CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 40-2024: A 56-Year-Old Woman with End-Stage Liver Disease and Headache

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PRESENTATION OF CASE

Dr. James Q. Zhou (Medicine): A 56-year-old woman with metabolic dysfunction–associated steatohepatitis and cirrhosis was admitted to this hospital because of end-stage liver disease.

The patient had been chronically ill and was healing from recent left hip surgery when new fatigue and abdominal pain developed 15 days before this admission. The patient did not take her routine, prescribed medications because of confusion. Thirteen days before this admission, when confusion prevented the patient from going to a scheduled appointment for therapeutic paracentesis, her husband took her to the emergency department of another hospital.

On evaluation, the patient reported abdominal pain and otherwise answered questions unreliably with one-word responses. She appeared jaundiced and was confused but oriented. Marked abdominal distention with bulging flanks and diffuse tenderness was observed. The left hip was bruised with a healing surgical wound with staples in place. Urinalysis was normal, and a urine toxicology screening was positive for opioids, oxycodone, and fentanyl, which had been prescribed. Other laboratory test results are shown in Table 1.

Dr. Benjamin M. Kozak: Radiography of the chest showed elevation of the right hemidiaphragm, increased opacification of the right hilum, and linear opacities in the left lower lung. Computed tomography (CT) of the abdomen and pelvis revealed a shrunken nodular cirrhotic liver contour and large-volume ascites; the gallbladder was surgically absent. Compression deformities of the lumbar spine, healed pubic rami fractures, and a left hip prosthesis were also noted. CT of the head revealed mild scattered hypodensities in the white matter, a finding consistent with chronic small-vessel disease.

Dr. Zhou: Empirical treatment with ceftriaxone was administered. The patient was admitted to the other hospital.

During the subsequent 12 days, lactulose and rifaximin were administered, and hepatic encephalopathy abated. Anemia worsened, and packed red cells were transfused. Esophagogastroduodenoscopy was performed, which reportedly revealed esophageal varices with evidence of previous band ligation and no active bleeding,

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N Engl J Med 2024;391:2361-9.
DOI: 10.1056/NEJMcpc2402504

CME

Table 1. Laboratory Data.*

Variable	Reference Range, Other Hospital	13 Days before Current Admission, Other Hospital	Reference Range, This Hospital†	On Current Admission, This Hospital
White-cell count (per μl)	3900–11,000	8390	4500–11,000	5460
Hematocrit (%)	34.0–46.0	26.4	36.0–46.0	26.7
Hemoglobin (g/dl)	11.0–15.0	8.0	12.0–16.0	8.3
Platelet count (per μl)	130,000–400,000	220,000	150,000–400,000	108,000
Prothrombin time (sec)	11.5–14.2	19.5	11.5–14.5	17.4
International normalized ratio for prothrombin time	0.9–1.1	1.8	0.9–1.1	1.5
Sodium (mmol/liter)	136–145	132	135–145	132
Potassium (mmol/liter)	3.4–5.1	4.9	3.4–5.0	5.1
Chloride (mmol/liter)	98–107	97	98–108	100
Carbon dioxide (mmol/liter)	20–31	21	23–32	21
Urea nitrogen (mg/dl)	6–20	43	8–25	73
Creatinine (mg/dl)	0.50–1.00	1.99	0.60–1.50	2.45
Glucose (mg/dl)	70–100	140	70–110	146
Calcium (mg/dl)	8.5–10.5	8.4	8.5–10.5	8.6
Aspartate aminotransferase (U/liter)	0–33	42	9–32	55
Alanine aminotransferase (U/liter)	0–34	16	7–33	19
Alkaline phosphatase (U/liter)	40–130	296	30–100	279
Total bilirubin (mg/dl)	0.0–1.2	3.7	0.0–1.0	3.1
Direct bilirubin (mg/dl)	0.0–0.3	1.8	0.0–0.4	0.9
Albumin (g/dl)	3.5–5.0	2.7	3.3–5.0	3.9
Total protein (g/dl)	6.4–8.3	6.2	6.0–8.3	6.0
Lipase (U/liter)	13–60	34	—	—
Lactic acid (mmol/liter)	0.5–2.2	2.0	—	—
Ethanol (mg/dl)	0–10	<10	—	—

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for lactic acid to milligrams per deciliter, divide by 0.1110. To convert the values for ethanol to millimoles per liter, multiply by 0.2171.

