Case Reports

Shigellemia

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SHIGELLEMIA (bacteremia caused by *Shigella* spp) is known to possibly complicate shigellosis. However, it is generally held to be a rare event that may occur at any time during the infection. Our experience with three patients who had shigellemia prompted a review of published information on the subject. From our review, we conclude that shigellemia is not rare, it occurs in patterns and it has prognostic importance.

Patients and Methods

We reviewed the records of blood cultures processed in the clinical microbiology laboratories of the University of California, Davis, Medical Center (UCDMC) from March 1971 through December 1980 and the Sacramento Kaiser-Permanente Hospital (SKPH) from June 1973 through March 1980. In addition, the reports of shigellemia published after 1948 were analyzed by grouping patients according to several criteria: underlying medical problems, age, survival and timing of bacteremia in relation to the clinical onset of disease.

Patients in whom shigellemia occurred in the presence of severe nutritional deficiency, pneumonia, cirrhosis, hepatitis, sickle cell anemia or diabetes mellitus were considered to be abnormal hosts. If shigellemia was detected before or within 24 hours of the clinical onset of colitis, the bacteremia was classified as *early;* shigellemia detected more than 24 hours after the onset of colitis was classified as *late*. Reports with insufficient information to permit such classification were excluded from analysis. When appropriate, differences in rates of occurrence were evaluated for statistical significance using either the χ^2 test (with the Yates' correction) or Fisher's exact test.*

Reports of Cases

CASE 1. The patient, a 35-year-old paraplegic homosexual man, had the sudden onset of lower abdominal cramping pain associated with watery, frequent diarrhea. As the diarrhea continued, the feces became blood-streaked and his temperature, taken orally, rose to 40°C (104°F). He was admitted to UCDMC 24 hours after onset of symptoms. There was no known exposure to anyone with diarrhea, and he recalled no change in his diet. However, he had been the recipient in rectal coitus about 24 hours before his illness began. He was an experienced recipient and recalled neither rectal pain nor tenderness. He said he had not had oral copulation.

On examination, his temperature was 37.8°C (100°F), his pulse rate was 120 per minute and his blood pressure 130/60 mm of mercury; the left side of his abdomen was tender. Blood-streaked feces was obtained at rectal examination; a Gram-stained smear showed large numbers of leukocytes and a variety of bacteria. *Shigella sonnei* was isolated from cultures of a fecal specimen and a blood specimen (one of two sets taken 24 hours after onset of symptoms). There were 6,800 leukocytes per μl in a blood specimen taken on admission, with 2% mature and 31% band form neutrophils, 23% lymphocytes, 22% monocytes, 9% metamyelocytes and 13% plasmacytoid lymphocytes.

The initial treatment with nafcillin sodium (one day) was changed to ampicillin, 200 mg per kg a day given intravenously every four hours as six equal portions for four days, then 30 mg per kg a day given by mouth every six hours as four equal portions for six days. Recovery was uneventful.

CASE 2. Severe headache, fatigue and fever began suddenly in a 17-year-old boy. Cramping with low abdominal pain presaged the passage of a single, loose, nonbloody bowel movement. His temperature, taken orally, was 40°C (104°F). There was no known exposure to anyone with diarrhea. He was admitted to SKPH six hours after his illness began.

On physical examination, the patient's temperature was 39.8°C (103.7°F), the pulse rate was 120 and there was postural hypotension (115/60 mm of mercury, supine; 68/36 mm of mercury, standing); there was no abdominal tenderness. *S sonnei* was isolated from cultures of a fecal specimen and a blood specimen (in one of five sets taken seven hours after onset of symptoms). There were 12,800 leukocytes per μl in the blood on admission, with 84% mature and 9% band form neutrophils, 3% lymphocytes and 4% monocytes. The initial treatment with ampicillin (one day) was changed to trimethoprim-sulfamethoxazole by mouth, two tablets (320 mg and 1,600 mg, respectively) every six hours for ten days. Recovery was uneventful.

CASE 3. The patient, a 4-year-old Asian-Indian boy,

*David Feigal, MD, provided statistical analysis.

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had diarrhea and a temperature rising to 38.9°C (102°F) (oral). Other family members had similar illnesses. He was admitted to UCDMC 96 hours after his illness began with dehydration, acidosis and hyponatremia.

