A newborn boy was admitted to the neonatal intensive care unit (NICU) of this hospital because of respiratory distress.

The patient was born at a gestational age of 29 weeks at another hospital by cesarean section for breech presentation, premature labor, and rupture of membranes of approximately 2 hours’ duration. He weighed 1275 g and appeared vigorous, with spontaneous respirations; the 1-minute and 5-minute Apgar scores were 7 and 9, respectively. Shortly thereafter, subcostal retractions developed. Analysis of umbilical arterial blood revealed a pH of 7.35, a partial pressure of oxygen of 47 mm Hg, and a partial pressure of carbon dioxide of 22 mm Hg. Continuous positive airway pressure (CPAP) was administered, and he was transferred to the nursery.

The temperature was 37.2°C under radiant heat, the blood pressure 58/44 mm Hg, the pulse 119 beats per minute, and the oxygen saturation 94 to 96% while the patient was breathing 50% oxygen with CPAP; the blood glucose level was 72 mg per deciliter (4.0 mmol per liter).

Transfer to this hospital was arranged; 1 hour after birth, the MassGeneral Hospital for Children NICU transport team arrived at the other hospital. On examination, the patient was nondysmorphic and the skin was pink and well perfused. There were moderate subcostal retractions, shallow respirations, and bronchial breath sounds that were slightly diminished in intensity; the remainder of the examination was normal for the gestational age. The trachea was intubated and assisted ventilation was begun; oxygen was administered to maintain hemoglobin saturation levels in the mid-90s percentage range. Proper position of the endotracheal tube was confirmed with the use of radiography. The blood glucose level decreased to 34 mg per deciliter (1.9 mmol per liter). A peripheral intravenous catheter was placed, and an infusion of 10% glucose was begun; the glucose level rose to 134 mg per deciliter (7.4 mmol per liter). He was transported by ambulance to this hospital and admitted to the NICU.

From the Departments of Pediatrics (E.A.C., H.S.W.), Medicine (H.S.W., M.L.-R.), Radiology (R.S.), and Pathology (M.L.), Massachusetts General Hospital; and the Departments of Pediatrics (E.A.C., H.S.W.), Medicine (H.S.W., M.L.-R.), Radiology (R.S.), and Pathology (M.L.), Harvard Medical School — both in Boston.

had received regular prenatal care and lived in a shelter. Medications during pregnancy included methadone, clonazepam, clonidine, and iron supplements. The maternal blood type was A, Rh-positive, with negative antibody screening. Prenatal testing for hepatitis C virus antibody was positive; testing for syphilis, the human immunodeficiency virus, hepatitis B virus, and gonococcal and chlamydial infections was negative. The newborn had a healthy half-sibling; there was no family history of genetic abnormalities.

On examination in the NICU, the patient’s temperature was 37.6°C, the blood pressure 60/30 mm Hg, the pulse 174 beats per minute (normal, 80 to 180), and the respiratory rate 56 breaths per minute (normal, 30 to 60). He attempted to cry around the endotracheal tube; breath sounds were decreased bilaterally. Heart sounds were normal, without murmurs; the extremities were warm and well perfused; testes were in the inguinal canals; the skin was ruddy and thin, with visible veins; no plantar creases were present; and there was no breast tissue. He moved all extremities, with resting posture in extension; the remainder of the examination was normal for his gestational age. Blood levels of phosphorus, magnesium, total and direct bilirubin, and creatinine were normal, as was the anion gap; other results are shown in Table 1. Chest radiographs showed diffuse, fine granular opacities and mild perihilar linear opacities bilaterally, features thought to be consistent with the respiratory distress syndrome of the newborn. Surfactant, caffeine, ampicillin, and gentamicin were administered. An umbilical venous catheter was placed.

On the patient’s second day of life, the neonatal abstinence syndrome developed (characterized by tremors, agitation, poor sleeping, and frantic behavior); screening of the urine for illicit drugs was negative. Morphine was administered, resulting in improvement. Radiographs showed improvement in the pulmonary opacities. The trachea was extubated, and nasal CPAP was administered transiently. Results of testing conducted by the Massachusetts newborn screening program were normal. Culture of blood drawn on admission was sterile, and the administration of antibiotic agents was stopped.

