Type IV Neonatal Early-Onset Group B Streptococcal Disease in a United States Hospital

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Group B streptococcus (GBS) serotypes causing neonatal disease vary by geographic region. Surveillance at the Brigham and Women’s Hospital in Boston, Massachusetts, revealed a case of neonatal early-onset sepsis caused by type IV GBS. Neonatal type IV disease occurs in the Middle East but has not recently been described in U.S. infants.

Maternal intrapartum antibiotic prophylaxis (IAP) against group B streptococcus (GBS) has significantly decreased the incidence of neonatal early-onset sepsis (EOS) caused by GBS (6). Early-onset disease has not been eliminated, however, with persistent disease primarily occurring in premature infants and in infants born to women who have falsely screened GBS negative (22). IAP has had no effect on the incidence of late-onset neonatal GBS sepsis (LOS) (6). In addition to causing neonatal disease, GBS is also a frequent cause of infection in pregnant women, a significant contributor to preterm birth, and a cause of serious infection in elderly and immunocompromised adults (23). The overall clinical problem of GBS disease in neonates and adult populations will best be addressed by the development of GBS vaccines (5).

Vaccine research to date has focused on the protective efficacy of antibodies to GBS capsular polysaccharide (19). The development of capsular polysaccharide-based vaccines is complicated by the multiple serotypes that cause neonatal disease. Nine antigenically and structurally distinct capsular GBS polysaccharide serotypes (types Ia, Ib, and II to VIII) have been described (8). The genetic basis for this diversity has recently been delineated (7). Geographic differences in the serotype distributions of isolates colonizing the rectovaginal region have been described (16, 17, 21). There has been a shift in the serotype distribution of invasive neonatal and adult disease isolates in the United States over the past 10 years, with the emergence of a significant proportion of type V serotype GBS (11, 14). Two recent studies of invasive disease isolates from neonates and pregnant women both found that serotypes Ia, III, and V were predominant, with the remaining isolates comprising serotypes Ib and II and nontypeable GBS (3, 11).

For the development of an effective multivalent GBS vaccine, ongoing surveillance is needed to detect further shifts in serotype distribution and to detect the potential emergence of historically less frequent serotypes. We conducted surveillance for neonatal GBS disease occurring in infants cared for in the neonatal intensive care unit (NICU) or newborn nurseries at the Brigham and Women’s Hospital (BWH) in Boston, Massachusetts, from January 2000 through August 2006. This research was conducted with the approval of the BWH Institutional Review Board. Cases were identified by an electronic search of Microbiology Laboratory records. Total births, birth weight, and clinical and microbiological data were obtained from a review of hospital medical and laboratory records. Identification of streptococcal isolates as GBS was performed in the hospital microbiology laboratory by use of a latex agglutination test (Streptex; Murex Diagnostics). Individual isolates were obtained from the hospital microbiology laboratory on blood agar plates. The capsular polysaccharide serotype was determined by using rabbit serum specific to each GBS capsular polysaccharide (CPS)-tetanus toxoid conjugate vaccine for serotypes Ia, Ib, II, III, IV, V, VI, and VIII, as described previously (20). The reference strains used were as follows: type Ia, strain 090; type Ib, strain H36B; type II, strain 18RS21; type III, strain M781; type IV, strain 3139; type V, strain CJB111; type VI, strain SS1214; and type VIII, strain JM9-130013. The alpha-like surface protein type was determined by PCR with primers specific for the alpha C protein, Alp-1, Alp-2, Alp-3, and Rib (L. C. Madoff, submitted for publication).