† 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.

as well as portal hypertensive gastropathy and erythematous duodenitis. Results of testing of the peritoneal fluid were not consistent with spontaneous bacterial peritonitis, and ceftriaxone was stopped. Treatment with furosemide and spironolactone was administered, and three therapeutic paracenteses were performed. The renal function worsened, the administration of diuretic agents was stopped, albumin was given intravenously, and treatment with midodrine and octreotide was started. On hospital day 13, the patient was transferred to this hospital for additional management of end-stage liver disease and acute renal injury, as well as evaluation for liver transplantation.

On transfer to this hospital, the patient described nausea and increasing abdominal distention and discomfort. A review of systems was notable for headache, heartburn, and pain in the left shoulder and hip.

The patient had a history of coronary artery disease, diabetes mellitus type 2, hyperlipidemia, obesity, gastroesophageal reflux disease, hypo-

thyroidism, anxiety, and depression. Migraines had occurred frequently in the past but had been rare after menopause. She had previously undergone a cesarean section, cholecystectomy, arthroplasty of the left shoulder, and recently, an open reduction and internal fixation involving the left femur. Medications included lactulose, midodrine, octreotide, ondansetron, pantoprazole, simethicone, insulin, gabapentin, duloxetine, and levothyroxine. Oxycodone and fentanyl patches started after the recent surgery were weaned and stopped, and the patient took acetaminophen as needed for pain. Treatment with azithromycin, trimethoprim–sulfamethoxazole, and hydromorphone had caused nausea and diarrhea; metoclopramide, promethazine, and prochlorperazine had caused anxiety. The patient lived in a rural area of New England with her husband and did not work because of medical disability. She did not drink alcohol, smoke cigarettes, or use illicit drugs.

On examination, the temporal temperature was 36.2°C, the blood pressure 92/55 mm Hg, and the pulse 78 beats per minute. The patient appeared chronically ill and jaundiced and was alert and oriented. The abdomen was tensely distended, with a fluid wave and diffuse tenderness. She had no asterixis, and trace swelling was present in both legs. No rash was present. The neurologic examination was normal. Laboratory test results are shown in Table 1. Treatment with midodrine and octreotide was stopped, and treatment with terlipressin was started.

On hospital day 2, the patient noted that headache, which had been present since admission to the other hospital, had increased in severity. The pain, which she described as "throbbing and pounding," was in the right frontal region and reminded her of previous migraines.

On hospital day 3, headache persisted, and the pain radiated to the back of her neck, which was not typical of her previous migraines. Butalbital–acetaminophen–caffeine was given, and a lidocaine patch was placed at the back of the neck; however, the pain did not abate after these treatments. On hospital day 4, nausea and abdominal distention increased, and therapeutic paracentesis was performed.

Dr. Kozak: CT of the head showed no changes from the previous imaging (Fig. 1).

Dr. Zhou: The administration of sumatriptan and intravenous magnesium and hydromorphone relieved the headache. However, on hospital day 5, headache worsened in severity throughout the day until the patient was tearful and rated the pain at 9 on a scale of 0 to 10, with 10 indicating the most severe pain. She had new photophobia, and blurred vision developed in the right eye. Intravenous hydromorphone was administered, and she subsequently rated the pain at 6 out of 10.

A diagnosis was made.