On examination, the rectal temperature was 37.7°C (99.8°F) and the pulse 128 (the blood pressure was not recorded). *Shigella flexneri* was isolated from cultures of a fecal specimen and a blood specimen obtained six days after onset of symptoms. The diarrhea persisted and the temperature increased to 40.4°C (104.8°F) on the third hospital day. There were 6,200 leukocytes per μl in a blood specimen taken on admission, with 5% mature and 44% band form neutrophils, 24% lymphocytes and 22% monocytes. Ampicillin was given intravenously in a dose of 150 mg per kg

TABLE 1.—*Reports of Shigellemia Grouped According to Species*

Study	*Number and Description of Cases*	*Outcomes*
	Shigella flexneri	
Henson, 1956[8]	1 normal child	Survived
Darasse, 1957[9]	1 child with kwashiorkor	Survived
Robertson, 1963[10]	3 normal children	Survived
Faucon and Duclous, 1964[11]	1 adult with hepatitis	Died
	1 normal adult	Survived
Spiller and Grant, 1966[12]	1 child with sickle cell anemia	Survived
Graber et al, 1966[13]	1 adult with diabetes mellitus	Died
Levin, 1967[14]	1 five-day-old neonate	Died
Kim and Hughes, 1968[15]	1 newborn	Died
Jackson and Kilgore, 1971[5]	1 nine-day-old neonate with meningitis	Died
Naveh and Friedman, 1973[16]	1 six-month-old infant	Survived
Kazal et al, 1976[17]	1 homosexual man with megacolon	Survived
Hallett and Scragg, 1978[2]	1 neonate	Survived
Scragg et al, 1978[3]	2 neonates	Died
	1 five-month old with kwashiorkor, pneumonia and typhoid	Died
	5 2-year-old children with pneumonia (4), kwashiorkor (2), marasmus (1)	All died
Phillips et al, 1979[18]	1 normal adult	Survived
De Mol et al, 1981[19]	2 normal children (5 and 33 months)	Survived
Cordle and Boltjes, 1963[20]	3 normal children	Survived
This study	1 normal child	Survived
	Shigella sonnei	
Henson, 1956[8]	1 child	Survived
Darasse, 1957[9]	1 adult with cirrhosis and ascites	Survived
Tatam et al, 1951[21]	1 child	Survived
Winter and Harding, 1962[22]	1 adult	Survived
Whitfield and Humphries, 1967[6]	1 neonate	Survived
Rubin et al, 1968[7]	1 child with sickle cell anemia and shigellal osteomyelitis	Survived
Kraybill and Controni, 1968[23]	1 neonate	Survived
Barrett-Connor and Connor, 1969[24]	3 normal children	Survived
Barrett-Connor and Connor, 1970[1]	1 normal child	Survived
Evans et al, 1972[25]	1 normal child	Survived
Fernhoff and Plotkin, 1973[26]	1 normal child	Survived
Moore, 1974[27]	1 neonate	Died
Spiers, 1974[28]	1 child with acute monocytic leukemia	Died
Neter et al, 1974[29]	1 adult postrenal transplant	Survived
Aldrich et al, 1979[4]	1 neonate	Died
Scragg et al, 1978[3]	25 children with pneumonia and marasmus	Survived
Lloret Caballeria et al, 1980[30]	1 neonate	Died
O'Connor and O'Callaghan, 1981[31]	1 adult with bone marrow aplasia and cecal perforation	Died
This study	2 normal adults	Survived
	Shigella dysenteriae	
Sodre et al, 1949[32]	1 normal child	Survived
	1 normal adult	Survived
Ullis and Rosenblatt, 1973[33]	1 normal child	Survived
Rahaman et al, 1974[34]	4 children, 3 with secondary hemolytic anemia	Unknown
Koshi et al, 1979[35]	6 children, 3 or 4 with marasmus, kwashiorkor and/or renal failure	All died
	Shigella boydii	
Barrett-Connor and Connor, 1969[36]	1 child with sickle cell anemia	Survived
	Multiple species and non-differentiable	
Hallett and Scragg, 1978[2]	22 cases, 17 *S flexneri*, 3 *S sonnei*, and 2 *S dysenteriae*. Except for 1 all had severe underlying malnutrition, pneumonia, typhoid and/or cirrhosis. 20 children younger than 2 years	8 died
	2 adults	1 died

of body weight a day as six equal portions every four hours for four days and then was given by mouth in a dose of 100 mg per kg a day (as four equal portions every six hours) for five days. Recovery was uneventful.

