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High-biodiversity probiotic promotes liver fibrosis regression; implications for radiotherapy

Abstract

Liver fibrosis, a progressive accumulation of extracellular matrix proteins, is a common pathological outcome of chronic liver diseases and a significant long-term complication of radiation-induced liver disease (RILD) following oncological radiotherapy. This case report details the notable improvement in an 83-year-old male patient with established liver fibrosis, objectively measured by elastography (FibroScan), who received daily supplementation with a high-biodiversity probiotic (Freeze Dried Bravo probiotic). After approximately six months, the patient's liver stiffness score significantly decreased from 7.6 kPa (moderate fibrosis, F2) to 3.6 kPa (absence of fibrosis, F0). This improvement was not confined to the liver alone. Concurrently, a remarkable trend toward normalization was observed in several key blood parameters, including Mean Corpuscular Hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), glycemia, serum creatine, and Blood Urea Nitrogen (BUN). A significant decrease in the White Blood Cell (WBC) count also suggests a reduction in systemic inflammation. The hepatic improvement is consistent with a prior observation presented in 2013 by one of the authors, involving a severe fibrosis case that regressed with probiotic use. We hypothesize that the unique biodiversity and postbiotic richness of Bravo probiotic, possessing immunomodulatory and detoxifying properties, contributed to these systemic and anti-fibrotic effects by improving gut barrier integrity and reducing inflammation. While acknowledging the limitations of a single case report, these findings suggest a promising non-pharmacological strategy for managing liver fibrosis across various etiologies, including potential applications in mitigating RILD. Further rigorous clinical trials are warranted to validate these observations and elucidate the underlying mechanisms.

Keywords: liver fibrosis, probiotic, elastography, fibroscan, gut-liver axis, metabolic improvement

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Introduction

Liver fibrosis is a complex pathological process defined by the excessive accumulation of extracellular matrix proteins, leading to architectural distortion and impaired liver function. This process represents a dysregulated and prolonged wound-healing response, where normal liver tissue is progressively replaced by fibrotic scar tissue. This scarring not only compromises the liver's intricate microvasculature but also directly impedes its critical functions, such as detoxification and protein synthesis.

While a majority of cases are attributed to chronic liver diseases such as viral hepatitis, non-alcoholic fatty liver disease (NAFLD), and alcohol-related liver disease, it is crucial to recognize less common etiologies, including drug toxicity and, notably, radiation exposure. In modern oncology, radiation therapy is a cornerstone treatment for a wide range of solid tumors. However, the liver's intrinsic sensitivity to radiation poses a significant clinical challenge, particularly for tumors situated within or near the liver parenchyma. Radiation-induced liver disease (RILD) is a well-established clinical syndrome that limits the total radiation dose that can be safely delivered. This hepatic toxicity can arise from various techniques, including older forms of external beam radiation therapy and, more critically, modern high-dose, image-guided approaches like Stereotactic Body Radiation Therapy (SBRT). The risk of liver damage is also a major consideration with internal radiotherapy methods, such as radioembolization, which delivers a high dose directly to the liver's vasculature.

RILD is a multifaceted condition with a spectrum of presentations, ranging from acute veno-occlusive disease to long-term chronic liver fibrosis and cirrhosis. The progression to fibrosis is a major long-term concern, as it can lead to severe complications such as portal hypertension and liver failure. Research in this field has highlighted that the risk and severity of RILD are highly dependent on the dose-volume parameters of the radiation treatment, with higher doses to larger volumes of the liver significantly increasing the risk of adverse outcomes.[1]

The mechanisms underlying radiation-induced liver injury are complex and involve a cascade of inflammatory and fibrogenic responses. Endothelial cell damage is a key initiating event, leading to sinusoid obstruction and subsequent hepatocellular injury. This cascade eventually activates hepatic stellate cells, which are the primary source of the excessive collagen deposition characteristic of fibrosis. A comprehensive understanding of the clinical and pathological features of RILD is essential for accurate diagnosis and management.[2] This is particularly relevant with the advent of advanced radiation techniques, such as SBRT, which delivers highly conformal, high-dose radiation. While SBRT can be highly effective, it also necessitates a re-evaluation of the long-term effects on the liver, as high-dose gradients could potentially trigger a fibrogenic response in the healthy liver tissue surrounding the target.