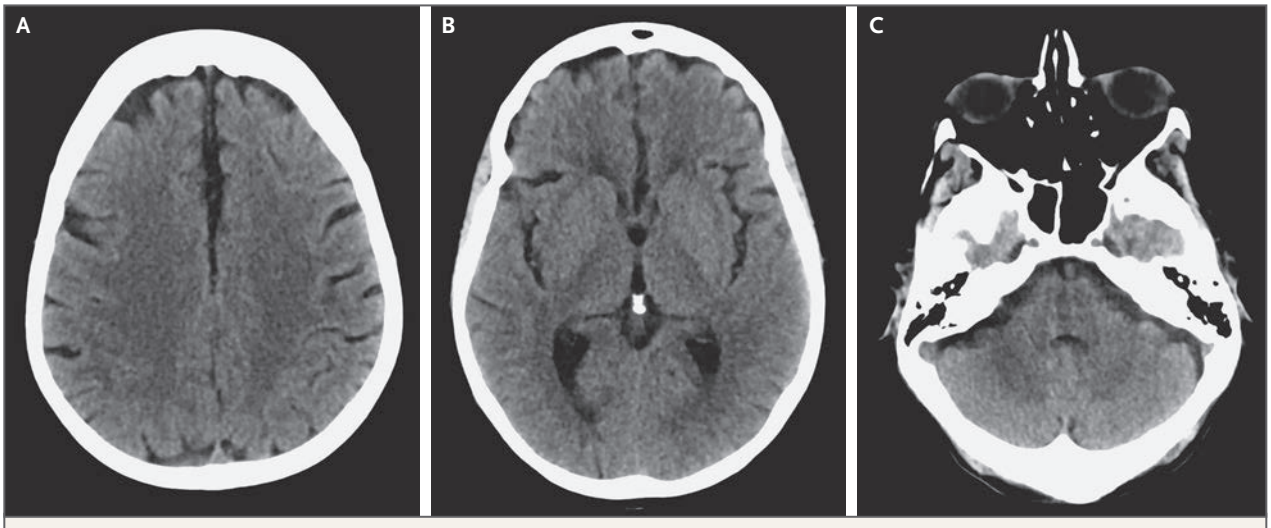

Figure 1. Initial CT of the Head.

CT of the head was performed without the use of intravenous contrast material. Axial images at the level of the centrum semiovale (Panel A), basal ganglia (Panel B), and posterior fossa (Panel C) show no radiologically significant abnormality except for mild scattered hypodensities in the white matter.

DIFFERENTIAL DIAGNOSIS

Dr. Shoshana J. Herzig: This 56-year-old woman had been chronically ill with end-stage liver disease, a history of migraines, and recent hip-fracture repair. She presented with confusion, abdominal pain and distention, and headache.

CONFUSION AND ABDOMINAL PAIN

Subacute confusion, as well as abdominal pain and distention, are common presenting symptoms for patients with end-stage liver disease. These findings typically indicate hepatic decompensation that leads to hepatic encephalopathy and the presence of ascites. This patient had been taking prescribed opioids for pain management after a recent hip-fracture repair. Opioids that are metabolized in the liver can accumulate in patients with hepatic impairment, which places patients with end-stage liver disease at heightened risk for opioid-related side effects, including the precipitation of hepatic encephalopathy. We are told that the confusion in this patient abated with the administration of lactulose and rifaximin and the continued holding of opioids, which supports the hypothesis that hepatic encephalopathy was the cause of this patient's initial confusion. Despite the decrease in confusion, other symptoms worsened. She appeared to have diuretic-refractory ascites, and progressive renal failure developed along with gradually worsening headache.

HEADACHE

Headache is one of the most common medical conditions reported by patients, and the majority fall within one of the primary headache syndromes, including migraine, cluster, and tension. This patient reported a history of migraines and noted that her headache was unilateral, pounding, and similar to previous migraines. All these initial features seem consistent with migraines. However, headache persisted and worsened in intensity, and the patient described differences in the characteristics of this headache relative to her usual migraines, including radiation to the posterior neck and eventually nausea, photophobia, and unilateral blurred vision. Although nausea and photophobia are common defining features of migraines, this patient's pain distribution changed from the initial presentation, and blurred vision developed in the right eye. Both of these features prompt consideration of a serious underlying disease as the cause of headache (i.e., secondary headache).