During the patient’s third day of life, when he was still in the NICU, a systolic ejection murmur was heard, respiratory distress recurred, and respiratory acidosis developed (Table 1). The trachea was reintubated, and a radiograph showed changes consistent with pulmonary edema and an increase in the size of the cardiac silhouette. Echocardiography revealed normal cardiac structures, normal ventricular function and thickness (left ventricular ejection fraction [LVEF], 69%), a patent ductus arteriosus (2.3 mm) with left-to-right shunting, estimated right ventricular systolic pressure of 55 mm Hg with systemic systolic pressure of 58 mm Hg, a patent foramen ovale, and no pericardial effusion. The administration of ampicillin and gentamicin was restarted, and ibuprofen was added. Feedings of pasteurized human milk, administered by gavage, were started. Ultrasonography of the brain revealed grade 1 hemorrhage into the germinal matrix bilaterally, with normal brain parenchyma. The patient’s respiratory status improved, clinical evidence of the patent ductus arteriosus resolved, and the trachea was extubated on the patient’s fifth day of life.

On the sixth day of life, the patient’s work of breathing increased suddenly and mottled skin developed; the trachea was reintubated, and stress doses of hydrocortisone, oxacillin, gentamicin, and intravenous saline were administered. Echocardiography revealed a small, concentric pericardial effusion, no evidence of tamponade, markedly thickened ventricular walls, near obliteration of right and left ventricular cavities, and underfilling of both ventricles; biventricular systolic function was preserved (LVEF, 61%). A radiograph showed increased opacification of the lungs. Hypotension and oxygen desaturation to 70% occurred. Dopamine, morphine, midazolam, vancomycin, normal saline, sodium bicarbonate, red cells, increased oxygen supplementation, and high-frequency oscillator ventilation were administered. Nitric oxide was administered, and oxygen saturation rose transiently to 86%, followed by worsening hypoxemia, anuria, and bradycardia. The neonate’s mother was informed and came to the NICU; she requested the presence of the hospital chaplain, who arrived shortly thereafter. Epinephrine was administered and positive-pressure ventilation and chest compressions were begun. However, refractory asystole developed, and the patient died early on his seventh day of life.

An autopsy was performed.
Differential Diagnosis

Dr. Elizabeth A. Catlin: May we review the imaging studies?

Dr. Randheer Shailam: A radiograph from the patient’s first day of life (Fig. 1A) shows that the lung volumes are normal; however, there are diffuse reticular and granular opacities bilaterally, features consistent with the respiratory distress syndrome. On the patient’s second day of life (Fig. 1B), there is a mild increase in the lung volumes as compared with the previous examination, but the volumes remain in the normal range. The reticular and granular opacities that are consistent with the respiratory distress syndrome persist in both lungs.

On the patient’s third day of life, ultrasonography of the brain revealed a hyperechoic area in the right caudothalamic groove that was consistent with hemorrhage in the germinal matrix; there was a smaller germinal-matrix hemorrhage in the left caudothalamic groove. The central portion on the right germinal-matrix hemorrhage was hypoechoic, suggesting that this is not acute. On the fifth day of life, a chest radiograph obtained after extubation showed normal lung volumes. However, there was a new hazy opacity in the right perihilar region and right upper lobe obscuring the costophrenic angle, and increased rightward cardiomedialstinal shift, features consistent with worsening atelectasis superimposed on findings of the respiratory distress syndrome.

A chest radiograph obtained after reintubation on the fifth day of life (Fig. 1C) showed worsening opacification at the right lateral base, obscuring the costophrenic angle, and increased rightward cardiomedialstinal shift, features consistent with worsening atelectasis in the right lung.

A radiograph obtained on the sixth day of life (Fig. 1D) showed diffuse abnormalities involving both lungs and completely obscuring the right cardiomedialstinal border. In the left upper lung zone was a new opacity with air bronchograms. The opacification in the right hemithorax had progressed. These findings were thought to represent worsening atelectasis and edema superimposed on the respiratory distress syndrome. Approximately 16 hours later, a chest radiograph showed progressive opacification of both hemithoraxes, new bilateral apical lateral opacities, and the appearance of pleural fluid.

