

Herpes Simplex Type-2 Encephalitis Masked by Diabetic Ketoacidosis

Yusuf Aydin, MD; Ihsan Ustun, MD; Kutlu Erol, MD; Etem Ozkaya, MD; Kamile Gul, MD; Dilek Berker, MD; Mustafa Unal, MD; Tuncay Delibasi, MD; Kadri Altundag, MD; and Serdar Guler, MD

Ankara, Turkey

Diabetic ketoacidosis is a life-threatening acute complication of type-1 diabetes mellitus. Infection is the most common precipitating factor for diabetic ketoacidosis and is responsible for more than 50% of the cases. Here, we present a case study of a young man with herpes simplex virus type-2 encephalitis masked by diabetic ketoacidosis. We aim to orient clinicians towards being vigilant against such clinical scenarios.

Key words: type-1 diabetes mellitus ■ diabetic ketoacidosis ■ herpes simplex virus type 2 ■ encephalitis

INTRODUCTION

Diabetic ketoacidosis (DKA) is a life-threatening acute complication of type-1 diabetes mellitus that may result from increased insulin requirements during the course of an infection, trauma, myocardial infarction or surgery.¹ During the course of DKA, the patient's neurological status may show impairment with symptoms of confusion, lethargy, stupor or even coma. Although the neurological status may be related to diabetes itself, occasionally, another etiology may play a role.

CASE REPORT

Subjective Information

A 22-year-old man with type-1 diabetes mellitus was admitted to the hospital with mental stupor. His diabetes had been diagnosed six years earlier, and since then he had receiving insulin therapy (four daily injections). Before admission to the hospital, his daily regimen was 30 U regular insulin and 10 U human neutral protamine Hagedorn insulin, and his average daily glucose levels had been 100–200 mg/dL. According to the history taken from his family, he had experienced high fever, nausea and vomiting for the last 24 hours. Mild dysarthria, gait instability and personality changes were also noticed. There was no history of any previous neurological disease. On physical examination, he had a fever of 39.2°C, pulse rate of 110/min, and Kussmaul respiration. He had fruity breath odor and abdominal rigidity. Neurological examination was normal except for lethargy and mild dysarthria.

Laboratory Findings

Initial laboratory evaluation showed a hemoglobin level of 12 g/dL, leukocyte count of 8200/μL, and an erythrocyte sedimentation rate of 10 mm/hour. Other biochemical values were as follows: serum glucose 905 mg/dL, blood urea nitrogen level 10 mg/dL, serum creatinine 0.7 mg/dL, sodium 123 mEq/L (135–145 mEq/L), potassium 3 mEq/L (3.5–

© 2005. From Division of Endocrinology and Metabolism, Department of Internal Medicine, Ankara Numune Education and Research Hospital (Aydin, Ustun, Erol, Gul, Berker, Unal, Delibasi, Guler); Refik Saydam National Hygiene Center, Virology Laboratory (Ozkaya); Department of Medical Oncology, Hacettepe University Medical School (Altundag), Ankara, Turkey. Send correspondence and reprint requests for *J Natl Med Assoc.* 2005;97:722–724 to: Kadri Altundag, MD, 8181 Fannin St., No. 728, Houston, TX 77054; phone: (713) 795-0438; fax: (713) 794-4385; e-mail: altundag@sbcglobal.net

5.5 mEq/L), chloride 92 mEq/L (95–110 mEq/L), hemoglobin A1c 9.3% (nondiabetic range, 4–6%). Arterial blood gas analysis revealed a bicarbonate level of 10 mEq/L and an arterial pH of 7.1.

