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Meningoencephalitis and Compartmentalization of the Cerebral Ventricles Caused by *Enterobacter sakazakii*

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A necrotizing meningoencephalitis complicated by ventricular compartmentalization and abscess formation caused by *Enterobacter sakazakii* in a previously healthy 5-week-old female is described. A detailed description of the isolate is presented. This communication firmly establishes the pathogenicity of *E. sakazakii*.

Important differences in deoxyribonucleic acid hybridization, pigment production, biochemical characteristics, and susceptibility to antimicrobial agents have prompted the differentiation of the yellow-pigmented *Enterobacter cloacae* into a new species, *Enterobacter sakazakii* (6). The full spectrum of pathogenicity of this new species is not well defined. A very rare cause of infection in humans, *E. sakazakii* has been reported to cause disease in neonates. To our knowledge, there has been only one report (7) of meningitis in a newborn in which the isolate is fully characterized and appears to be consistent with *E. sakazakii*.

The present report describes a previously healthy 5-week-old infant who developed severe meningitis caused by *E. sakazakii* and describes the characteristics of the isolate. The infection resulted in necrotizing cerebritis (2, 3) with abscess formation and compartmentalization of the cerebral ventricles (8) and was extremely difficult to clear. This experience firmly establishes the pathogenicity of *E. sakazakii* in an infant beyond the first month of life.

Case report. A 5-week-old full-term female developed fever, a bulging fontanelle, and grand mal seizures. The cerebrospinal fluid contained 15,600 leukocytes per mm^3, 95% of which were polymorphonuclear leukocytes, and had a protein concentration of 295 mg/dl and a glucose concentration of 4 mg/dl. Courses of intravenous ampicillin (400 mg/kg administered every 24 h) and chloramphenicol (100 mg/kg administered every 24 h) were begun. Cultures of the cerebrospinal fluid grew *E. sakazakii*, and treatment was continued with intravenous ampicillin alone. Serosanguineous fluid from bilateral subdural taps on day 6 grew *E. sakazakii*, and a course of intravenous gentamicin (7.5 mg/kg administered every 24 h) was begun. Cultures of subdural fluid continued to grow *E. sakazakii*, and computerized tomography (CT) scan on day 15 showed massive ventricular dilatation. The patient was then transferred to Riley Children's Hospital.

At admission, the infant was irritable and afebrile. There was no clinical or laboratory evidence of congenital malformation of the urinary tract, gastrointestinal tract, or central nervous system. Intravenous ampicillin and gentamicin was continued. Cultures of the ventricular fluid were again positive on day 21 of treatment, and a 10-day course of intraventricular gentamicin (3 mg, injected bilaterally) was begun on day 27 after admission. Ampicillin and gentamicin continued to be administered parenterally for 21 days after the last culture-positive ventricular tap. The ventricular fluid was sterile 24 h after the first dose of intraventricular gentamicin and remained sterile after the antibiotics were discontinued. CT scan at the time of discharge showed multiple loculated fluid collections throughout the brain. Samples of ventricular fluid obtained from different sites contained 800 to 2,100 leukocytes per mm^3, the majority of which were polymorphonuclear leukocytes.

Two months after discharge, the head circumference rapidly increased, necessitating the placement of a ventriculoperitoneal shunt. Developmental milestones were severely delayed.

The organism was isolated after 2 days of incubation at 35°C on a chocolate agar plate in 10% CO_2–90% air and on CDC-anaerobe blood agar (Carr-Scarborough Microbiologicals, Stone Mountain, Ga.) in 10% H_2–5% CO_2–85% N_2. Subcultures showed excellent aerobic growth after overnight incubation. Subcultures on sheep blood agar incubated overnight revealed colonies that were 2 to 3 mm in diameter, tan,

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opaque, raised, convex, and nonhemolytic. The organism was lactose positive on MacConkey medium. Colonies were bright yellow on plain Trypticase soy agar (BBL Microbiology Systems) incubated at 25°C for 2 days. The yellow pigment was obvious on agar medium containing blood and on MacConkey agar after the plates had been incubated for 3 to 4 days at room temperature.

