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Case Report

Bacteraemia caused by *Lactobacillus rhamnosus* given as a probiotic in a patient with a central venous catheter: a WGS case report

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SUMMARY

Introduction: *Lactobacilli*, especially *Lactobacillus (L.) rhamnosus*, are common and well-documented components of commercial probiotics [1]. Whole genome sequencing (WGS) is often used to compare bacterial genomes and their relatedness. In outbreak situations, it is used to investigate the transmission of pathogenic bacteria. WGS has also been used to determine safety in probiotics, by looking at potential virulence factors and resistance genes.

Case presentation: This case report describes a 56-year old multi-traumatised, immunocompetent woman who was given *L. rhamnosus* GG as a probiotic, and later developed a blood stream infection with *L. rhamnosus* GG.

The patient was fed by a nasogastric tube, and she also had a central venous catheter for parenteral feeding. When the patient developed diarrhoea after long-term hospitalisation, she was given *L. rhamnosus* GG, as a probiotic, which was standard care on the ward where she was hospitalised. In this case report we describe the use of WGS to demonstrate that a patient fed with *L. rhamnosus* GG as a probiotic, developed a blood stream infection with the same strain.

Conclusion: In this case WGS was applied to show the relatedness of a probiotic and a pathogenic strain of *L. rhamnosus* GG. This case emphasises the need for caution when administering probiotics to patients with indwelling catheters. The patient was immunocompetent and she cleared the infection without the need for antibiotics.

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Background

Lactobacilli are some of the most well-documented and used probiotics [1,2]. Probiotics are "live microorganisms, that when administered in adequate amounts, confer a health benefit on the host" [3]. The use of probiotics is widespread and from a survey undertaken by the National Health Interview Service, 1.6% of the adult US population had ingested pro- or prebiotics within the last 30 days [4]. Probiotics are commonly used as prevention of antibiotic induced diarrhoea [5]. There is also evidence suggesting their potential antimicrobial effects against bacterial pathogens of the gastrointestinal tract as well as some viruses, such as rotavirus [6].

Case

This case describes a 56-year old woman hospitalised for specialised neurorehabilitation after having been involved in a traffic accident, where she became multi-traumatised with severe intra-abdominal injuries as well as widespread, hypoxic cerebral injury. Clinically the patient presented with left-sided, spastic hemiparesis, aphasia, truncal instability as well as diarrhoea, nausea, vomiting and periodic weight loss. Sufficient nutrition could not be attained with a nasogastric tube, and parenteral nutrition via a central venous catheter was initiated.

During the admission, the patient became febrile, without features of sepsis. Antibiotic treatment was therefore not initiated, but blood cultures were performed. Three of four blood cultures from the central venous catheter showed growth of *L. rhamnosus*. The central venous catheter was removed, and the tip was cultured but was negative. In the days leading up to the febrile episode the patient had received probiotics in the form of a capsule (commercially available, proprietary probiotic containing L. rhamnosus), where the capsule was opened and the content mixed with water, and fed to the patient via a nasogastric tube. Probiotics were routinely used on the ward as a standard treatment for patients with diarrhoea.

As the patient remained clinically stable and with no increase in infectious parameters, antibiotics were not initiated. The probiotics were discontinued. The infectious parameters were checked daily and remained low. Control blood cultures on day two and five came back negative, and the patient had thus cleared the *L. rhamnosus* bacteraemia without need for antimicrobial therapy.

To examine whether the isolate of *L. rhamnosus* from the patient's blood came from the ingested probiotics, WGS was performed on the Illumina MiSeq platform (Illumina Inc., San Diego, USA), producing 150 bp paired-reads as previously described [7]. The sequencing reads generated were compared to a publicly available sequence of *L. rhamnosus* GG from the probiotic manufacturer (NCBI Sequence Read Archive run no. SRR8313513) [8] and full-length *L. rhamnosus* genomes downloaded from NCBI GenBank. This was done using NASP (Northern Arizona SNP Pipeline) [9], a pipeline for comparison of genomic data and identification of single nucleotide polymorphisms (SNPs) between genomes, with *L. rhamnosus* GG whole genome sequence, strain GG (ATCC 53103) (Genbank accession no. NC_013198.1) as reference. From the results of NASP, SNP distances were calculated using the program snp-dist [10] and a phylogenetic tree was built with fasttree v. 2.1.11 [11] using FastTreeDbl (double precision) to obtain correct branch length estimations for very similar sequences. Our analysis identified 0 SNPs between *L. rhamnosus* isolated from the blood and *L. rhamnosus* GG from the probiotic capsule (DSM 33156), and close clustering of these and other *L. rhamnosus* GG genomes in the phylogenetic tree (Figure 1 and Supplementary table 1). A maximum of 13 SNPs was identified between the *L. rhamnosus* genomes shown in the subtree highlighted in the top left corner of the figure. Based on these analyses, results indicate that the *L. rhamnosus* isolate from the blood of the patient originated from the *L. rhamnosus* GG in the probiotic from the capsule.

Discussion

Lactobacilli are low-virulent bacteria, seldomly giving rise to invasive clinical infections and they are often used as probiotics to treat diarrhoea after a long-term antibiotic treatment [5].

This case report sheds light on the need to use caution when using probiotics for patients with indwelling intravascular catheters. The patient described in this case was healthy apart from her trauma, and was therefore immunocompetent, which may explain why her bacteraemia cleared rapidly and without the need for antibiotics. The probiotic could have entered the blood through the central venous catheter, seen in the light of its proximity to the nasogastric tube or possibly through bacterial translocation from the intestine. The patient was not known to suffer from any intestinal bowel diseases that could have disrupted the intestinal mucosa, however, she had diarrhoea, and had suffered intraabdominal injuries, so this is still a possibility.