Treatment

After 24 hours of treatment with intravenous insulin, blood glucose was 180 mg/dL, and serum sodium was 133 mEq/dL. Urinalysis showed no ketones, and arterial pH was 7.35. In spite of the improvement of the laboratory data, the patient's clinical status remained the same. Since his fever and lethargy continued, lumbar puncture was performed to rule out bacterial meningitis. Cerebro-spinal fluid (CSF) findings revealed mild lymphocytic pleocytosis with a cell count of 20 cells/mm³, glucose of 105 mg/dL and protein level of 53 mg/dL. Gram, India ink and acid-fast stains were all negative for microorganisms. Blood and CSF bacterial cultures and serology for brucellosis were also negative. Results of magnetic resonance imaging (MRI) of the brain were normal. A second lumbar puncture, performed seven days after the first one, yielded a positive polymerase chain reaction (PCR) for herpes simplex virus (HSV) type 2 and a negative result for HSV type 1. CSF was added to a Vero cell culture, and a cytopathic effect was observed on the fourth day of culture. Intravenous administration of acyclovir (10 mg/kg) was started on the 10th day, and the patient's mental status began to improve one week later. The patient was discharged without any neurologic sequelae after three weeks of acyclovir therapy.

DISCUSSION

DKA is an acute complication of type-1 diabetes mellitus and is associated with further serious complications if not diagnosed promptly and treated appropriately. In patients with type-1 diabetes mellitus, DKA is commonly precipitated by a lapse in insulin treatment or by an acute infection, trauma or infarction that makes usual insulin treatment inadequate.¹ The most important causes of mortality in persons with type-1 diabetes mellitus are DKA, infections and chronic complications.² When both type-1 and type-2 diabetes mellitus patients are taken into account, infections are the leading cause of mortality (25.8%) followed by cardiovascular diseases (18.5%), cerebrovascular diseases (11.3%), uremia (8.6%) and DKA (1.3%).³ Infection is the most common precipitating factor for DKA and is responsible for more than 50% of the cases. Diabetic patients with infection may decrease or skip insulin doses unintentionally, and this might further contribute to DKA.⁴

The causative agent in our case was HSV type 2, a relatively rare cause of encephalitis outside the

neonatal period.^{5,6} In the current literature, we have found one report of suspected herpes simplex type-2 encephalitis (HSE) occurring with DKA.⁷ While the exact incidence of HSE is not known, it has been estimated at about one case per million per year. Patients with fever, headache, confusion, aphasia, personality change, clouding of consciousness and even coma should be further evaluated for encephalitis.⁶ Patients with DKA can also present with an altered state of consciousness. On admission, our patient had fever (39.2°C), Kussmaul respiration, tachycardia, abdominal rigidity and unconsciousness, which are all compatible with DKA. After treatment of the patient for DKA, his mental stupor did not improve, causing us to further seek other underlying etiologies.

The diagnosis of HSE is usually established clinically and with radiological interventions. MRI is the best imaging technique in HSE and may show evidence of focal edema in the medial region of the temporal and orbital surface of the frontal lobes, insular cortex and angular gyrus.⁶ However, radiological findings may occasionally be normal in HSE as they had been in our patient.^{5,6} CSF examination is of crucial diagnostic value in HSE and should be performed after computed tomography or MRI.⁷ The characteristic profile of CSF in HSE consists of a normal or raised pressure, pleocytosis (typically 10–200 cells/mm³), normal glucose and increased protein (0.6–6 g/L). CSF findings of our patient were compatible with encephalitis, revealing a mild lymphocytic pleocytosis with a cell count of 20 cells/mm³, slightly elevated protein level (53 mg/dL), elevated glucose level (105 mg/dL) and no red blood cells. PCR test for HSV DNA on CSF has been suggested to be the gold standard for diagnosing HSE.⁶ In our patient, the results of the PCR test from CSF were positive for HSV type 2 and negative for HSV type 1.

Treatment with the nucleoside analogue acyclovir should be started as soon as the diagnosis of HSE is suspected, since the mortality and morbidity of patients have been dramatically reduced by this treatment.^{5,6,8} In the literature, acyclovir therapy is recommended for at least 10 days. In immunocompromised patients, the duration of therapy can be extended to 21 days to prevent a relapse.^{5,6,8}

In conclusion, clinicians should consider HSE in all cases of encephalopathy even in the presence of normal results for imaging studies, and HSE infection should further be ruled out with PCR. Additionally, if a diagnosis of HSE is suspected, acyclovir should be started as soon as possible. Although the outcome of treatment may be favorable, patients may still suffer from subsequent significant neurologic sequelae.

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