Infection of Central Nervous System by Motile *Enterococcus*: First Case Report

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A 66-year-old man with four indwelling ventriculoperitoneal shunts for multiloculated hydrocephalus from a complicated case of meningitis a year before developed shunt infection based on a syndrome of fever, drowsiness, and cerebrospinal fluid neutrophil pleocytosis in the background of repeated surgical manipulation to relieve successive shunt blockages. The cerebrospinal fluid culture, which yielded a motile *Enterococcus* species, was believed to originate from the gut. This isolate was lost in storage and could not be characterized further. The patient improved with vancomycin and high-dose ampicillin therapy. He relapsed a month later with *Enterococcus gallinarum* shunt infection, which responded to high-dose ampicillin and gentamicin therapy. This is probably the first case report of motile *Enterococcus* infection of the central nervous system.

CASE REPORT

A 64-year-old man was admitted to a public hospital in early March 1999 for fever for 2 days. He had a background history of listeria meningitis a year ago, which was complicated by multiloculated hydrocephalus requiring four indwelling ventriculoperitoneal (VP) shunts. He also had mild Parkinson's disease for which he was not on any specific treatment and a recent admission, 2 months ago, to another hospital for aspiration pneumonia after which he was on a nasogastric tube for feeding. On examination, he was febrile (temperature, 38.0°C) and lethargic but oriented. His neck was supple, and the 4-VP shunts were palpable. A computed tomography (CT) scan of the brain showed no hydrocephalus, and the 4-VP shunts were in situ. He was empirically treated for presumed aspiration pneumonia with ceftriaxone and metronidazole, although the chest X-ray was unremarkable. As his fever persisted, therapy was changed to ceftazidime and vancomycin. The fever settled after about a week of treatment, and the antibiotics were stopped. Four days later, vancomycin was restarted because he became febrile and drowsy after a shunt revision from which cultures of the shunt and cerebrospinal fluid (CSF) were sterile. Subsequently, he required two further shunt revisions during the first week of April 1999. Cultures from the CSF fluid from these revisions yielded a motile *Enterococcus* species which correlated with significant neutrophil pleocytosis from the specimens of the CSF on both occasions. The organism was intermediate in its sensitivity to vancomycin (the vancomycin MIC was 8 mg/liter) and was sensitive to ampicillin, penicillin (the MIC of penicillin was 0.38 mg/liter), and gentamicin synergy. Shunt infection was diagnosed based on the preceding features and the ongoing fever and drowsiness in the patient. High-dose ampicillin was added to vancomycin, resulting in marked defervescence after 2 days. The treatment was contin-

ued for 3 weeks with good response. The shunts remained indwelling, as the surgeons were not keen to remove them. He underwent another shunt revision 2 weeks later, and this time the CSF culture was sterile. He was discharged after 6 weeks of hospitalization to a rehabilitation facility.

In May 1999, he was admitted to a private hospital for another episode of shunt infection. Obstruction of all the shunts was noted together with encystment of their peritoneal ends. There was no evidence of intestinal perforation that could have led to the encystment. All four shunts were removed, and new shunts were inserted. Culture from the peritoneal end of the left parietal catheter tip yielded *Citrobacter* species, *Pseudomonas aeruginosa*, and *Proteus mirabilis*, whereas culture of the left lateral ventricle catheter tip isolated *Klebsiella* species and group B *Streptococcus*. Details of the inpatient stay at this hospital were not available, but he apparently received intravenous ampicillin, vancomycin, and gentamicin for 4 weeks with good recovery.

However, he deteriorated with symptoms of fever and drowsiness in late May 1999 and was transferred back to the public hospital, where he was noted to have a Glasgow Coma Scale value of 12 and power of grade 3/5 for all his limbs. There was no evidence of peritonitis, and a CT scan of the abdomen was unremarkable. A CT brain scan showed significant hydrocephalus. This time, all four shunts were externalized, and he was treated with intravenous meropenem and vancomycin pending cultures.