Dr. Manuella Lahoud-Rahme: The first echocardiogram, obtained on the third day of life (Fig. 2A, 2B, and 2C), showed normal segmental anatomy, normal biventricular systolic function (LVEF, 69%), a patent foramen ovale with left-to-right shunting, a patent ductus arteriosus (2.3 mm) with left-to-right shunting across it, and a peak systolic gradient of 14 mm Hg suggesting pulmonary pressures that were elevated but were 80% of systemic pressures. The study was normal for age, with a moderately large patent ductus arteriosus and elevated pulmonary pressures.

On the sixth day of life, a repeat echocardiogram (Fig. 2D through 2G), obtained semiurgently, showed concentric biventricular hypertrophy, small ventricular cavities, preserved biventricular function (LVEF, 61%), and no evidence of shunting across a patent ductus arteriosus. With the use of color Doppler imaging, the patent foramen ovale was again seen with left-to-right shunting. In addition, there was a small inferior pericardial effusion and no evidence of tamponade.

In this patient, biventricular hypertrophy developed over a period of 3 days, with preserved systolic function. The biventricular hypertrophy was most likely due to intravascular depletion and underfilling of both ventricles.

Dr. Catlin: I am aware of the diagnosis in this case. This newborn boy, born prematurely at a gestational age of 29 weeks, had a relatively typical course in the NICU until suddenly, on his sixth day of life, progressive multiorgan system failure developed, and he died early on his seventh day of life. For diagnostic possibilities, I considered four categories of neonatal disorders: inborn errors of metabolism, respiratory failure, cardiomyopathy, and bacterial or viral sepsis.

Inborn Errors of Metabolism

This patient’s catastrophic clinical collapse at the end of his first week of life raises the possibility of an inborn error of metabolism. Inborn errors of metabolism in newborns consist of a heterogeneous group of disorders with similar presentations. Pregnancy and delivery are usually uncomplicated; neonates are often healthy at birth, as in this case, but metabolic imbalances may develop during the first week of life, in association with poor feeding, vomiting, excessive sleepiness, and lethargy. A number of features suggested a metabolic disorder in this patient, including rapid and stunning clinical deterioration, lack of...
Table 1. Laboratory Data.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range, Age-Adjusted†</th>
<th>On Admission to the NICU, 3.75 Hr after Birth</th>
<th>12 to 16 Hr after Birth</th>
<th>3rd Day of Life</th>
<th>6th Day of Life</th>
<th>7th Day of Life</th>
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<tr>
<td>Hematocrit (%)</td>
<td>45.0–67.0</td>
<td>49.7 (ref 42.0–60.0)</td>
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<td>42.0</td>
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<td>Hemoglobin (g/dl)</td>
<td>14.5–22.5</td>
<td>16.7 (ref 13.5–19.5)</td>
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<td>White-cell count (mm³)</td>
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<td>8100 (ref 9000–30,000)</td>
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<td>6200</td>
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<td>Differential count (% adjusted for nucleated red cells)</td>
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<td>Polymorphonuclear leukocytes</td>
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<td>51 (ref 66–87)</td>
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<td>Band forms</td>
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<td>Lymphocytes</td>
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<td>32 (ref 22–37)</td>
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<td>33</td>
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<td>Monocytes</td>
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<td>5</td>
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<td>3 promyelocytes, 9 myelocytes, 4 metamyelocytes</td>
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<td>Nucleated red cells (per 100 white cells)</td>
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<td>15</td>
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<td>Platelet count (mm³)</td>
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<td>164,000</td>
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<td>Peripheral smear description</td>
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<td>1+ anisocytosis, 1+ polychromasia, 2+ hypochromasia, 3+ macrocytes, 1+ schistocytes</td>
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<td>Sodium (mmol/liter)</td>
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<td>Potassium (mmol/liter)</td>
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<td>Chloride (mmol/liter)</td>
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<td>Carbon dioxide (mmol/liter)</td>
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<td>Glucose (mg/dl)</td>
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<td>99</td>
<td>103</td>
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<td>169</td>
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<td>Urea nitrogen (mg/dl)</td>
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<td>27</td>
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<td>Calcium (mg/dl)</td>
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<td>9.8</td>
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<td>Ionized calcium (mmol/liter)</td>
<td>1.14–1.30</td>
<td>1.48</td>
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response to antibiotics, cardiac hypertrophy and shock, metabolic acidosis, lethargy, and multiorgan-system dysfunction.2