During the study period, 62,033 births occurred at BWH and 1,364 very-low-birth-weight (VLBW; birth weight, <1,500 g) infants were cared for in the BWH NICU. Twenty-eight cases of neonatal invasive GBS disease were identified: 20 cases of EOS and 8 cases of LOS (Tables 1 and 2). We have previously reported the clinical characteristics, but not the serotype, of the early-onset cases that occurred from 2000 to 2003 (22). Most of the EOS cases occurred in term infants, with an average gestational age of 36.9 weeks (range, 25 to 42 weeks) and an average birth weight of 2,969 g (range, 850 to 4,370 g). The overall incidence of EOS from 2000 to 2006 was 0.32 cases/1,000 live births; the incidence for 2004 to 2006 was 0.18 cases/1,000 live births. The EOS cases that occurred from 2004 to 2006 continued trends that we observed previously: EOS occurred in two infants born to mothers with negative prenatal GBS screening cultures, i.e., in one premature infant whose
sera found evidence of multiple CPS gene types, but no type IV United States from 1992 to 2002 (3, 4, 11, 13, 14, 17, 25). A EOS caused by type IV GBS was reported in studies from the Neither disease, colonization in pregnant women, nor neonatal gene that is specific to the type IV capsule cluster (7, 15).

ers designed to be specific for a unique portion of the CpsH factor for recurrent disease (8, 12).

3% of infected infants, and prematurity is a significant risk disease. Recurrent GBS disease is known to occur in up to the isolates from both episodes were of identical serotype and clinical status, but there were no cases of meningitis or death average gestational age of 26.4 weeks (range, 24 to 28 weeks). average birth weight of 968 g (range, 650 to 1,360 g) and an admissions. All eight cases occurred in VLBW infants with an birth circumstance did not allow the administration of IAP and in one term infant whose GBS-positive mother did not receive IAP due to obstetrical error. The clinical isolates were available for serotyping in 14/20 (75%) of EOS cases. The predominant serotypes were type Ia (36%), type V (29%), and type III (21%), consistent with those reported in the two most recent multicenter reports (3, 11).

The overall incidence of LOS was 5.9 cases/1,000 VLBW admissions. All eight cases occurred in VLBW infants with an average birth weight of 968 g (range, 650 to 1,360 g) and an average gestational age of 26.4 weeks (range, 24 to 28 weeks). The average age of onset of illness was 37 days (range, 18 to 85 days). All infants became significantly ill beyond their baseline clinical status, but there were no cases of meningitis or death directly attributable to the GBS infection. Two cases occurred in the same infant (LOS cases 3 and 4). This infant received standard antibiotic therapy for the first episode of GBS sepsis. The isolates from both episodes were of identical serotype and surface protein type, suggesting that illness was due to recurrent disease. Recurrent GBS disease is known to occur in up to 3% of infected infants, and prematurity is a significant risk factor for recurrent disease (8, 12).

We identified one case of EOS caused by type IV GBS. The serotype was confirmed both by exclusive reactivity with type IV-specific antisera and by genetic means by a PCR with primers designed to be specific for a unique portion of the CpsH gene that is specific to the type IV capsule cluster (7, 15). Neither disease, colonization in pregnant women, nor neonatal EOS caused by type IV GBS was reported to occur in the United States from 1992 to 2002 (3, 4, 11, 13, 14, 17, 25). A recent PCR-based genetic study of a series of American GBS isolates that were nontypeable with the use of CPS reference sera found evidence of multiple CPS gene types, but no type IV genes were identified (24). A single case of invasive nonpregnant adult disease type IV GBS was reported in a surveillance study in Maryland in 1992 (13). Type IV has been reported to be the dominant colonizing serotype in a recent study of pregnant women in the United Arab Emirates (2) and the second most common colonizing serotype in a study of pregnant women in Turkey (9). Other reports from Kuwait (1), Israel (18), and Turkey (10) have not found a significant proportion of type IV GBS isolates in studies of maternal GBS colonization, suggesting that type IV GBS transmission is found in highly localized populations even in similar geographic regions. The mother of the case infant in our study was Caucasi-an, was born in the United States, and had no known recent travel history. This case illustrates the importance of ongoing surveillance for the emergence of historically less frequent serotypes as efforts to develop and market a multivalent GBS vaccine proceed.

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**REFERENCES**


