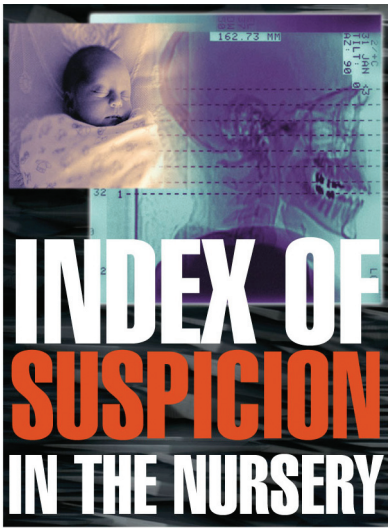

The reader is encouraged to write possible diagnoses for each case before turning to the discussion. We invite readers to contribute case presentations and discussions. Please inquire first by contacting Dr. Philip at aphilip@stanford.edu.

Author Disclosure

Drs Balighian, Lee, Hassoun, Maqbool, and Mahajan have disclosed no financial relationships relevant to these cases. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Case 1: Skull Swelling 14 Hours After Birth
Case 2: Fever and Eye Discharge at 11 Days of Age

Case 1 Presentation

A 3.3-kg male term infant is born via vacuum-assisted vaginal delivery to a 26-year-old G2P1001, now P2002, woman whose serology results were within normal parameters. Membranes ruptured 4 hours before delivery, and Apgar scores are 9 and 9 at 1 and 5 minutes, respectively. A hematocrit obtained shortly after birth is 46% (0.5). At 14 hours after birth, the infant has swelling around the posterior scalp that increases in size over the next 6 hours. The swelling is fluctuant and shifts with movement of the infant's head and body. The infant appears pale, and a complete blood count is obtained.

The infant's hematocrit 22 hours after birth is 12% (0.12). Skull radiographs appear normal. The infant is transfused with packed red blood cells. Coagulation studies reveal a prothrombin time of 15.8 sec, International Normalized Ratio of 1.3, and partial thromboplastin time of 60 sec. The infant is transferred to a tertiary care hospital neonatology unit for further management.

Case 2 Presentation

A previously well 11-day-old infant is brought to the emergency department for evaluation of fever and eye discharge. The maximum temperature measured at home was 39.2°C. The mother mentions that the baby is sleepier and has had reduced oral intake of formula as well as redness in one eye over the past 24 hours.

The baby was born at term via spontaneous vaginal delivery and had uncomplicated prenatal and perinatal periods.

Physical examination in the emergency department reveals a well-appearing febrile infant whose rectal temperature is 39.5°C, heart rate is 176 beats/min, respiratory rate is 32 beats/min, and oxygen saturation is 100%. He does not appear to be in any distress and is alert and easily consolable. The rest of the physical examination findings are within normal limits, except for right eye injection and discharge.

A complete sepsis evaluation is performed in the emergency department, including a complete blood count, urinalysis, cerebrospinal fluid analysis, and samples for cultures of blood, urine, right eye discharge, and cerebrospinal fluid are obtained. The results are a white cell count of $10.1\times10^3/\mu L$ ($10.1\times10^9/L$) with 66% neutrophils and normal urine and cerebrospinal fluid analysis results. The clinician administers ampicillin and cefotaxime in the emergency department and admits the infant for further management.

Case 1 Discussion

The Diagnosis

Subgaleal hemorrhage was diagnosed at the tertiary hospital. A subgaleal hemorrhage occurs when shearing and traction force of the scalp during delivery causes blood to accumulate into the space between the periosteum of the skull and the aponeurosis. The space allows for potentially massive blood loss, volume depletion, shock, and up to 14% mortality. Subgaleal hemorrhage presents as diffuse and fluctuant swelling that shifts with movement. Infants delivered by vacuum assistance are 15 times more likely to have a subgaleal hemorrhage than infants who do not receive such assistance.

In contrast, a caput succedaneum is a benign swelling of the scalp above the periosteum that crosses sutures lines. Another cause of scalp swelling, a cephalohematoma, involves localized subperiosteal swelling that does not cross suture lines.

When asked if there were any bleeding problems in the family, the mother revealed that her father had hemophilia. The family history and infant's clinical course made a diagnosis of hemophilia highly likely.

The Condition

The hemophilias are a group of inherited bleeding disorders. The term hemophilia most often refers to either factor VIII deficiency (hemophilia A) or factor IX deficiency (hemophilia B). Both hemophilia A and B are X-linked recessive diseases that produce a varied clinical spectrum. The combined incidence of hemophilia in male live births is 1 in 5,000, with 80% of affected infants having hemophilia A. One third of cases are due to new mutations. Intracranial bleeding occurs more commonly in vaginal deliveries than caesarean sections among patients who have hemophilia.

Treatment

The therapy for a significant bleeding episode is replacement of the deficient factor. The mother of this patient was unsure if her father had hemophilia A or B, but after contacting her mother, the clinicians learned the father had hemophilia A. Therefore, this infant required immediate intravenous replacement factor VIII, which should be administered in consultation with a pediatric hematologist. Fresh frozen plasma, which contains both factors VIII and IX, can be used if the exact diagnosis is uncertain. Head ultrasonography of the infant did not show intraventricular hemorrhage. The infant's bleeding stopped, and he recovered well and was discharged 6 days after birth.