Although migraines can be associated with visual aura, the aura typically precedes or occurs with headache rather than developing after it abates, usually includes positive visual phenomena (e.g., geometric shapes or shimmering), typically progresses to include a quadrant or hemifield of visual loss in both eyes rather than unilateral blurred vision, and rarely lasts longer than an hour. Additional "red flag" features that should prompt consideration of an underlying cause include features of the headache and characteristics of the patient. This patient is over 50 years of age, with functional immunosuppression due to end-stage liver disease. In addition, she had persistent headache with features reported as atypical of her usual migraines, which progressed to include unilateral blurred vision. These signs and symptoms are consistent with headache secondary to serious underlying disease.

SECONDARY HEADACHE

The differential diagnosis of secondary headache is broad, including vascular, infectious, inflammatory, neoplastic, and other causes. The first differentiating feature that stands out in this patient's case is the subacute nature of her headache. The patient noted that headache had been present since the initial admission, indicating persistence over at least 2 to 3 weeks. Typically, vascular causes of headache, such as hemorrhage or arterial dissection, come on quickly and can be diagnosed by performing CT of the head. Similarly, typical bacterial or viral meningitis usually develops over hours to days, rather than weeks, and is associated with fever. Space-occupying lesions of the central nervous system (e.g., tumors, cysts, or abscesses) can cause subacute headache; however, the unremarkable findings on head CT make these conditions unlikely causes of this patient's illness.

The eventual development of unilateral blurred vision is another important differentiating feature that helps to further narrow the differential diagnosis of secondary headache. Causes of subacute headache that can result in blurred vision include conditions that lead to papilledema due to elevated intracranial pressure (e.g., idiopathic intracranial hypertension and meningoencephalitis), conditions that affect the ophthalmic

vessels (e.g., cerebral venous thrombosis and giant-cell arteritis), and conditions that increase intraocular pressure (e.g., orbital tumor and sarcoidosis). Giant-cell arteritis is a diagnosis that must be considered promptly, since failure to initiate treatment with high-dose glucocorticoids can result in permanent vision loss. However, headache from giant-cell arteritis is usually temporal and is often associated with scalp tenderness or nodularity over the temporal arteries. Patients with cerebral venous thrombosis or idiopathic intracranial hypertension can present with subacute headache and vision changes (symmetric or unilateral) associated with papilledema due to elevated intracranial pressure. I would strongly consider both of these conditions in this patient's case, as well as sarcoidosis, a protean condition that can affect any part of the central or peripheral nervous system and any part of the eye. Finally, although this patient's presentation is too protracted for typical bacterial or viral meningitis, certain less common pathogens can cause a more subacute meningitis and would need to be strongly considered as well.

Patients with end-stage liver disease can have cirrhosis-associated immune dysfunction, which can impair all effector arms of the immune system, resulting in functional immunosuppression.[1] In these cases, inflammatory conditions, such as vasculitis and sarcoidosis, are unlikely causes of headache, and infections would rise to the top of my differential diagnosis.

SUBACUTE MENINGOENCEPHALITIS

The differential diagnosis of subacute meningoencephalitis is broad and includes bacterial, viral, fungal, and parasitic pathogens. Most bacterial pathogens result in infection that manifests with systemic signs and symptoms (e.g., fever and weight loss), as well as pathogen-specific organ involvement. A thorough social history is an invaluable tool to additionally narrow the differential diagnosis. We are told that this patient does not work because of medical disability, and she has no epidemiologic risk factors associated with acquisition of tickborne pathogens and zoonotic infections. A patient's geographic area of residence and travel history can further substantially raise or lower the probability of certain diagnoses. This patient resides in the northeastern United States, and we are not told of any travel outside the country, which makes some parasites and endemic mycoses (e.g., coccidioidomycosis, histoplasmosis, paracoccidioidomycosis, and blastomycosis) unlikely causes in this case.