The inborn errors of metabolism that present dramatically in newborns include organic acidemias, primary lactic acidoses, urea-cycle defects, disorders of carbohydrate metabolism, disorders of amino acid metabolism, and fatty-acid oxidation defects.3 Some infants with organic acidemias have distinctive urinary odors (e.g., the odor of maple syrup in maple syrup urine disease or the odor of sweaty socks in isovaleric acidemia). This patient had no unusual odors, and severe lactic acidosis developed only in the context of progressive hypoxemia and hypotension, making a primary lactic acidosis unlikely.

Galactosemia was not considered likely, because the patient did not have vomiting or pathologic jaundice. Patients with fatty-acid oxidation defects may present with features similar to those seen in this patient, including cardiomegaly and possible pulmonary edema, but this patient did not have other characteristic features such as seizures, encephalopathy, hypotonia, or hypoglycemia. The results of this patient’s panel of tests conducted by the Massachusetts newborn screening program showed no evidence of an inborn error of metabolism.3,4

NEONATAL RESPIRATORY FAILURE

This neonate showed signs of respiratory distress immediately after birth. In a patient with a gestational age of 29 weeks, the fetal lungs are biochemically and morphologically immature; approximately 30% of such neonates have the respiratory distress syndrome. In this newborn, the progressive respiratory insufficiency, findings on chest radiographs, and favorable response to intratracheal surfactant supported the diagnosis of the respiratory distress syndrome. Neonatal pneumonia may be radiographically indistinguishable from the respiratory distress syndrome, which is why treatment with antibiotics is typically instituted.5

The patient’s second episode of respiratory failure was most likely caused by a patent ductus arteriosus in which left-to-right shunting of blood caused cardiomegaly, pulmonary edema, and ventilation–perfusion mismatch. Pharmacologic closure of the patent ductus arteriosus correlated with resolution of the second episode of respiratory insufficiency.6

When a third episode of respiratory failure oc-
curred, a consideration was that the ductus arteriosus had reopened or that pneumonia had developed. Antibiotic coverage was broadened for the possibility of a new pneumonia. Radiographic evidence consistent with pulmonary edema and clinical decline prompted repeat echocardiography. The results unexpectedly showed that biventricular hypertrophy had developed, suggesting that some of the clinical findings had a cardiogenic cause, such as a cardiomyopathy.

**Neonatal Cardiomyopathy**

Neonatal cardiomyopathies are uncommon and may be part of systemic diseases, including genetic syndromes, metabolic diseases, and neuromuscular disorders. On physical examination,

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**Figure 1. Radiographic Studies.**

A chest radiograph obtained within 24 hours after the patient’s admission to this hospital (Panel A) shows bilateral diffuse reticular and granular opacities (arrows), findings compatible with the respiratory distress syndrome. The lung volumes are normal in this intubated patient. A radiograph obtained after the first extubation (Panel B) shows mild reticular and granular opacities (arrows), findings compatible with the respiratory distress syndrome. The lung volumes remain normal after extubation. A chest radiograph obtained after a third episode of respiratory failure and reintubation (Panel C) shows multifocal patchy opacities (arrows) in the right upper, middle, and lower lung zones, features suggestive of atelectasis superimposed on the respiratory distress syndrome (arrowhead). Hazy opacities are suggestive of pulmonary edema. A radiograph obtained during the final period of clinical deterioration (Panel D) shows bilateral patchy opacities with air bronchograms (arrowheads) and small bilateral pleural effusions (arrows).
this neonate was entirely nondysmorphic, and his neuromuscular examination was consistently normal for his gestational age. The two cardiac ultrasound studies showed preserved systolic function and no evidence of pericardial effusion. In a color-flow Doppler image (Panel C) of the main and branch pulmonary arteries, the blue area indicates antegrade flow of blood into the branch pulmonary arteries and the red area indicates flow across the patent ductus arteriosus. On the sixth day of life, by comparison, the parasternal long-axis view (Panels D and E) shows marked thickening of the right and left ventricle and near obliteration of the left ventricular cavity in systole. Panel F shows a color-flow Doppler image within the left ventricle, with the blue area indicating acceleration of flow across the left ventricular outflow tract. Doppler investigation of the flow shows a gradient of 25 mm Hg within the ventricle. A subcostal view of the heart (Panel G) shows a small inferior pericardial effusion.