The management of liver fibrosis, whether it arises from chronic diseases or is a complication of radiation therapy, is a multifaceted challenge. The primary strategy for non-radiotherapy-induced fibrosis is to address the underlying cause, such as achieving sustained virological response in hepatitis C, managing metabolic syndrome in NAFLD, or promoting abstinence in alcohol-related liver disease. However, for established fibrosis, several pharmacological and

non-pharmacological approaches are being explored. Anti-fibrotic drugs, though largely still in the clinical trial phase, include agents that target specific pathways involved in stellate cell activation and collagen synthesis. These include inhibitors of growth factors like Transforming Growth Factor-beta (TGF-β) and Platelet-Derived Growth Factor (PDGF), and antagonists of angiotensin II, which have shown promising results in pre-clinical studies.

In the context of RILD, the treatment landscape is more complex. Prevention is paramount, and it relies on meticulous treatment planning to minimize the dose to the healthy liver parenchyma, often utilizing techniques like dose-volume histograms and advanced delivery systems such as SBRT with dose-sparing protocols. Once RILD and subsequent fibrosis have developed, management becomes largely supportive, focusing on treating symptoms such as ascites and portal hypertension. Therefore, there is a growing interest in therapeutic interventions that can mitigate RILD.

A promising, albeit nascent, area of research is the role of the gut-liver axis and the potential for probiotics in modulating liver fibrosis. The gut microbiome influences liver health through various pathways, including the production of short-chain fatty acids and the modulation of inflammation. Dysbiosis, or an imbalance in the gut microbiota, can exacerbate liver injury and fibrosis by increasing intestinal permeability and promoting the translocation of bacterial products that stimulate inflammatory and fibrogenic responses in the liver. Probiotic supplementation, which aims to restore a healthy gut microbiome, has been shown in some studies to reduce liver inflammation and fibrosis in animal models of NAFLD and other chronic liver diseases. While the evidence for its role in radiation-induced fibrosis is still limited, the potential to modulate the inflammatory cascade and mitigate liver injury through the gut-liver axis makes it an intriguing area for future investigation.[3,4]

Based on the growing body of evidence linking the gut-liver axis to liver health, we present a compelling case that underscores the potential of probiotic intervention. This report details the clinical course of a patient with established liver fibrosis, as objectively measured by vibration controlled transient elastography (FibroScan), a recognized non-invasive method for assessing liver stiffness.[5] Following the initiation of a specific probiotic formulation, chosen for its high biodiversity and richness in postbiotic metabolites, the patient experienced a significant clinical improvement. Serial elastography measurements demonstrated a progressive and meaningful reduction in liver stiffness, indicating a reversal of the fibrotic process. This improvement was not confined to the liver alone. Concurrently, a remarkable trend toward normalization was observed in several key blood parameters, including Mean Corpuscular Hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), glycemia, serum creatine, and Blood Urea Nitrogen (BUN). A significant decrease in the White Blood Cell (WBC) count also suggests a reduction in systemic inflammation. This case illustrates a strong association between the use of this specialized probiotic and a positive impact on both hepatic function and broader systemic markers. The findings suggest that modulating the gut microbiome with a high-biodiversity formulation may offer a novel therapeutic avenue for patients with liver fibrosis, and they highlight the need for further investigation into this promising approach.[6]

Case presentation

The patient described in this case report is an 83-year-old male, a long-term client of Cultivate True Health clinic, where he undergoes periodic check-ups for a range of chronic, age-related issues. These include digestive problems, constipation, altered cholesterolemia, and hand tremors. Of note, the patient had a history of bladder cancer, which was previously treated with surgery and a subsequent 6-week course of BCG (Bacillus Calmette–Guérin) bladder instillation.

In January 2025, in addition to his ongoing therapies and supplements, the patient began taking the lyophilized probiotic Freeze Dried Bravo to support his gut microbiome and address his hand tremors as well as the digestive and constipation issues. The decision to initiate Bravo probiotic therapy was primarily based on the patient's hand tremors, as a similar intervention had previously shown positive results in another elderly male patient. This specialized probiotic, developed by Silver Spring (Switzerland), is obtained through a fermentation process of bovine milk and colostrum. The product is characterized by a unique microbial biodiversity, encompassing hundreds of different strains, phages, and plasmids,[7,8] and possesses immunomodulatory and detoxifying properties.[9,10] The patient was prescribed one capsule of the probiotic daily.