Cryptococcus, on the other hand, is a fungal pathogen that is ubiquitous in the United States. In addition, cryptococcus has a propensity to cause central nervous system disease. Furthermore, patients with end-stage liver disease have an increased risk of cryptococcosis, as well as an increased risk of disseminated disease and death.[2] The findings on chest radiography in this patient, which included opacification in the right hilar region and linear opacities in the left lower lung, are consistent with recent infection with cryptococcus, given that the lungs are typically the portal of entry.

Thus, although several diseases remain on the differential diagnosis, disseminated cryptococcal disease is a unifying diagnosis that would explain the majority of the clinical findings in this patient's case. I suspect that this patient has cryptococcal meningitis. To confirm this diagnosis, I would perform a lumbar puncture in order to measure the opening pressure and obtain cerebrospinal fluid (CSF) for analysis, microbiologic studies, and cryptococcal antigen testing.

DR. SHOSHANA J. HERZIG'S DIAGNOSIS

Cryptococcal meningitis.

HOSPITAL COURSE

Dr. Cesar G. Berto (Medicine): Lumbar puncture was requested, but it was delayed because the international normalized ratio for prothrombin time (INR) increased to 1.8 (reference range, 0.9 to 1.1). Fresh-frozen plasma and vitamin K were administered intravenously. In the meantime, blood testing for cryptococcal antigen was performed, and additional imaging studies were requested.

IMAGING STUDIES

Dr. Kozak: CT of the head performed 6 days after the previous head CT showed new small rounded hypodensities in the basal ganglia (Fig. 2A).

Magnetic resonance imaging (MRI) of the head was performed the following day and revealed new hyperintense foci in the basal ganglia on T2-weighted fluid-attenuated inversion recovery (FLAIR) images (Fig. 2B), a finding that corresponded with the abnormalities seen on the most recent head CT. Diffuse FLAIR hyperintensity within the cerebral sulci was present without abnormal sulcal enhancement or susceptibility signal abnormality. The findings in the basal ganglia showed restricted diffusion (Fig. 2C) and no abnormal enhancement (Fig. 2D).

DIAGNOSTIC TESTING

Dr. Sarah E. Turbett: The initial diagnostic test was a serum cryptococcal antigen test, which was positive at a titer of 1:64. This result prompted a lumbar puncture, which revealed an opening intracranial pressure of 31 cm of water (reference range, 10 to 20). On CSF analysis, the glucose level was 80 mg per deciliter (4.4 mmol per liter; reference range, 50 to 75 mg per deciliter [2.8 to 4.2 mmol per liter]), the total protein level 114 mg per deciliter (reference range, 5 to 55), and the white-cell count 41 per microliter, with a mononuclear cell predominance. Calcofluor white staining of a wet-mount preparation of CSF revealed large round yeast forms. Cryptococcal antigen testing of CSF was positive at a titer of 1:2048. Fungal cultures of CSF grew a yeast that was ultimately identified as *Cryptococcus neoformans.*

A diagnosis of infection with *C. neoformans* can be made with numerous methods, as shown in this case. Patients with cryptococcal meningoencephalitis typically have elevated intracranial pressure, low CSF glucose levels, high CSF total protein levels, and a mononuclear pleocytosis in CSF.[3] Direct staining of CSF with fluorochrome stains such as calcofluor, when positive, can suggest infection with *C. neoformans*; however, negative staining of CSF cannot rule out this infection, given its low overall sensitivity.[3] Fungal culture of CSF remains the standard testing method for the diagnosis of cryptococcal meningoencephalitis, and it is also a useful marker for monitoring the response to treatment.[3] The main limitation to this method is a prolonged time to organism growth (average, 3 to 4 days; maximum, 11 days), which can lead to diagnostic delays.[4]