The proximal tips of two of the shunts and culture of the CSF yielded *Enterococcus gallinarum*. The MIC of vancomycin was 4 mg/liter, and it was sensitive to penicillin, ampicillin, and gentamicin synergy. The tips of the other two shunts were sterile. The antibiotic regimen was changed to high-dose ampicillin and gentamicin. Subsequent CSF cultures from the external ventricular drain were repeatedly sterile. He had a VP shunt inserted in mid-July, following which the antibiotics were stopped. He made progressive improvement and was dis-

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charged to a rehabilitation facility. At clinic review a month after discharge, he remained well.

From the microbiology laboratory record, the first isolate had characteristics typical of an enterococcus. There were growth in 6.5% NaCl broth and blackening of the bile esculin slant. The organism was positive for pyrrolindonylarylamidase using the PYR disc (Murex, Dartford, England) and possessed the Lancefield group D antigen (Murex). It was sensitive to ampicillin, and there was no high-level resistance to gentamicin by the Kirby-Bauer disc diffusion method using NCCLS criteria (13). The MIC of vancomycin was 8 mg/liter, and the MIC of penicillin was 0.38 mg/liter using the E test (AB Biodisk, Solna, Sweden). A wet mount prepared from a fresh 4-h growth in nutrient broth showed that the organism was motile. A commercial identification kit, the API 20 Strep, was used, and the analytical profile number generated was 5217551. It gave a good identification for *Enterococcus casseliflavus*, with a confidence level of 98.5% using database version 5.1 for API 20 Strep (APILab version 3.2.2.). Unfortunately, the detection of yellow pigmentation by observing a swab of the colonies from a sheep blood agar plate was omitted. This isolate was lost in storage and could not be characterized further.

The second isolate had characteristics similar to those of an enterococcus. The MIC of vancomycin was 4 mg/liter using the E test (AB Biodisk), and it was sensitive to ampicillin and gentamicin synergy by the Kirby-Bauer disc diffusion method using NCCLS criteria (13). It was motile by wet mounting, lacked pigmentation, and gave the profile number 5157551 when API 20 Strep was used. When the updated database version 6 for API 20 Strep found in the current APILab version 3.3.3 was used, it yielded *Enterococcus faecium* with a confidence level of 97%. However, by use of the Gram Positive Identification Card from the automated Vitek method, software version R06.01, the bionumber 77325270530 was generated. This yielded *E. gallinarum* at a 73% confidence level. The organism was further characterized by the conventional test scheme previously described by Facklam and Collins (7). There was deamination of arginine in Moeller's decarboxylase broth; the organism was motile; there was no pigmentation; and there was fermentation of 1% mannitol, arabinose, and lactose in heart infusion broth. Sorbitol was not fermented. Its motility and lack of pigmentation distinguished *E. gallinarum* from *E. faecium* (2, 7). A PCR was performed to determine the presence of C1 or C2-C3 ligase genes using primer pairs C1 and C2 (for *vanC1*) and D1 and D2 (for *vanC2*) as described previously (6). The result showed that an 822-bp product was amplified, consistent with the presence of *vanC1*, which is specific for *E. gallinarum* (6, 11) (Fig. 1). The presence of *vanC1* confirmed that the second isolate was *E. gallinarum* (2, 6).

E. faecium, *E. gallinarum*, and *E. casseliflavus* share many similar biochemical and phenotypic characteristics (16). The most useful tests used to identify these species were those for motility and pigmentation (7). This may highlight a problem for routine laboratories that use a commercial test kit to identify the motile *Enterococcus* species, especially if they are not aware of the additional tests required to identify these organisms. The updated version 6 of the API 20 Strep contained modifications to the percentages in its database, and currently *E. casseliflavus* cannot be identified directly but only with additional tests.

FIG. 1. Multiplex PCR performed using primers C1 and C2 and D1 and D2. This isolate was in lane 6. Lane 1, 100-bp ladder. Lanes 2 and 5, two unrelated clinical strains of *E. gallinarum*. Lane 3, clinical strain of *E. faecalis*. Lane 4, clinical strain of *E. casseliflavus*. Clinical strains were identified using the Vitek method, which was supplemented by wet mounting for motility and pigmentation testing.

