial pressure can be seen with bacterial meningitis as a consequence of cytotoxic edema from ischemia, vasogenic edema secondary to endothelial damage, and impaired venous drainage from venous or sinus thrombosis [1]. As in NCC, corticosteroids are thought to be beneficial in reducing intracranial pressure and cerebral edema in pneumococcal meningitis [16]. Unfortunately, no guidelines exist on how to manage the vascular complications seen in bacterial meningitis. There are reports of decent recovery with steroids and there are reports that deterioration may occur with tapering of steroids. However, no evidence supports the use of steroids for a more prolonged period of time [7,17].

All three cases described demonstrate that CNS infections need to be considered in the differential diagnosis of CVAs presenting with fevers. Case 2 most clearly depicts how, in the absence of diagnostic studies like LP, a CNS infection may be misdiagnosed. The signs and symptoms of non-CNS infections associated with CVAs may be clinically indistinguishable from those of CNS infections. The outcomes of untreated CNS infections are extremely poor. It is thus imperative that one have a high index of suspicion for CNS infection when evaluating CVAs with fevers or other signs of infection and order the appropriate workup, so that these infections are not overlooked.

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