Cryptococcal antigen testing of CSF has become a useful diagnostic tool for cryptococcal meningoencephalitis. The assay detects glucuronoxylomannan (GXM), a polysaccharide present in the cell wall of the organism.[5] GXM is released during growth and can be found in both CSF and serum of patients with cryptococcal meningoencephalitis. The test can be rapidly and easily performed at clinical laboratories, and overall, it has high sensitivity and specificity for the diagnosis of cryptococcal infection.[3] The cryptococcal antigen test is semiquantitative, and the titer can have prognostic implications. A titer of more than 1:1024 has been shown to be associated with an increased risk of death.[6] False negative tests can occur at the extremes of infection, both in cases with a low disease burden and in cases with a high disease burden, which has been associated with an inhibition of precipitates by excess antigen (postzone effect).[5] Although the test is highly specific, false positive cryptococcal antigen tests have been reported in patients infected with trichosporon species.[7] Such false positives are thought to result from a cross-reactive polysaccharide that is present in the cell wall of this organism.

LABORATORY DIAGNOSIS

Cryptococcus neoformans meningoencephalitis.

DISCUSSION OF INFECTIOUS DISEASE MANAGEMENT

Dr. Camille N. Kotton: Among patients with cirrhosis, the morbidity and mortality associated with cryptococcal disease is even higher than that among people with human immunodeficiency virus (HIV), a group known to have a high risk of complications and death from cryptococcal disease. In one case series, mortality from cryptococcal disease was reported to be 80% in patients with end-stage liver disease, as compared with 23% in those who were HIV-negative, and 14% in those with HIV.[8] The risk of death from cryptococcal disease is higher among patients with severe cirrhosis (defined by an elevated Model for End-Stage Liver Disease [MELD] score), those undergoing hemodialysis or mechanical ventilation, patients with fungemia, and those with altered mental status. Cirrhosis leads to profound immune suppression, which includes impairment of innate and cell-mediated immunity, complement deficiencies, altered neutrophil chemotaxis, and lymphocyte hyporesponsiveness.[9-11]

