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Severe *Serratia liquefaciens* Sepsis following Vitamin C Infusion Treatment by a Naturopathic Practitioner

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A 66-year-old female patient developed severe *Serratia liquefaciens* sepsis following vitamin C infusion treatment by a naturopathic practitioner. The clinical course of the infection was characterized by several complications, and the direct costs of the hospital stay amounted to about 40,000 Euro. Genotypically identical *S. liquefaciens* was isolated from the residue of the infusate given to the patient, as well as from the washbasin overflow and from two other infusion bottles. A careful inspection of the dispensing facilities and review of procedures used to prepare the infusate revealed several indications of poor hygiene. However, the source of contamination could not be fully clarified. This case report raises questions about the local facilities and personal qualifications required for naturopathic practitioners to conduct invasive procedures and demonstrates that lapses in hygiene can lead to severe morbidity and high cost.

CASE REPORT

A 66-year-old female patient presented with symptoms of septic shock, meningism, and loss of consciousness. Her medical history revealed a carcinoma of the cervix (stage IIIb) successfully treated by primary radiotherapy 3 years previously. The day before, she had received an intravenous infusion containing 200 ml (i.e., 30 g) of vitamin C, 50 ml of lactopurum (homeopathic dilution [D4] of lactic acid in water for injection), and 250 ml of isotonic 0.9% sodium chloride solution via a peripherally inserted venous catheter. Immediately after termination of the infusion, the patient suffered from neck pain, vomiting, and fever. First, she was given symptomatic medication (i.e., antipyretic and antiemetic drugs), but during the night, her state worsened dramatically.

On admission to the intensive care unit, the patient was comatose, her skin was pale and cyanotic, and the peripheral pulses were not palpable. Clinically, we found signs of meningism. The leukocyte count was 22.8×10^9/liter, and the level of vitamin C in serum was 55.9 mg/liter (reference value, 5.0 to 15.0 mg/liter). Blood cultures revealed growth of *S. liquefaciens* that was sensitive to piperacillin plus tazobactam, cotrimoxazole, cefotaxime, ceftriaxone, and gentamicin, but insensitive to ampicillin, cefazolin, cefuroxime, and nitrofurantoin. At the time of admission, piperacillin and tazobactam were given empirically as antibiotic medication. A sample from the remainder of the original infusate was obtained for culture and also revealed growth of *S. liquefaciens*, as confirmed by API 20E (BioMerieux). The initial antibiotic therapy was conducted until the 11th day after admission, and *S. liquefaciens* could not be isolated any longer after this initial period.

The further clinical course was characterized by a protracted septic shock with disseminated intravascular coagulation (D-dimers > 20 mg/liter); the clinical picture of systemic inflammatory response syndrome, with a great need for catecholamines to support circulation; adult respiratory distress syndrome; reversible acute renal failure; severe anasarca;, and transient hypothyreosis. Mechanical ventilation had to be conducted for about 1 month. On the 37th day after admission, the patient was transferred to a medical unit, and on the 68th day, the patient, who was in a reduced physical and psychic state (reactive depression), was dismissed from the hospital to receive further treatment in a rehabilitation center.

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S. liquefaciens is an infrequent but increasingly recognized cause of transfusion-related sepsis and is associated with a high rate of mortality (1, 7). Recently, two outbreaks of *S. liquefaciens* bloodstream infections in a critical care unit (4) and at a hemodialysis center (3) have been described; however, the environmental sources of *S. liquefaciens* remained unclear. In this paper, we present a case report of severe *S. liquefaciens* sepsis following administration of a vitamin C infusion by a naturopathic practitioner, which was associated with a contaminated washbasin overflow and poor hygienic practice.

Inspection and microbiological investigations. After notification to the local health administration, we were asked to assist in the investigation of the case. First, we conducted a careful inspection of the dispensing facilities. The room where the infusion was prepared and administered was small, and there was only limited workspace for preparation of infusions. The washbasin was constructed with an overflow hole, a type of design that is not recommended for use in German hospitals. A dispenser for hand disinfectant solution was lacking.

Second, we undertook a review of the procedure used to prepare the infusate. This revealed several examples of poor aseptic technique. (i) Some of the infusion components were taken from multiply punctured bottles. (ii) In order to remove air bubbles, the infusion tubing was wound around the tap with

the distal end of the tubing touching the washbasin overflow hole. (The washbasin overflow is a safeguard to prevent flooding in case a tap is left running while the plug is in; the overflow hole is located at the top of the washbasin.) (iii) Compliance with hand disinfection was poor. Finally, (iv) the puncture site of the infusion container was not disinfected.

Samples were taken from the table surface and from different sites of the washbasin (water, faucet aerator, armatures, surface, and overflow hole) for microbiological analysis. Except for two samples from the overflow, none of the samples revealed growth of *S. liquefaciens*. The residual fluid in another two repeatedly punctured infusion bottles containing water for injection and isotonic 0.9% sodium chloride solution drawn from the same room also revealed growth of *S. liquefaciens.* Samples from sealed containers (identical batches) of the infusion components (i.e., vitamin C, lactopurum, and isotonic 0.9% sodium chloride solution) as supplied by the manufacturers revealed no bacterial growth. Pulsed-field gel electrophoresis (PFGE) showed that all isolates were genotypically identical to the *S. liquefaciens* isolates from the patient's blood and from the original infusate given to the patient. Figure 1 shows the PFGE fingerprint patterns of clinical and environmental *S. liquefaciens* strains.