Discussion. Enterococci rank third as agents causing nosocomial infections (3). The taxonomy of *Enterococcus* species has evolved progressively over the last 2 decades, with 14 accepted species in the genus *Enterococcus* (1, 4). The most common species causing human infections, *Enterococcus faecalis* and *E. faecium*, together account for more than 90% of clinical isolates. The other species, including *E. gallinarum*, are rarely encountered in human clinical specimens and are primarily found in the gastrointestinal tracts of various animals (5).

Enterococcal infections of the central nervous system can occur but are very rare. This case illustrates infection of the central nervous system by a motile *Enterococcus* species which has not been documented previously according to a MEDLINE search in the English language. The clinical significance of a particular isolate must weigh in the ubiquitous nature of the enterococci. But in this case, there was evidence of central nervous system infection, as demonstrated by fever, drowsiness, and CSF neutrophil pleocytosis in the background of repeated surgical manipulation to relieve blockages in the indwelling VP shunts. The organism may have colonized the gut.

E. casseliflavus and *E. gallinarum* have the capacity to express low-level resistance to vancomycin, which is an intrinsic feature conferred by the genes *vanC1* (in *E. gallinarum*) and *vanC2* (in *E. casseliflavus*) (10, 17). The vancomycin MICs can range from 2 to 32 mg/liter (11).

It could be argued that the shunt infection may have been caused by only one species of motile *Enterococcus* but was perhaps misidentified as two separate ones. This patient may have had a relapsing VP shunt infection with *E. gallinarum*. Unfortunately, the first isolate was lost, and the case could not be proven conclusively. However, it is clear that the patient had two episodes of shunt infection due to a motile *Enterococcus* species with intrinsic low-level resistance to vancomycin.

The enterococcus is predominantly an enteric organism. A shunt infection due to this organism may signal an infection beginning from the peritoneal end of the shunt. Asymptomatic intestinal perforation by the VP shunt tubing could occur and has been reported (9, 14). This could have occurred here. Although the VP shunt tube was not removed and replaced due to several factors, the patient had clinical improvement on high-dose intravenous ampicillin without gentamicin for synergy.

Less than a month after discharge, the patient had signs and symptoms of shunt infection again. This time, the tubings and shunts were apparently replaced during surgery in the private hospital. The culture of the peritoneal end of the shunt catheter essentially yielded enteric organisms, which suggested that the infection ascended from the peritoneal end. Since the tubings were not removed during the earlier admission, they probably provided a nidus for reinfection which was protected from the effect of antibiotics.

When the patient's condition did not improve, he had a third surgery to remove all the shunts and externalize the CSF drainage. Culture of the shunts this time yielded *E. gallinarum*. The patient responded to high-dose ampicillin along with gentamicin. Subsequent CSF cultures from the external ventricular drains were sterile, as was the case the first time that the patient presented. A cure may finally have been effected this time, because the infected shunts were all removed and the CSF was drained externally. New shunts were inserted after the patient had completed a prolonged course of antibiotics.

There was no report on treatment of central nervous system infections due to motile *Enterococcus*, but there was a recent report on bacteremia due to these organisms (15) in which the author noted that vancomycin was not an effective form of treatment.

Because the enterococcus has innate resistance to antibiotics (16), the use of gentamicin for synergy is recommended for endocarditis due to enterococci without high-level resistance to gentamicin. In some references (8, 12), gentamicin for synergy is also recommended for central nervous system infections due to enterococci. However, there has been no study that shows improved mortality for central nervous system infections due to enterococci treated with combination antibiotics rather than with a beta-lactam alone.

The finding of a motile *Enterococcus* species with intermediate vancomycin resistance is not an indication for strict isolation precautions for the patient, as the intrinsic resistance is not transferable and the organism is susceptible to other drugs.

In conclusion, this case serves to increase awareness of infection with a motile *Enterococcus* species particularly in the central nervous system. It is probably prudent to use penicillin and aminoglycoside synergy together with expedient indwelling shunt removal for prompt cure of shunt-related infections.

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