Case Report

Septicemia: As a result of erroneous parenteral administration of probiotic

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ABSTRACT

Probiotics are formulations of live microbial cells that are administered orally to contribute to intestinal microbial balance. *Bacillus clausii* is one such aerobic, spore-forming bacterium that is able to survive in the acidic environment of the stomach and is used as a probiotic. In the past few years, probiotic use has increased to a greater extent. However, there is growing global evidence that the use of probiotics in patients with organ failure, the immunocompromised state can cause infections, but it is extremely rare in immunocompetent persons when given through peroral route. However, it can cause severe sepsis in even immunocompetent individuals when given intravenously inadvertently. This case report shows the importance of establishing safety guidelines for probiotic use and particularly for dispensing probiotics in liquid formulations.

Key words: *Bacillus clausii*, Parenteral, Probiotics, Septicemia

It is a well-established incontrovertible fact that intestinal microflora performs several important functions including metabolic, trophic, and protective ones for the body. Probiotics play an important role in maintaining disturbed gastrointestinal microbial balance in various situations and also help to increases immunity. It is well-known fact that live probiotics can cause septicemia in immunocompromised patients, but it is extremely rare in immunocompetent persons when given through peroral route. *Bacillus clausii* is an aerobic, rod-shaped, and gram-positive spore-forming bacterium that is able to survive transit through the acidic environment of the stomach and colonize the intestine even in the presence of antibiotics [1]. *B. clausii* exhibits probiotic properties and being a spore-forming probiotic, which is stable over a good range of temperatures. A systematic review focusing on randomized controlled trials of *B. clausii* in acute childhood diarrhea revealed a reduction in duration of diarrhea by a mean of 9.12 h [1]. *B clausii* is available for oral use as a liquid formulation of 2 billion spores/5 ml [2]. The spores belong to four strains that are resistant to different classes of antibiotics [3].

Here, we report a case of accidental intravenous (IV) injection of *B. clausii* suspension. To our greatest knowledge, this is the second reported case of an accidental probiotic injection overall and first in the pediatric population.

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CASE REPORT

A 4-year-old male child presented to the pediatric emergency department of our hospital with complaints of generalized body swelling, high-grade fever, acute vomiting (multiple episodes), and lethargy for the past 2 days. There was a history of fever and loose stools 4 days back and was managed by oral rehydration solutions and oral antibiotics by the medical practitioner elsewhere. On day 3rd of the illness, the parents noticed frank blood in stool and took the child to a nearby hospital where he was treated with IV fluids, vitamin K, and probiotics.

On admission, the patient was tachypneic with a respiratory rate of 42 breaths/min, heart rate of around 112 beats/min, and blood pressure recorded from the right upper limb was 76/50 mm Hg which was less than the third centile.

On detailed history, the parents revealed accidental IV administration of probiotic suspension (Fig. 1a) containing 2 billion spores of *B. clausii* in 5 ml by paramedical staff (Fig. 1b). High-grade fever, vomiting, and generalized edema started on the 4th day of illness, and the patient was brought to our hospital. Baseline investigations were repeated on admission, which showed a drastic change from reports done before this accidental administration of probiotics. Along with the drastic rise in total leucocyte count, there was a fall in Hb, platelet counts, and the associated rise in C-reactive protein (CRP) (Q) was noted along with mildly increased serum glutamic pyruvic transaminase to 60 U/L (Table 1). Ultrasound whole abdomen revealed mild gallbladder wall edema and cortical echogenicity of the kidney

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Table 1: Baseline investigation and after IV probiotic administration

Parameters	Before IV probiotic	After inadvertent IV probiotic administration	2 weeks after IV probiotic
Total leucocyte count	6800/mm^3	24800/mm^3	7900/mm^3
Hemoglobin	8.1 g/dL	7.4 g/dl	9.2 g/dl
Platelet	3.24 Lakhs/mm^3	2.7 Lakhs/mm^3	3.5 Lakhs/mm
C-reactive protein (Q)	8.48 mg/dl	93.6 mg/dl	6.2 mg/dl