Experimental methodology

As part of routine health monitoring, the patient undergoes periodic blood and urine tests and, approximately once a year, an elastography examination (Fibroscan) to further evaluate liver health. For the purpose of this case report, we consider the results of blood tests performed in November 2024, prior to probiotic administration, and those performed at the end of May 2025, approximately six months after continuous probiotic intake. In particular, we focus on the most significant changes observed. Regarding liver elastography, results obtained in May 2024 are compared with those from May 2025.

Among the most significant changes observed in the hematochemical parameters, it's notable that MCHC values normalized, increasing from 31.2 g/dL to 32.8 g/dL (normal range 32-36 g/dL). MCH increased from 29.3 pg to 30.6 pg (normal range 28-33 pg). WBC count decreased from 5.9 bil/L to 4.5 bil/L (normal range 3.5-10.1 bil/L). Blood glucose levels decreased from 103 to 87 mg/dL (normal range 70-99 mg/dL); serum creatine values decreased from 0.9 to 0.76 mg/dL (normal range 0.60-1.30 mg/dL); and BUN decreased from 22 to 20 mg/dL (normal range 7-25 mg/dL). Collectively, these variations are consistent with a trend towards an improvement in the patient's metabolic condition, concerning sugar and protein/nitrogenous compound metabolism. This trend is further supported by the decrease in the WBC count, which can be interpreted as a reduction of a chronic systemic inflammatory state, often associated with metabolic dysfunction.

All other hematochemical parameters [Red Blood Cells count; Hemoglobin; Hematocrit; Mean Corpuscular Volume (MCV); Platelets count and Mean Platelet Volume (MPV); WBC formula; Sodium (Na); Potassium (K); Chloride (Cl); Carbon Dioxide (CO2) or Bicarbonate; Calcium; Albumin; Total Protein; Alanine Aminotransferase (ALT); Aspartate Aminotransferase (AST); Alkaline Phosphatase (ALP)] were within the normal range.

Regarding the results of the liver elastography examination, the liver stiffness score decreased from 7.6 kPa, indicative of moderate fibrosis (F2: presence of fibrosis with expansion of most portal areas and occasional bridging fibrosis), to 3.6 kPa, values considered compatible with the absence of liver fibrosis.

As a side note, following four months of Bravo probiotic use, the patient experienced a significant improvement in his hand tremors.

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Discussion

The striking improvements in the patient's hematochemical parameters following Bravo probiotic supplementation warrant discussion, particularly given the product's unique composition. The increase of both MCHC and MCH, along with significant reductions in blood glucose, serum creatine, and BUN, suggests a powerful systemic impact. This systemic effect is further evidenced by the decrease in the WBC count, which points to a reduction in chronic systemic inflammation and underscores the probiotic's positive influence well beyond just liver health.

One plausible hypothesis centers on the gut-liver-kidney axis and the role of a healthy microbiome in modulating metabolic processes and reducing systemic inflammation. The highly diverse microbial profile and postbiotic richness of Bravo probiotic[7,8] could enhance gut barrier integrity, thereby reducing the translocation of bacterial toxins (e.g., lipopolysaccharides) into the bloodstream. This reduction in endotoxemia is known to lessen systemic inflammation, which can, in turn, improve insulin sensitivity and glucose metabolism, potentially explaining the decrease in blood glucose.[11]

Furthermore, a healthier gut microbiome can influence kidney function by altering the production and reabsorption of various metabolites. For instance, dysbiosis can lead to an accumulation of uremic toxins. The observed improvements in creatine and BUN levels might reflect a more efficient nitrogen waste metabolism, potentially through enhanced microbial breakdown of protein by-products or reduced absorption of specific compounds that contribute to kidney burden.[12] The immunomodulatory and detoxifying properties attributed to Bravo probiotic[9,10] could also contribute to these systemic effects, fostering a less inflammatory environment that benefits multiple organ systems. While a single case report limits definitive conclusions, these findings underscore the interconnectedness of gut health with broader metabolic and renal functions, suggesting a promising avenue for multi-systemic improvements with targeted microbiome interventions.

The observed improvement in liver stiffness from 7.6 kPa (F2) to 3.6 kPa (F0) in the current patient, as measured by elastography, is a highly significant finding, indicating a remarkable reversal of liver fibrosis. This effect on liver fibrosis is reminiscent of an analogous observation presented by one of the authors of this work (MR) at a conference in 2013.

