*American Journal of Internal Medicine*
2024, Vol. 12, No. 6, pp. 120-124
https://doi.org/10.11648/j.ajim.20241206.13

Case Report

# Autologous Bone Marrow-Derived Mesenchymal Stem Cell Transplantation for Decompensated Post-Hepatitis B Cirrhosis: A Case Report

**Muhammad Saeed[1], Siyab Aamir[2], Nida Hassan[3], Karrar Shaaban Imran[4], Gulnaz Bahtiyarova[5], Younes Nabgouri[5], Nnamdi Cletus Opara[6], Zhang Ming[7, *]**

[1]Department of Internal Medicine, Polyclinic Hospital, Islamabad, Pakistan
[2]Department of Surgery, Zhejiang Chinese Medical University, Hangzhou, China
[3]Department of Medicine, Holy Family Hospital, Rawalpindi, Pakistan
[4]Faculty of Medicine, University of Warith Al-Anbiya, Karbala, Iraq
[5]Department of Internal Medicine, Formerly: First Pavlov State Medical University, Saint Petersburg, Russia
[6]College of Medicine, Imo State University, Orlu, Nigeria
[7]Department of Internal Medicine, First Affiliated Hospital of Zhejiang University, Hangzhou, China

## Abstract

End-stage liver disease (ESLD) represents the terminal phase of chronic liver injury, characterized by overt clinical manifestations and severe complications that significantly impair the quality of life. The condition often culminates in a variety of symptoms, including jaundice, ascites, and hepatic encephalopathy, which reflect the liver's inability to perform its essential functions. Liver transplantation remains the definitive treatment for ESLD; however, limitations in donor organ availability necessitate exploration of alternative therapeutic strategies. we present a case of a 71-year-old Asian male with decompensated post-hepatitis B cirrhosis, who had a one-year history of hematemesis and melena. Endoscopic evaluation confirmed the presence of esophageal-gastric varices, further corroborating portal hypertension and hypersplenism. This patient underwent treatment with autologous bone marrow-derived mesenchymal stem cell (BM-MSC) transplantation. Following the procedure, the patient demonstrated significant clinical improvement, suggesting the safety and potential feasibility of BM-MSC transplantation for patients with ESLD. The field of BM-MSC transplantation has witnessed significant progress in recent years, emerging as a promising therapeutic approach for ESLD. This innovative treatment modality harnesses the regenerative capabilities of stem cells to promote liver repair and function. Notably, BM-MSCs possess immunomodulatory properties that may mitigate inflammation and fibrosis in the liver, thereby addressing some of the underlying pathophysiology associated with ESLD. This case presentation highlights the potential application of BM-MSC therapy in patients with decompensated cirrhosis. The findings underscore the need for further research and refinement of clinical application techniques to fully realize the broad therapeutic possibilities of BM-MSC transplantation for ESLD. As we advance our understanding of stem cell therapies, it is crucial to conduct larger studies to evaluate long-term outcomes and establish standardized protocols for treatment.

[*]Corresponding author: zhangming1993@yahoo.com (Zhang Ming)

**Received:** 4 October 2024; **Accepted:** 23 October 2024; **Published:** 28 November 2024

## Keywords

Stem Cells, End-Stage Liver Disease (ESLD), Hepatitis B

## 1. Introduction

Chronic Liver Disease and End-Stage Liver Disease (ESLD):