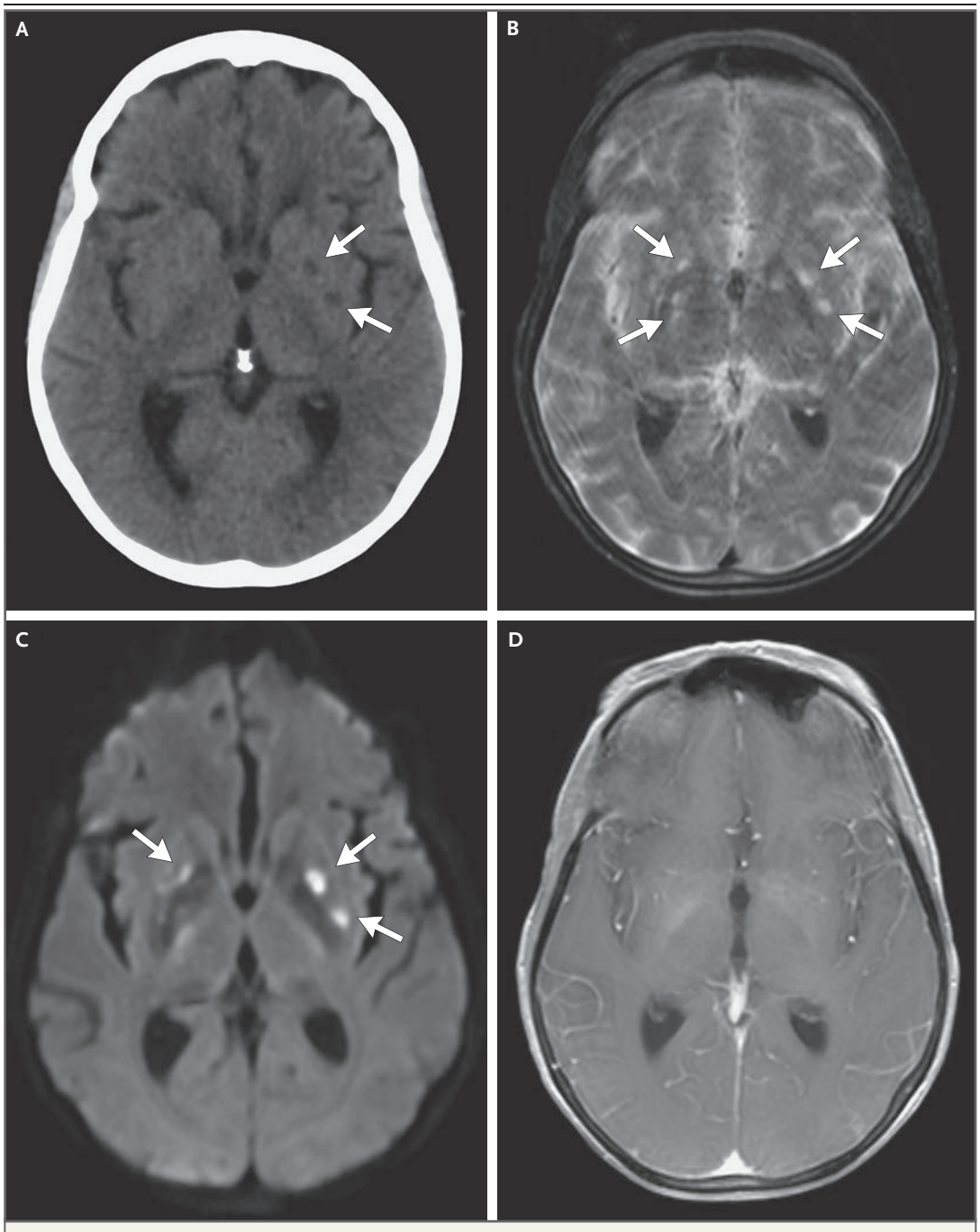

Figure 2. Additional Imaging Studies.

CT of the head was performed without the use of intravenous contrast material. An axial image at the level of the basal ganglia (Panel A) shows new small hypodensities in the basal ganglia (arrows). MRI of the head was performed with and without the use of intravenous contrast material. An axial, T2-weighted fluid-attenuated inversion recovery (FLAIR) image (Panel B) is degraded by motion but shows new hyperintense foci in the basal ganglia (arrows) and diffuse hyperintense signal in the cerebral sulci. An axial diffusion-weighted image through the basal ganglia (Panel C) shows hyperintense signal associated with the abnormalities in the basal ganglia (arrows). A corresponding hypointense signal was present on the apparent diffusion coefficient map (not shown). An axial, T1-weighted image, obtained after the administration of intravenous contrast material (Panel D), shows no abnormal enhancement in the basal ganglia or within the cerebral sulci.

Treatment of disseminated cryptococcal disease involves three phases: induction, consolidation, and maintenance. For induction, guidelines recommend treatment with either amphotericin B deoxycholate or liposomal amphotericin B given with flucytosine.[12-15] Guidelines vary regarding the recommended duration of therapeutics; however, a recent report suggests that, in those with HIV, a one-time dose of liposomal amphotericin B (10 mg per kilogram of body weight) with flucytosine and fluconazole is effective.[14] Although similar data in HIV-negative patients are lacking, a recent survey showed that the majority of practicing physicians in North America typically treat patients with cryptococcal meningitis with amphotericin B (either deoxycholate or liposomal) plus flucytosine for at least 2 weeks.[16]

Consolidation therapy usually includes the administration of high-dose fluconazole (400 to 800 mg per day) for 8 weeks. The dose should be adjusted, if needed, on the basis of the patient's renal function, and drug interactions should be evaluated. Given the increasing recognition of fluconazole resistance in cryptococcus species, susceptibility testing may help determine the dose of fluconazole and improve outcomes. Fluconazole administered at a high dose may result in unacceptable side effects in patients with cirrhosis; liver function should be closely monitored, and prolongation of the corrected QT interval (QTc) may be seen (which may be additive, since QTc prolongation can be seen in up to 50% of patients with cirrhosis).[17] Once consolidation therapy is complete, patients can be transitioned to maintenance therapy with fluconazole (200 to 400 mg per day) for at least 12 months. The appropriate duration of maintenance therapy is unknown, given that we do not have defined predictive markers.