**Neonatal Sepsis**

Neonates with very low birth weight (<1500 g), such as this patient, are at increased risk for bacterial or viral sepsis. Bacterial pathogens include gram-negative organisms (Escherichia coli, klebsiella), streptococcus, staphylococcus species, or listeria. Causes of viral sepsis include enterovirus, adenovirus, and herpes simplex virus (HSV). Presenting signs are nonspecific and protean and could have had an atypical presentation of an evolving cardiomyopathy.
include temperature instability, lethargy, apnea, jaundice, respiratory distress, rashes, poor perfusion, irritability, and poor feeding. This patient had several of these signs, leading to the clinical suspicion of severe sepsis syndrome.

SUMMARY
In conclusion, I believed this patient's illness and death were probably due to overwhelming bacterial or viral sepsis. I believed that the sepsis led to irreversible systemic hypotension, hypoxic respiratory failure (due to pneumonitis and pulmonary edema), severe metabolic acidosis, and acute renal failure.

DR. ELIZABETH A. CATLIN’S DIAGNOSIS
Multiorgan system failure, probably due to overwhelming bacterial or viral infection with sepsis; a cardiomyopathy cannot be ruled out.

PATHOLOGICAL DISCUSSION

Dr. Madelyn Lew: There were two major clinical concerns that we were asked to address at the autopsy: the cause of respiratory distress and the possibility of a cardiomyopathy to explain the sudden cardiac decompensation.

The patient weighed 1340 g and had a crown–rump length of 24.3 cm, features consistent with a newborn at a gestational age of 29 weeks. There were bilateral serous pleural effusions measuring approximately 25 ml and 20 ml in the right and left pleural cavities, respectively. The lungs were pale, firm, and heavy, weighing 49.1 g in combination (normal weight for a gestational age of 29 weeks, 25.3±12.6). Examination of the heart revealed slight cardiomegaly (10.2 g; normal weight for a gestational age of 29 weeks, 7.2±2.7) and a probe-patent ductus arteriosus. The remainder of the gross examination revealed structurally normal organs with diffuse mottling.

Histologic examination of the heart revealed a normal myocardium with no hypertrophy, inflammation, or necrosis to indicate involvement by a myocarditis or cardiomyopathy. More than 50% of the evaluated lung parenchyma contained multiple hemorrhagic infarcts with adjacent air spaces filled with fibrin and inflammatory cells. The interstitium adjacent to these infarcts contained enlarged cells with cherry-red nuclear inclusions, findings consistent with viral inclusions (Fig. 3A). Multiple microscopical fields of the liver (Fig. 3B) and adrenal glands (Fig. 3C) contained similar patches of necrosis associated with cells containing nuclear inclusions. The differential diagnosis of nuclear inclusions includes many viral causes, including cytomegalovirus, HSV, parvovirus, varicella–zoster virus, and measles virus. However, the morphologic features of these nuclear inclusions and the pattern of organ involvement are most consistent with infection with HSV type 1 (HSV-1) or type 2 (HSV-2). Immunohistochemical analysis (Fig. 3D) showed staining of these cells for HSV-1 and HSV-2. The immunohistochemical stains for HSV-1 and HSV-2 use antibodies that react to common antigens present in both serotypes.

Neuropathological examination revealed a germinal-matrix hemorrhage that extended into the right lateral ventricle. There was focal infarction in the developing white matter underly- ing the germinal matrix. Immunohistochemical analysis for HSV-1 and HSV-2 was negative. There was no evidence of meningitis or encephalitis.