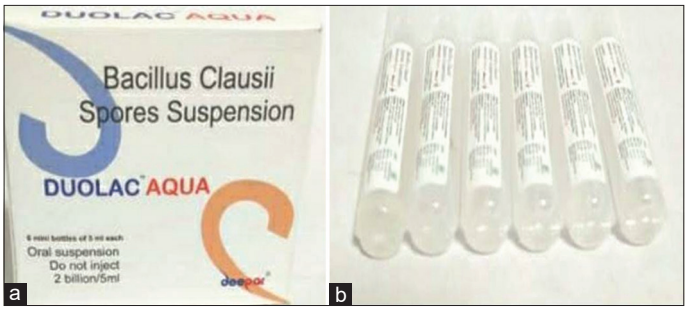

Figure 1: (a and b) Accidental IV administration of probiotic suspension containing 2 billion spores of *Bacillus clausii* in 5 ml by paramedical staff

was normal. Lactate dehydrogenase level, renal function test, and urine microscopy were within normal limits and these exclude the possibility of Shigella dysentery and hemolytic uremic syndrome.

Empirical antibiotic treatment with symptomatic and supportive treatment was started. Ciprofloxacin (15 mg/kg/day), vancomycin (40 mg/kg/day), and gentamycin (7.5 mg/kg/day) were used based on the sensitivity of *B. clausii* as reported in the literature [3]. Two blood culture samples from different sites were sent to the microbiology department. The blood culture report came as sterile. 2D echo revealed no signs of infective endocarditis. Fever and generalized edema subsided on day 3rd of antibiotics.

The patient was discharged successfully after 7 days of parenteral antibiotics and sent on oral ciprofloxacin in the dose of 10 mg/kg/d and advised for 7 days follow-up. On follow-up, repeat investigations came out to be normal, and repeat blood culture was sterile.

DISCUSSION

This report depicted the first known case of sepsis in a 4-year-old male immunocompetent child caused by the probiotic *B. clausii*. To our greatest knowledge, this is the second reported case of an accidental probiotic injection overall and first in the pediatric population. This infection resulted due to direct inoculation of bacterial suspension in the bloodstream caused by the accidental injection of probiotic which was meant for oral use.

Previous reports also confirmed sepsis caused by IV probiotics. Monnerat *et al*. reported an accidental IV probiotic injection in a 25-year-old backpacker who developed septicemia which was evident from the blood culture reports showing *B. clausii* consistently for 3 months that antibiotics were given for 5 months albeit clinical symptoms subsided by 2 weeks [4]. A study conducted by Kochan *et al*. stated *Lactobacillus rhamnosus* administration orally caused sepsis in cardiosurgical patients [5]. Princess *et al*. reported an immunocompetent adult patient on oral probiotic for antibiotic-induced loose stools following cranioplasty resulted in septicemia and blood culture report showed *B. clausii*. The patient was treated with teicoplanin [6].

A serious challenge in treating *B. clausii* sepsis is due to the limited therapeutic options as it is known to carry multiple drug-resistant genes [7]. Initiation of an appropriate antibiotic inadequate dosage was another positive aspect of our case which resulted in better patient outcome. This emphasizes the importance of thorough knowledge of resistance patterns in handling infections caused by exotic/unusual organisms. As good bacteria carry drug-resistant genes, they can turn dangerous in some situations [8], due to which they might not respond to the primary line therapy that necessitates the use of high-end antibiotic therapy.

Bacterial strains used as probiotics can become virulent and establish themselves as pathogens in some situations. Further, research is necessary on this issue as the mechanism of virulence of these bacterial strains remains questionable, especially in normal individuals. Here in this case, in spite of highly positive CRP values suggesting sepsis, the blood culture came out to be sterile as the patient received antibiotics before the sample was sent for culture. A drastic change in CRP quantitative values within a day is more in favor of probiotic administration-related septicemia.

CONCLUSION

Although probiotics are shown to profit the majority of patients on treatment, the risks may outweigh the advantages in immunosuppressed cases as evident in the literature. To date, there is insufficient standardization of safety and administration protocols for probiotics. Due to the paucity of data regarding the mechanism through which probiotics act, appropriate administrative regimens, and probiotic interaction, this issue continues to thrive among scientists around the world. This responsibility should be concomitant with the establishment of the latest safety standards in this area. This case report can, thus, be taken as a warning call for creating judicious use of probiotics and special measures should be taken in dispensing probiotics in liquid formulations to avoid accidental IV administration.

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