Discussion. There is no doubt that the severe *S. liquefaciens* sepsis described in this case report was acquired from a contaminated naturopathic vitamin C infusion. The protracted course and several complications associated with this case underline the severe morbidity associated with gram-negative sepsis. In transfusion-related *S. liquefaciens* sepsis, the fatality rate is reported to be as high as 75% (7). The direct cost of the hospital stay is estimated at 40,000 Euro, the range previously estimated for nosocomial bloodstream infections (6).

Our findings strongly suggest that contamination of the infusion had occurred on the premises of the naturopathic practitioner, although the mode of contamination could not be fully clarified. The possibility of intrinsic contamination of one of the components used to prepare the infusion could be largely eliminated, since samples from other containers from the batches supplied by the manufacturers were found to be sterile. In addition, the same *S. liquefaciens* strain was isolated in used components from different manufacturers. Based on a careful inspection and review of dispensing procedures, we found several indications of poor aseptic technique that could have contributed to the contamination of the infusate. Our first hypothesis was that while removing the air bubbles from the tubing, the distal end of the tubing could have touched the overflow hole of the washbasin, which was also found to be contaminated with genotypically identical *S. liquefaciens*. However, this hypothesis did not satisfactorily explain the contamination of the remainder of the infusate within the bottle, which was largely protected from contamination in this tubing by the drip chamber. Moreover, the time between preparation of the infusate and administration to the patient was too short to allow sufficient growth of *S. liquefaciens* within the bottle to produce the observed clinical picture: i.e., the occurrence of the febrile reaction immediately after administration of the infusion suggested the presence of considerable amounts of lipopolysaccharides. In most reported cases of *S. liquefaciens* contamination of blood, the implicated erythrocyte units were older than 14 days, with a mean age of 28 days (7, 9).

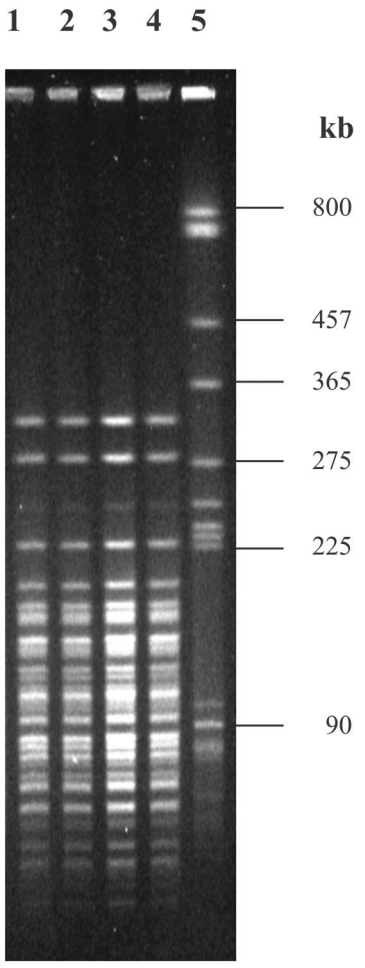

FIG. 1. PFGE fingerprint patterns of *S. liquefaciens* strains from environmental and clinical samples. Lanes: 1 and 2, washbasin overflow hole; 3, remainder of the infusate given to the patient; 4, patient's blood culture; 5, standard *S. typhimurium* strain LT2.

More likely, *S. liquefaciens* was inoculated into the infusion bottle by improper multiple puncturing. Grohskopf and coworkers (3) described an outbreak of *S. liquefaciens* bloodstream infections at a hemodialysis center caused by puncturing single-use vials multiple times and pooling preservative-free residual epoetin alfa. Sharing of unlabeled heparin and insulin vials was also observed in an outbreak of *S. liquefaciens* bloodstream infections in a critical care unit (4), although this was not proven to be directly implicated in the outbreak.

To our knowledge, the identification of an overflow as an environmental reservoir of *S. liquefaciens* is unique in the scientific literature. Although its role in the contamination of the infusate remains speculative, the recommendation to install washbasins without an overflow hole in German hospitals (5) is further supported by these findings. In the study of Grohskopf et al., the *S. liquefaciens* in the epoetin alfa probably originated from the hands of health care personnel transiently contaminated by soap or hand lotion (3). In our study, the soap was not investigated.

Our case report raises questions about the local facilities and personal qualifications required for naturopathic practitioners

and groups with related occupations to conduct invasive procedures, such as infusion treatments. Systematic data on the frequency of infectious complications in naturopathic medicine are lacking (2), and only a few case reports exist: e.g., a case of endocarditis in a patient with prosthetic heart valves caused by *Propionibacterium acnes* after a series of "vitamin" injections and semipermanent acupuncture needle procedures by a natural healer (8). These incidents suggest that that the hygienic prerequisites in naturopathic settings should be on a level comparable with that in conventional ambulatory medicine. As a consequence of the case described in this paper, the local health authorities now offer special vocational training to natural practitioners to improve aseptic techniques and have implemented a stronger focus on hygiene in their examination procedure.

In summary, our case report demonstrates that infusion therapy should be performed under proper hygienic conditions and that failures can lead to severe morbidity and high cost.

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