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PERINATAL/NEONATAL CASE PRESENTATION

Gestational diabetes insipidus, HELLP syndrome and eclampsia in a twin pregnancy: a case report

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We report a case of eclampsia in a twin pregnancy complicated by HELLP syndrome and diabetes insipidus. This confluence of disease processes suggests that a modification of common magnesium sulfate treatment protocols may be appropriate in a certain subset of patients.
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Introduction

The association between diabetes insipidus (DI) and liver dysfunction in a preeclamptic patient has been established in multiple case reports.[1] This case is an important example that illustrates how the pathophysiology of DI and the pharmacokinetics of magnesium sulfate affect patient management in the setting of preeclampsia. To our knowledge, no cases have been reported regarding DI and Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome associated with a case of eclampsia. Medline and Ovid database searches using the terms 'eclampsia,' 'diabetes insipidus' and 'HELLP,' failed to show any reports.

Case

An 18-year-old African-American primigravida at 34-weeks gestational age presented from an outlying facility for the management of preeclampsia. The pregnancy was complicated by dichorionic, diamniotic twin gestation, but was otherwise unremarkable. On admission, the patient reported headache, right upper quadrant abdominal pain, blurry vision and was on a continuous infusion of magnesium sulfate at 2 g per hour. The patient's initial blood pressure levels at the outlying facility were elevated to 188/106 mmHg. Vital signs on admission were unremarkable, except for blood pressure of 140/93 mmHg. Fetal heart tracings were both reactive. Laboratory values were normal except as follows: hemoglobin, 11.1 g per 100 ml; hematocrit, 32.2%; platelets, 106 000 per μl; potassium, 3.2 mg per 100 ml; creatinine, 0.72 mg per 100 ml; aspartate aminotransferase, 127 U l^{-1}; alanine aminotransferase, 65 U l^{-1}; and lactate dehydrogenase, 390 U l^{-1}. A 24-h urine collection was begun to quantify proteinuria.

During the first night of hospitalization, the patient developed marked polyuria and polydipsia. Urine output increased to 1500 cc h^{-1} by the early morning totaling 12 l for the entire night. Repeat electrolytes were unchanged. The endocrinology service was then consulted for the management of presumptive DI. Therapy with the administration of dDAVP (1-deamino-8-D-arginine vasopressin) orally twice daily was initiated. Serum osmolality was increased at 296 mOsm kg^{-1}, and urine osmolality was decreased to 71 mOsm kg^{-1} with a specific gravity of 1.000. The 24-h urine results showed a total protein of 780 mg. The patient denied the previously reported headaches, blurry vision and right upper quadrant pain, and her blood pressures remained 140 to 155 mmHg (systolic) and 80 to 95 mmHg (diastolic), consistent with a diagnosis of mild preeclampsia. Magnesium infusion was subsequently discontinued, and the patient was kept in the hospital for continued bed rest and monitoring of her electrolytes, urine output, blood pressures and other laboratory values.

Shortly after the discontinuation of the magnesium infusion in the morning of hospital day 2, the patient had a 2-min seizure. A 4-g bolus of magnesium sulfate was administered followed by a continuous infusion of 2 g per hour. Urine output at this time continued to be elevated. Laboratory values showed mildly elevated sodium of 144 mequiv., decreasing platelets of 61 000 per μl, as well as mildly elevated alanine aminotransferase and aspartate aminotransferase of 65 and 58 U l^{-1}, respectively. Delivery through Cesarean section was then performed under general anesthesia secondary to complete breech presentation of the first fetus.

Postoperatively, the patient continued on 24 h of magnesium sulfate infusion and developed severely increased blood pressures requiring treatment with hydralazine. Platelets reached a nadir of 24 000 per μl, then increased to 124 000 per μl. Urine output improved to 100 cc h^{-1}, and liver enzymes were normalized by discharge on postoperative day 4. The patient continued on dDAVP after discharge and was followed by endocrinology on an outpatient basis.

Comment

Diabetes insipidus occurs in 4 of 100 000 pregnancies and is believed to result from the activity of a placental N-terminal

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aminopeptidase that degrades endogenous arginine vasopressin (AVP).[2,3] Overt diuresis occurs with a decrease of 80 to 85% in the circulating amount of AVP, resulting in a small (1 to 2%) decrease in total body water and marked polydipsia. This manifests in hypo-osmolar urine and, especially in the setting of preeclampsia, in concentrated serum with electrolyte imbalances, including hypernatremia and hypokalemia. Central DI in both pregnant and nonpregnant women is typically treated with dDAVP, a synthetic form of AVP with a different N terminus that lends resistance to degradation by the placental vasopressinase, essentially reversing the diuretic effects. Administration may be oral, intranasal or intravenous.[3]

Several mechanisms for decreased AVP were present in this patient. Increased placental tissue in a multifetal gestation could have produced more vasopressinase than one placenta in a singleton gestation. Katz and Bowes[4] reported a similar case of transient DI and preeclampsia in a triplet gestation in 1987.[4] Although no studies have attempted to evaluate this association, it follows that increased placental tissue would increase levels of vasopressinase, thereby further lowering the circulating levels of AVP and increasing the risk of development of DI. A second factor is this patient's liver dysfunction, which decreases the liver's ability to clear the body of placenta-produced vasopressinase, also decreasing the available circulating AVP.

Magnesium sulfate has been the cornerstone for the prevention of eclamptic seizures in preeclamptic patients for decades. It is so effective that eclampsia may be seen as a preventable disease.[5] However, its exact mechanism of action is unknown. Magnesium is renally excreted and has a half-life of 4 h with normal renal function.[6] When glomerular filtration decreases, the half-life of magnesium increases,[6] and it follows that the converse would be true as well; as the glomerular filtration rate increases, so does the excretion of magnesium, decreasing its half-life. Our institution uses a typical regimen of a 4-g loading dose followed by a continuous intravenous infusion of 2 g per hour.[7] Patients are monitored clinically by examining patellar reflexes, vital signs and urine output >100 cc every 4 h to prevent magnesium toxicity.[3] Serum magnesium levels are not routinely monitored.

In our patient, the interaction between the massive diuresis and recently discontinued magnesium infusion likely contributed to inadequate serum levels for seizure prophylaxis. Monitoring urine output has been a mainstay of the prevention of magnesium toxicity. Conversely, this case shows that excessive diuresis may signal subtherapeutic magnesium levels through a decreased half-life. These patients might require more intensive monitoring or a higher rate of magnesium infusion to compensate for the renal dysfunction until the diseases resolve. Although no magnesium levels were drawn during this patient's hospital course, it likely would have proven useful in guiding magnesium therapy during the period of massive diuresis. Either increasing the magnesium infusion rate beyond 2 g per hour or increasing the utilization of serum magnesium levels, or both may be beneficial when preeclampsia is complicated by DI for the prevention of eclampsia.

Conflict of interest

The authors declare no conflict of interest.

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