The slides and paraffin blocks of specimens obtained from the placenta were evaluated at Massachusetts General Hospital. There was no evidence of chronic villitis, chorionic-plate thrombi, plasma-cell deciduitis, or viral inclusions to indicate HSV infection. Immunohistochemical analysis for HSV-1 and HSV-2 was negative.

In summary, the autopsy findings are diagnostic of systemic HSV infection involving the liver, adrenal glands, and lungs. We concluded that the patient’s respiratory distress was due to viral pneumonia and the shock was due to viral sepsis. The brain infarct was most likely secondary to stress, including sepsis, whereby shunted blood flow to the heart and lungs led to ischemic changes in the brain.

NEONATAL HSV INFECTION

Dr. H. Shaw Warren: Both HSV-1 and HSV-2 are common in pregnant women and can cause neonatal infection. Neonatal HSV infection occurs in approximately 1 in 3200 deliveries and may present with three syndromes that frequently overlap: involvement of skin, eyes, mouth, or a combination; neurologic infection; and disseminated infection. Disseminated infection, seen in this patient, is difficult to diagnose because nonspecific signs of severe organ failure predominate, as they did in this case. Diagnosis is
often delayed, and infection with HSV is often discovered only at autopsy, as in this case.

When and where did this newborn acquire HSV? In utero infection is rare (estimated at approximately 1 in 100,000 deliveries) and is unlikely in this patient because of the uninvolved placenta and because such neonates usually have signs of chronic skin, eye, and neurologic involvement. An estimated 85% of cases are acquired at birth. Risk factors for transmission include the presence of HSV in the birth canal, prolonged rupture of membranes, vaginal delivery, and the use of fetal monitors. Both the short duration of ruptured membranes and the cesarean section would have reduced the risk of transmission from the mother in this case. The highest risk to the neonate (risk of transmission, 30 to 50%) is primary maternal infection close to delivery, leading to a high quantity of virus and an absence of type-specific HSV antibody passed to the neonate. The risk of transmission from mothers who have recurrent infection at the time of delivery is much lower (risk of transmission, <3%). Both primary and recurrent infections are often asymptomatic in pregnant women, so the absence of a symptomatic lesion does not rule out the diagnosis in this case.

No diagnostic samples for HSV were obtained from the patient, so we are left to interpret the testing of the mother’s serum, obtained 24 days post partum and sent to an outside laboratory. The test results showed that the IgG antibody level for a combination of HSV-1 and HSV-2 was markedly elevated, the HSV-2 type-specific IgG antibody level slightly elevated, and the IgM antibody level for a combination of HSV-1 and

Figure 3. Pathological Findings at Autopsy.
Panel A (hematoxylin and eosin) shows a hemorrhagic pulmonary infarct (arrow), with viral inclusions in cells adjacent to the infarct (inset). Panel B (hematoxylin and eosin) shows an infarct in the liver (arrow), adjacent to the central vein; cells adjacent to the infarct show viral inclusions (inset). Panel C (hematoxylin and eosin) shows adrenal cortical infarcts (arrow), with viral inclusions in adjacent cells (inset). Immunohistochemical analysis of a specimen of the lung for HSV-1 and HSV-2 (Panel D and inset, immunoperoxidase stain for HSV-1 and HSV-2) shows staining of the cells that have inclusions.
HSV-2 very slightly elevated. Many laboratories use assays that cross-react between HSV-1 and HSV-2, mixed-antigen preparations, or both, as was done here. Furthermore, titers of IgM antibodies to HSV can increase with recurrent episodes of HSV infection, so that an elevated IgM titer does not necessarily prove primary infection. Although the antibody levels are consistent with the possibility that the mother had a primary infection with one type and an old infection with the other type, the results are not definitive. Postnatal acquisition of HSV through exposure to a caregiver is estimated to cause about 10% of cases of neonatal HSV. On balance, it seems most likely that the patient acquired the infection from the mother at the time of birth.

Even poring over this case retrospectively, there were no clear clues to the diagnosis that might have prompted antiviral treatment with acyclovir. Many infections can cause severe sepsis in a 6-day-old neonate, including infection with many strains of bacteria and with viruses such as adenovirus and enterovirus, in addition to HSV. Sepsis is common in this population, and occult disseminated HSV is rare; therefore, empirical treatment with acyclovir of all neonates with sepsis syndrome is not warranted.