The isolate was characterized biochemically with a microtube plate system (MIC-2000; Dynatech Laboratories, Inc., Alexandria, Va.) that is ordinarily used in our laboratory for simultaneous identification and susceptibility testing of *Enterobacteriaceae* (E. E. Harris, D. R. Venturini, and S. D. Allen, Abstr. Annu. Meet. Am. Soc. Microbiol. 1978, C76, p. 289). It was also characterized biochemically with the API-20E system (profile no. 3305373; Analytab Products, Plainview, N.Y.) and was definitively identified by using the conventional biochemical methods of Edwards and Ewing (5) and the identification criteria of Farmer et al. (6). The following conventional tests were positive: Voges-Proskauer, citrate, deoxyribonuclease (delayed 4 days), arginine dihydrolase, ornithine decarboxylase, phenylalanine deaminase (weak), glucose, lactose, sucrose, mannitol, salicin, inositol, arabinose, raffinose, rhamnose, trehalose, and xylose. Reactions were negative for indole, H_2S, urea, lysine decarboxylase, malonate, dulcitol, adonitol, and sorbitol. The isolate was confirmed as *E. sakazakii* biogroup 1 by the Enteric Section of the Centers for Disease Control.

Yellow colonies, the negative D-sorbitol fermentation test, and the delayed positive deoxyribonuclease reaction are key characteristics of *E. sakazakii* which help to differentiate this species from *E. cloacae*. Otherwise, the biochemical characteristics of *E. cloacae* are similar to *E. sakazakii*. Other *Enterobacteriaceae* which may have yellow colonies include *Escherichia coli* (B. R. Davis, C. F. Riddle, and S. D. Allen, Abstr. Annu. Meet. Am. Soc. Microbiol. 1977, C12, p. 60) and *Enterobacter agglomerans* (J. K. Leete, A. C. McWhorter, and D. J. Brenner, Abstr. Annu. Meet. Am. Soc. Microbiol. 1977, C155, p. 61). Thus, yellow pigment alone cannot be relied upon as a criterion for separating *E. sakazakii* from other species without the use of additional differential tests (5, 6).

It is difficult to confirm a pathogenic role for *E. sakazakii* in reports of infections due to yellow-pigmented organisms in which a detailed biochemical description of the isolate was not included. Urmenyi and Franklin, in 1961, described two infants, one of 32 weeks and the other of 38 weeks gestation, who died within 2 days of each other with generalized sepsis due to "pigmented organisms belonging to the cloacae group A" (11). Each infant experienced complications during the peripartum period, became septic at days 5 and 11, respectively, and died within 48 h after diagnosis. Necrotic hemorrhagic cerebral inflammation (4) was found at postmortem examination. Jøker et al. (7) reported that from the cerebrospinal fluid of a 4-day-old infant with meningitis born after a complicated delivery, an organism consistent with *E. sakazakii* was isolated. Multiple antibiotics were used for treatment, and the course was complicated by hydrocephalus and a brain abscess which communicated with a lateral ventricle. Monroe and Tift (9) has recently described a previously normal 7-day-old infant with sepsis unassociated with meningitis who responded promptly to a 10-day course of parenteral ampicillin. We are unaware of other reports of documented infection due to this organism.

The results of tests of susceptibility to antimicrobial agents were in good agreement with published data (6, 9). Our strain of *E. sakazakii* was susceptible to ampicillin, amikacin, carbenicillin, cefamandole, cefoxitin, chloramphenicol, tetracycline, kanamycin, gentamicin, tobramycin, and sulfamethoxazole but was moderately resistant to cephalothin (minimal inhibitory concentration, 16 μg/ml [10]). In contrast, *E. cloacae* strains isolated in our laboratory showed different susceptibility patterns. Of 211 *E. cloacae* strains isolated in 1979, 54% were resistant to tetracycline, 63% were resistant to cefoxitin, 44% were resistant to cefamandole, and 97% were resistant to ampicillin (J. K. Reynolds and J. W. Smith, unpublished data based on the disk method of Bauer et al. [1]).

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