Lessons for the Clinician

Hemophilia is an X-linked bleeding disorder that may present during the newborn period in otherwise healthy male infants. This disease should be suspected with prolonged or severe bleeding of any type and especially after circumcision. Circumcision should not be performed in patients who have a family history of hemophilia until the patient is tested. Identifying affected patients early is crucial for comprehensive care and anticipatory guidance, including potential complications and therapeutic options. Also, asking specific questions about specific diseases when obtaining a family history is sometimes enlightening. (*Eric Balighian, MD, Pediatrics Instructor, Johns Hopkins Hospital, St. Agnes Hospital Hospitalist; Calvin Lee, MD, Clinical Fellow, Pediatric Hematology and Oncology, Johns Hopkins Hospital, Baltimore, MD*)

American Board of Pediatrics Neonatal-Perinatal Medicine Content Specifications

- Know the inheritance patterns of the common factor deficiencies.
- Know the causes and pathophysiology of congenital defects in hemostasis.
- Know the clinical manifestations, laboratory findings, and management of congenital defects in hemostasis.
- Know the diagnostic, clinical, and imaging features of extracranial hemorrhage, including cephalohematoma and subgaleal hemorrhage.

Suggested Reading

Carcao M, Aledort L. Prophylactic factor replacement in hemophilia. *Blood Rev*. 2004;18:101–113

Chalmers E. Hemophilia and the newborn. *Blood Rev*. 2004;18:85–92

Chalmers E. Neonatal coagulation problems. *Arch Dis Child Fetal Neonatal Ed*. 2004;89:F475–F478

Kenet G, Chan AK, Soucie JM, Kulkarni R. Bleeding disorders in neonates. *Haemophilia*. 2010;16(suppl 5):168–175

Case 2 Discussion

Diagnosis

The patient's blood culture grew *Listeria monocytogenes* within 24 hours, prompting the diagnosis of neonatal listeriosis.

Listeriosis is an uncommon serious condition. This foodborne disease usually affects the elderly, immunocompromised individuals, infants, and pregnant women.

Pregnant women are 20 times more likely to acquire listeriosis than the general population and represent one third of all confirmed cases. (1) Although infection can occur throughout pregnancy, it is more likely in the third trimester, when T-cell-mediated immunity is weakened. (2) Most neonatal infections are acquired transplacentally. The in-

cidence of disease due to *L monocytogenes* has decreased substantially in the recent years, with the most recent incidence figures from the Centers for Disease Control and Prevention placing it at 1.9 per 100,000 in children younger than 1 year of age. This decline in incidence is largely due to improved sanitation, education, and control of *L monocytogenes* contamination at food processing plants, (3) along with increasing use of ampicillin for prophylactic management of group B *Streptococcus* infection.

Listeriosis in pregnancy can lead to stillbirth, preterm birth or full-term newborns who can develop septicemia or meningitis, even if the mother is asymptomatic. Transmission is transplacental, and exposure can occur through the birth canal or after delivery.

Neonatal listeriosis can be classified as early-onset (0 to 6 days) and late-onset (7 to 42 days) disease. Early-onset disease is more severe and usually leads to preterm delivery and neonatal sepsis. Newborns manifest signs of sepsis within 24 to 48 hours after birth. In severe cases, this results in disseminated infection involving the lungs, skin, and intestine, a condition termed granulomatosis infantisepticum. (4) This condition is fatal in one third of cases, despite adequate antimicrobial therapy. (5) Late-onset disease is more likely to occur in infants following uncomplicated term pregnancies. Meningitis is more common than generalized septicemia. Manifestations can vary, with some infants having fever with or without signs of lethargy and irritability.

Although leukocytosis is common, this patient's complete blood count showed a white blood cell count of $10.1\times10^3/\mu L$ ($10.1\times10^9/L$) with 66% neutrophils and no bands, hemoglobin of 17 g/dL (170 g/L), and platelet count of $176\times10^3/\mu L$ ($176\times10^9/L$). In most cases of *Listeria* meningitis, the cerebrospinal fluid appears purulent and has a polymorphonuclear predominance. The protein concentrations in the cerebrospinal fluid are usually high and correlate directly with the prognosis. Blood cultures are positive in up to 75% of cases, unlike for other bacterial causes of meningitis in which blood cultures are frequently negative. The placental pathology of affected fetuses usually shows acute intervillositis or intervillous abscesses, (6) which was the only finding in this case before presentation.

Ampicillin is effective in 70% of cases of listeriosis and is the first line of treatment. Nearly 30% of affected newborns die unless effective antimicrobial therapy with a combination of an aminopenicillin and an aminoglycoside is used. (7) Antibiotic resistance is emerging, with multiple reports indicating decreased susceptibility of some *L monocytogenes* strains to ampicillin.

Lessons for the Clinician

Neonatal listeriosis is an uncommon serious illness that should be considered in all cases of suspected sepsis. Placental pathology could be a valuable tool, if available, in identifying such subtle cases. Sepsis can be a late presentation of the disease in a healthy term newborn. (*Ameer Hassoun, MD, Shazia Maqbool, MD, Prashant Mahajan, MD, MPH, MBA, Division of Pediatric Emergency Medicine, Carman & Ann Adams Department of Pediatrics, Children's Hospital of Michigan, Detroit, MI*)

American Board of Pediatrics Neonatal-Perinatal Medicine Content Specifications

- Know the epidemiology, pathogenesis, prevention, clinical manifestations, and diagnostic features of perinatal *Listeria monocytogenes* infection.
- Know the treatment and complications of perinatal *Listeria monocytogenes* infection.

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4. Posfay-Barbe KM, Wald ER. Listeriosis. *Semin Fetal Neonatal Med*. 2009;14: 228–233
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