The mechanisms by which the Bravo probiotic, with its rich biodiversity of strains, phages, and plasmids,[7,8] along with its postbiotic components, could mediate such a profound anti-fibrotic effect are hypothesized to be multifaceted. Firstly, the immunomodulatory properties of Bravo[9,10] may play a crucial role by dampening chronic low-grade inflammation in the liver, a key driver of fibrogenesis. By restoring gut barrier integrity and reducing the translocation of pro-inflammatory bacterial products from the gut to the liver (the "gut-liver axis"), the probiotic could decrease the activation of hepatic stellate cells, which are central to collagen deposition.

Secondly, the detoxifying properties attributed to Bravo probiotic[9,10] might contribute by alleviating the metabolic burden on the liver, allowing for improved hepatocellular function and regeneration. The postbiotic substances, which are metabolic by-products of the probiotic fermentation, could directly exert anti-fibrotic effects or enhance the liver's natural repair mechanisms. While the exact interplay between the diverse microbial components and the host's hepatic response requires further elucidation, these observations suggest that a comprehensive microbiome modulation strategy can significantly impact the progression and even regression of liver fibrosis, offering a promising non-pharmacological approach for patients with chronic liver disease.

Conclusion

The present case report offers compelling insights into the potential systemic and hepatic benefits of probiotic supplementation. While the patient in this specific case did not present with RILD, the striking reversal of liver fibrosis, as evidenced by elastography, and the concurrent normalization of metabolic and renal parameters (blood glucose, creatine, and BUN) are highly relevant to the field of radiation oncology and broader liver health. The mechanisms of liver fibrosis, whether induced by radiation, metabolic dysfunction, or other chronic conditions, share common pathways involving inflammation and stellate cell activation. Therefore, an intervention that effectively modulates these pathways, as hypothesized for Bravo probiotic, holds significant promise across diverse etiologies of liver fibrosis.

For patients undergoing or having undergone radiotherapy near the liver, preventing or mitigating RILD and subsequent fibrosis is a critical challenge. Current strategies focus primarily on dose-sparing techniques. However, the observed anti-fibrotic effect in this case, coupled with the previously noted analogous observation from 2013, suggests that gut microbiome modulation could serve as a valuable adjunctive therapy. By potentially reducing systemic inflammation and enhancing liver regeneration, highly diverse probiotic formulations like Bravo probiotic might help protect healthy liver tissue from radiation-induced damage or even promote recovery in established RILD. This opens a new frontier for improving the therapeutic ratio of liver-directed radiation therapy, potentially allowing for higher tumor doses while safeguarding liver function.

The strengths of this case report lie in the objective measurements of liver stiffness via elastography and the clear documentation of pre- and post-intervention hematochemical values, providing concrete evidence of the observed changes. The consistency with a prior observation further reinforces the potential of this intervention. However, it's crucial to acknowledge the inherent limitations of a single case report. This is an observational study without a control group, making it impossible to definitively attribute the improvements solely to the probiotic, as other confounding factors or spontaneous regression cannot be entirely excluded.

Despite these limitations, this case highlights a critical area for future research. Prospective, placebo-controlled clinical trials are warranted to rigorously evaluate the efficacy and mechanisms of Bravo probiotic in various forms of liver fibrosis, including RILD. Further investigations should focus on characterizing the specific microbial and postbiotic components responsible for these effects, as well as elucidating the precise molecular pathways involved in both fibrosis regression and broader metabolic improvements. Such research could pave the way for novel, biologically targeted strategies to combat liver fibrosis, offering hope for patients across a spectrum of chronic liver diseases and those at risk from oncological treatments.

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Competing interests: RB is the founder of Cultivate True Health, a clinic dedicated to holistic natural health and nutrition. MR is the founder of Silver Spring Sagl, the company producing the probiotic used in this experience. MR served as CEO of the company until his retirement in 2020. He had no prior knowledge of the nutritional plan followed by the subject of this article nor of the results. RB communicated the results to MR only after completion of the experience.

Patient consent for publication: Consent obtained directly from patient. Since this is a single case report that does not produce generalizable knowledge, nor is it an investigation of an FDA regulated product, it is accepted that Institutional Review Board (IRB) review is not required for this activity.[13]

Advisory: No information in this paper is intended or implied to be a substitute for professional medical advice, diagnosis or treatment.

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