**Dr. Nancy Lee Harris** (Pathology): Dr. Ecker, would you comment on strategies for prevention of maternal–fetal HSV infection?

**Dr. Jeffrey L. Ecker** (Maternal–Fetal Medicine): Women with a history of HSV infection are often prescribed acyclovir in the last weeks of pregnancy to reduce the risk of recurrence and the risk of neonatal HSV infection at the time of delivery. Regardless of such prophylaxis, obstetricians will plan cesarean delivery in cases of genital lesions or symptoms suggestive of recurrent HSV at the time of labor, of rupture of membranes, or of an otherwise indicated or planned delivery. Delivery during a primary HSV infection is associated with a high risk of neonatal HSV infection, but reducing transmission may be challenging, especially if there are no symptoms or lesions that are suspicious for genital HSV. Some researchers and clinicians have suggested that discordant couples — in which the woman has no serologic evidence of past HSV infection and her partner does have such evidence — may be encouraged to make behavioral changes (e.g., the use of barrier methods) to prevent primary maternal HSV infection during pregnancy. Such strategies remain a matter of debate, discussion, and study.

**Dr. Catlin:** This newborn’s death was devastating to her mother. Parents never completely recover from the death of a child, for many parents, it is the single most traumatic event in their lives. The NICU health care providers also grieve, struggle to make sense of the situation, and experience stress when a newborn patient dies. I was in close contact with the patient’s mother while we awaited postmortem results. Once the diagnosis of systemic herpes infection, without placental involvement, was made, concern was raised about acquisition of herpes by the newborn in the hospital. We have a policy in all the nurseries that staff members with herpetic lesions cannot work until cleared by Occupational Health services. Nonetheless, Margaret D. Settle, R.N., Ph.D., NICU Nurse Director, systematically reviewed staffing assignments for this patient, and each caregiver was interviewed regarding herpetic lesions. We similarly questioned the physicians. No herpetic lesions were discovered. Thus, we were relatively confident that the herpes infection was not acquired in this hospital.

I reported the results of the postmortem examination to the mother and suggested that she be checked for HSV infection. She went to the clinic, asking to be checked for herpes. Serologic samples were drawn, but a physical examination was not performed, so we do not know whether she had a current lesion. She now seems to be doing well emotionally.

**Dr. Harris:** What is the status of a possible HSV vaccine?

**Dr. Warren:** To date, attempts to develop such a vaccine have not been successful.

**ANATOMICAL DIAGNOSIS**

Neonatal herpes simplex virus infection, involving the lungs, liver, and adrenal glands, with sepsis.

This case was presented at the Pediatric Grand Rounds.

Dr. Catlin reports receiving consulting fees from Medical Professional Mutual Insurance. No other potential conflict of interest relevant to this article was reported.

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

We thank Dr. Drucilla Roberts for supervising the postmortem examination and assisting in the preparation of the pathological discussion and images.
REFERENCES


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LANTERN SLIDES UPDATED: COMPLETE POWERPOINT SLIDE SETS FROM THE CLINICOPATHOLOGICAL CONFERENCES

Any reader of the Journal who uses the Case Records of the Massachusetts General Hospital as a teaching exercise or reference material is now eligible to receive a complete set of PowerPoint slides, including digital images, with identifying legends, shown at the live Clinico-pathological Conference (CPC) that is the basis of the Case Record. This slide set contains all of the images from the CPC, not only those published in the Journal. Radiographic, neurologic, and cardiac studies, gross specimens, and photomicrographs, as well as unpublished text slides, tables, and diagrams, are included. Every year 40 sets are produced, averaging 50-60 slides per set. Each set is supplied on a compact disc and is mailed to coincide with the publication of the Case Record.

The cost of an annual subscription is $600, or individual sets may be purchased for $50 each. Application forms for the current subscription year, which began in January, may be obtained from the Lantern Slides Service, Department of Pathology, Massachusetts General Hospital, Boston, MA 02114 (telephone 617-726-2974) or e-mail Pathphotoslides@partners.org.