Results

As shown in Table 1, our three cases plus the 87 cases reported by others yield 90 cases of shigellemia documented since 1948.[1-36] Of these, 48 (53%) were caused by *S flexneri,* 26 (29%) by *S sonnei,* 15 (17%) by *Shigella dysenteriae* and 1 (1%) by *Shigella boydii.* The case death rates were 2 of 32 (6%) in patients who had no underlying abnormality ("normals"), 19 of 44 (43%) abnormal hosts and 8 of 12 (67%) neonates; ($P<.001$, comparing the abnormal hosts and the neonates with the normals using the χ^2 test with Yates' correction factor).

Through evaluation of those reports in which the timing or number (or both) of blood cultures was ascertainable, two patterns of shigellemia became apparent. With *S sonnei,* the bacteremia was detected during the first 24 hours of illness in 14 of 18 (78%) episodes, whereas with *S flexneri,* 20 of 24 (83%) episodes were detected after the first 24 hours of illness ($P<.001$ by Fisher's exact test). Only 1 of the 22 patients with *S sonnei* had two positive blood cultures, whereas 5 of the 37 patients with *S flexneri* had 11 separate blood cultures that yielded the shigellae (not a statistically significant difference by Fisher's exact test).

Discussion

The presumption of the rarity of shigellemia is based on several early reports of failure or infrequent identification of *Shigella* spp in blood specimens from patients proved to have shigellosis by culture of feces.[1,37-39] However, more recently 3.2% to 6.4% of cultures of blood specimens yielded *Shigella* spp.[2,3,40,41] This apparent discrepancy may be related to (1) the use of the wrong technique in culturing the blood, (2) inhibition of bloodborne *Shigella* spp by humoral antibodies and leukocytes, (3) failure to get a blood specimen at the proper time in the illness and (4) a change in the kind of patient now seen with shigellosis.

With regard to the first reason, it should be noted that *Shigella* spp are not fastidious in their nutritional requirements. However, controlled evaluations enabling definition of the optimal volume of blood to be added to a given volume of liquid culture medium have not been done and the relative nutritional adequacy of various formulations has not been determined.

The putative inhibitory effect of humoral antibodies and leukocytes on the outgrowth of bloodborne shigellae would be nullified by the additive sodium polyanethol sulfonate in culture mediums currently in use. This additive is an effective anticoagulant that also inactivates complement and leukocytes.[42] Such actions may be important in view of the demonstrated killing of shigellae in vitro by serum from humans containing IgM and complement—acting through either the classical or an alternate pathway.[43] The susceptibility of shigellae was unrelated to either the titer of antibody or prior exposure of the donor to *Shigella* spp. However, susceptibility to killing does vary considerably according to species and serotype, in order of increasing resistance: *S sonnei*=*S flexneri* 1; *S flexneri* 2; *S flexneri* 3.[43] This variation in susceptibility of *Shigella* to humoral defenses appears to correlate with the persistence of shigellemia.

It is clinically apparent that bacteremia caused by *S sonnei* is most likely to be detected during the first 24 hours of illness. Although this is the optimal time for detecting shigellemia, patients do not always seek medical attention during this period. Those who do see a physician are generally treated symptomatically and cultures are not done. If the disease persists or progresses, cultures of fecal specimens are usually done, but less frequently of a blood specimen. The result could be a skewing of the data toward a falsely low incidence of shigellemia and an apparently high mortality. In a prospective study of mildly to moderately severely ill patients, however, the incidence of shigellemia did not correlate with the severity of the disease.[40]

Immunocompromised and neonatal patients appear to be less able to confine *Shigella* spp to the intestine. As a consequence, their fatality rates are greatly increased, as is the probability of occurrences of extraenteric shigellosis, such as meningitis,[5,6,44] pyelonephritis,[44] osteomyelitis[7] and otitis media.[44] Because the detection of shigellemia in immunocompromised and neonatal patients appears to have grave prognostic importance, the blood should be cultured even when the illness appears to be trivial.

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