L. rhamnosus can give rise to clinically invasive infections among immunocompromised patients. It has been described in a range of infections, such as abscesses, endocarditis and bacteraemia [12]. Bacteraemia with *L. rhamnosus* is furthermore described in patients with central venous catheters on Intensive Care Units. This is why experts recommend thorough hand hygiene after handling these catheters by healthcare workers, who have previously handled probiotic formulations [13]. *L. rhamnosus* bacteraemia is also described among immunocompetent patients with ischemic colitis and ulcerative colitis, where a possible bacterial translocation, due to disruption of the intestinal mucosa, has taken place [14]. In this case, we describe an immunologically healthy patient who had been multi-traumatised and therefore was clearly compromised as well as having diarrhoea which could facilitate translocation. Probiotics should therefore also be handled with care in patients suffering from intraabdominal trauma.

In conclusion, this is the first case using WGS to show that the exact same strain that was used as a probiotic in a patient, gave rise to a subsequent blood stream infection.

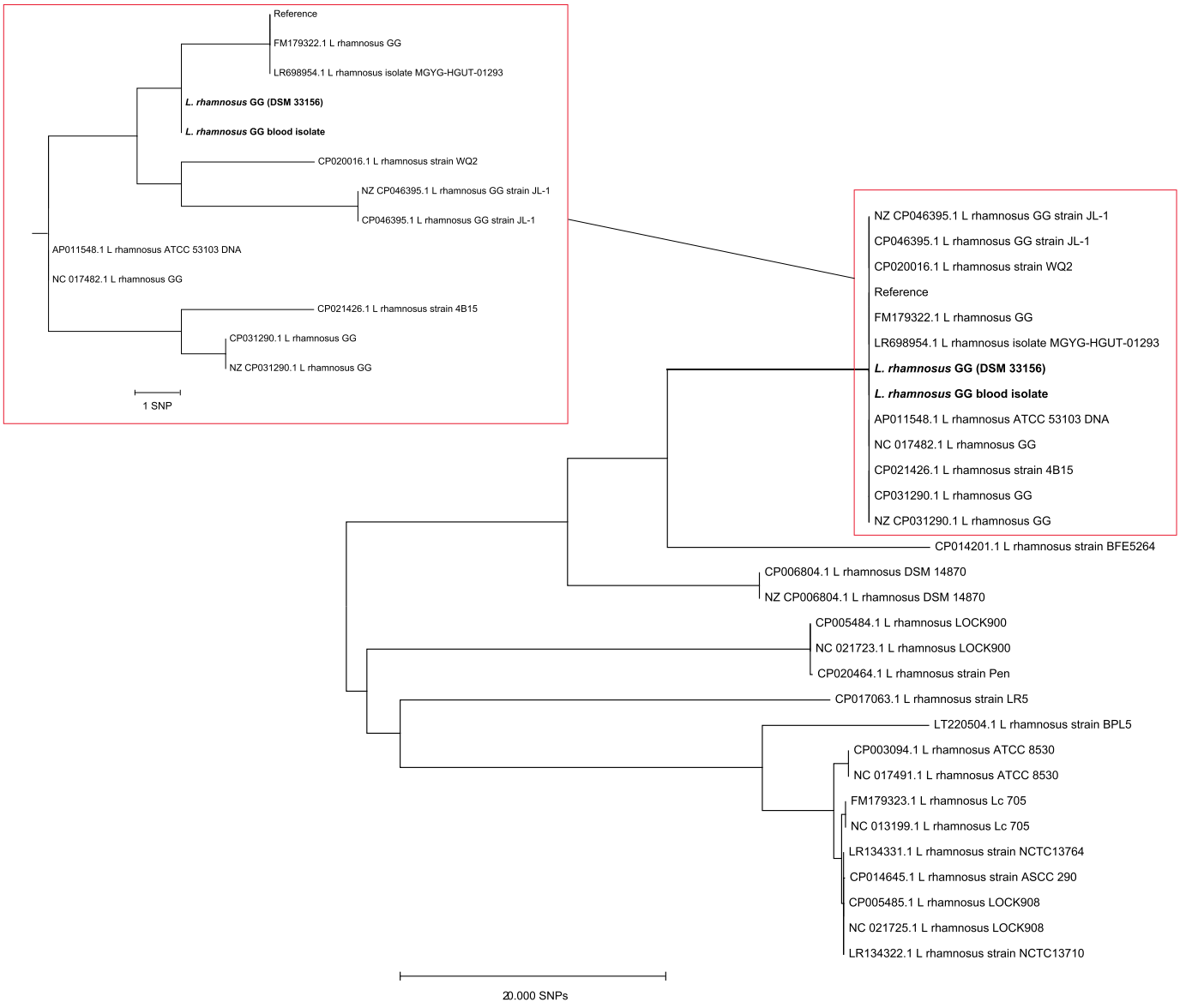

Figure 1. Phylogenetic tree showing the relatedness between *L. rhamnosus* genomes publicly available at NCBI GenBank, and *L. rhamnosus* GG from the blood of the patient as well as *L. rhamnosus* GG from the probiotic manufacturer (*L. rhamnosus* GG (DSM 33156)). The tree on the right includes all available *L. rhamnosus* genomes, while the subtree at the top left only includes genome closely related to *L. rhamnosus* GG from the blood of the patient and the probiotic capsule. SNP: Single nucleotide polymorphisms.

Ethical declaration

Written informed consent has been given and retained by authors.

Conflict of interest statement

The authors declare no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.infpip.2022.100200.

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