Increased intracranial pressure is common, and expert management is imperative, since this feature is associated with clinically significant complications and an increased risk of death. Guidelines recommend aggressive management, including serial lumbar puncture, lumbar drain placement, and if needed, ventriculoperitoneal shunting. Treatment with one lumbar puncture in the first week of treatment, irrespective of baseline opening pressure, has been associated with a 69% relative survival benefit in the first 10 days.[18] Experts recommend "that at a minimum, scheduled lumbar puncture be performed on day 3 after diagnosis and prior to discharge in all persons with cryptococcal meningitis, irrespective of baseline opening pressure."[19]

FOLLOW-UP

Dr. Berto: A serum cryptococcal antigen test was positive on hospital day 6, and treatment with fluconazole and flucytosine was started. After the lumbar puncture was performed on hospital day 7, fluconazole was discontinued, and induction treatment with liposomal amphotericin B was initiated. During the subsequent 5 days, serial therapeutic lumbar punctures were performed because the patient had only transient relief of headache. A lumbar drain was placed on hospital day 13 and removed when intracranial pressure stabilized 1 week later. Of note, culture of CSF obtained at the time of drain removal showed no growth. Treatment was switched to consolidation therapy with fluconazole in hospital week 4, and the patient was discharged.

Unfortunately, the patient was readmitted to this hospital 3 weeks later because of shock, hepatic encephalopathy, and acute kidney failure. Opening pressure during lumbar puncture and culture of CSF were normal. No cause of the multiorgan failure in this patient was identified. The goals of care were transitioned to comfort measures, and the patient died in the hospital.

Dr. Kathy M. Tran (Medicine): How should the coagulation profile be considered in the decision for diagnostic and therapeutic lumbar puncture and drainage?

Dr. Annemarie E. Fogerty: The hematology consult service was asked to provide strategies to decrease the INR in an effort to minimize the bleeding risk associated with lumbar puncture. Data suggest that when the INR is less than 2, as in this case, fresh-frozen plasma has little benefit. INR reduction with transfusion of fresh-frozen plasma is a factor of the pretransfusion INR, such that meaningful INR reduction is only observed when the INR is greater than 4.[20] More importantly, data show that INR does not predict bleeding risk. In a series of 852 invasive procedures performed in 363 patients with cirrhosis, only 10 bleeding events were observed, which were unrelated to platelet count, INR, Child-Pugh grade, or the use of fresh-frozen plasma. In this series, no bleeding events occurred in patients with a platelet count less than 50,000 per microliter, including those who also had an INR greater than 1.3.[21]

INR and prothrombin time do not predict bleeding risk because they only reflect the role of procoagulant proteins. Patients with liver disease, however, have a rebalanced hemostasis in which both procoagulants and the endogenous anticoagulants protein C and protein S are reduced. Of note, the thrombin generation assay, which is able to examine the contribution of both anticoagulants and procoagulants, was normal when performed in patients with cirrhosis.[22]

The INR cannot be used to predict bleeding in patients with cirrhosis. In this case, no clinically significant bleeding was observed, the platelet count was above 50,000 per microliter, and the INR was less than 2 throughout hospitalization. Thus, there was no role for preprocedural transfusion with fresh-frozen plasma or platelets, which may also cause harm from unnecessary volume expansion.

FINAL DIAGNOSIS

Cryptococcal meningoencephalitis.

CASE RECORDS EDITORS' NOTE — LESSONS LEARNED

1. Patients with end-stage liver disease can have cirrhosis-associated immune dysfunction that results in functional immunosuppression.

2. Patients with end-stage liver disease are at increased risk for disseminated cryptococcal disease and also have an increased risk of disease-associated death.

3. Therapeutic serial lumbar puncture is a key strategy in the treatment of patients with elevated intracranial pressure.

4. The INR cannot be used to predict bleeding risk in patients with cirrhosis.

5. There is usually no role for preprocedural transfusions of fresh-frozen plasma or platelets when the platelet count is above 50,000 per microliter.

This case was presented at the Medicine Case Conference.

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

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