Chronic liver disease encompasses a spectrum of pathological processes characterized by ongoing hepatic injury and fibrosis. A hallmark feature is cirrhosis, a progressive and irreversible scarring of the liver parenchyma. This scarring disrupts normal liver architecture and impairs vital functions such as detoxification, protein synthesis, and bile production [8]. Various chronic insults can lead to cirrhosis, including chronic viral hepatitis (e.g., hepatitis C), alcoholic liver disease, autoimmune hepatitis, and cholestatic liver diseases (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, cystic fibrosis) [7, 8]. ESLD represents the most advanced stage of chronic liver disease, characterized by decompensated liver function and the emergence of overt clinical manifestations. Unlike earlier stages, ESLD patients typically experience a constellation of symptoms, including abdominal pain, particularly in the right upper quadrant, hepatomegaly, and jaundice [10, 11]. Depending on the underlying etiology, the cirrhotic liver may exhibit significant inflammation and fibrosis. Furthermore, patients often develop complications such as ascites, esophageal varices, and dark-colored urine [5, 6]. Cutaneous manifestations, including rashes, can also occur. Unfortunately, ESLD is currently considered an irreversible condition. Liver transplantation remains the sole curative therapeutic option [2, 11]. However, widespread application of liver transplantation is hampered by a critical shortage of donor organs and the associated high costs. This highlights the urgent need for alternative therapeutic strategies for ESLD patients. The case presented here explores the potential application of bone marrow-derived mesenchymal stem cells (BM-MSCs) as a novel treatment approach.

## 2. Case Report

A 71-year-old Asian male with a 32-year history of chronic hepatitis B presented to the hospital on September 9$^{th}$, 2022, with a one-year history of hematemesis (vomiting blood) and melena (black stools). Chronic hepatitis B diagnosed 32 years prior, currently managed with entecavir 0.5mg daily (antiviral therapy). Type 2 diabetes mellitus diagnosed 4 years prior, treated with metformin hydrochloride 0.5g daily. Hernia repair surgery in 2016.

Denies history of hypertension, heart disease, other infectious diseases (tuberculosis), additional surgeries, trauma, contact with epidemic areas, tobacco or alcohol use, exposure to industrial toxins, dust, or radioactive substances.

## 3. Physical Examination

Mild jaundice of the skin and sclerae.

Positive spider nevi on the palms, suggestive of chronic liver disease. Flat, soft abdomen without tenderness, rebound tenderness, or muscle guarding. Old, well-healed surgical scar present. No flank pain (Maxwell's sign), no umbilical hernia (Mohr's sign), no abdominal fluid accumulation on percussion. Normal bowel sounds, mobile flanks, and mild bilateral lower limb edema. Esophagogastroduodenoscopy (EGD) likely revealed multiple, worm-like impressions on the lower esophageal wall, consistent with esophageal varices. Upper abdominal CT scan confirmed: Liver cirrhosis, Splenomegaly, Portal hypertension,

Esophageal and gastric varices Small amount of ascite and Gallstones. Decompensated stage of post-hepatitis B cirrhosis, esophageal-gastric varices, portal hypertension, and speen enlargement was finally established. Laboratory examination showed abnormal biochemical indicators as in Table 1 on 17$^{th}$ May, 2020.

***Table 1.*** *Biochemical indicators when first admitted to hospital.*

| Biochemical indicator | Concentration | Change |
|---|---|---|
| Hemoglobin | 93.0 g/L | ↓ |
| Platelet Count | $62*10^9$/L | ↓ |
| Total Leukocytes count | $1.40*10^9$/L | ↓ |
| Indirect bilirubin | 18.6 | ↑ |
| Albumin | 34.9 g/L | ↓ |
| Prothrombin time | 18.6s | ↑ |
| Fibrinogen | 1.47 g/L | ↓ |

Six days following admission, the patient underwent splenectomy and esophagogastric vein devascularization under general anesthesia. This surgical approach aims to address both the enlarged spleen (hypersplenism) and the bleeding esophageal and gastric varices. Pathological examination of

the resected spleen confirmed chronic congestive splenomegaly. The spleen measured 18 x 10 x 5 cm, weighed 473g, and exhibited a solid, gray-red appearance on section. The patient demonstrated a favorable postoperative recovery and was discharged two weeks later. Unfortunately, the patient experienced recurrent hematemesis and melena within a year of discharge. Endoscopic variceal ligation (EVL) was performed on August 19th, 2020 (Figure 1) to address the bleeding varices. Details of the laboratory evaluation are presented in Table 2.

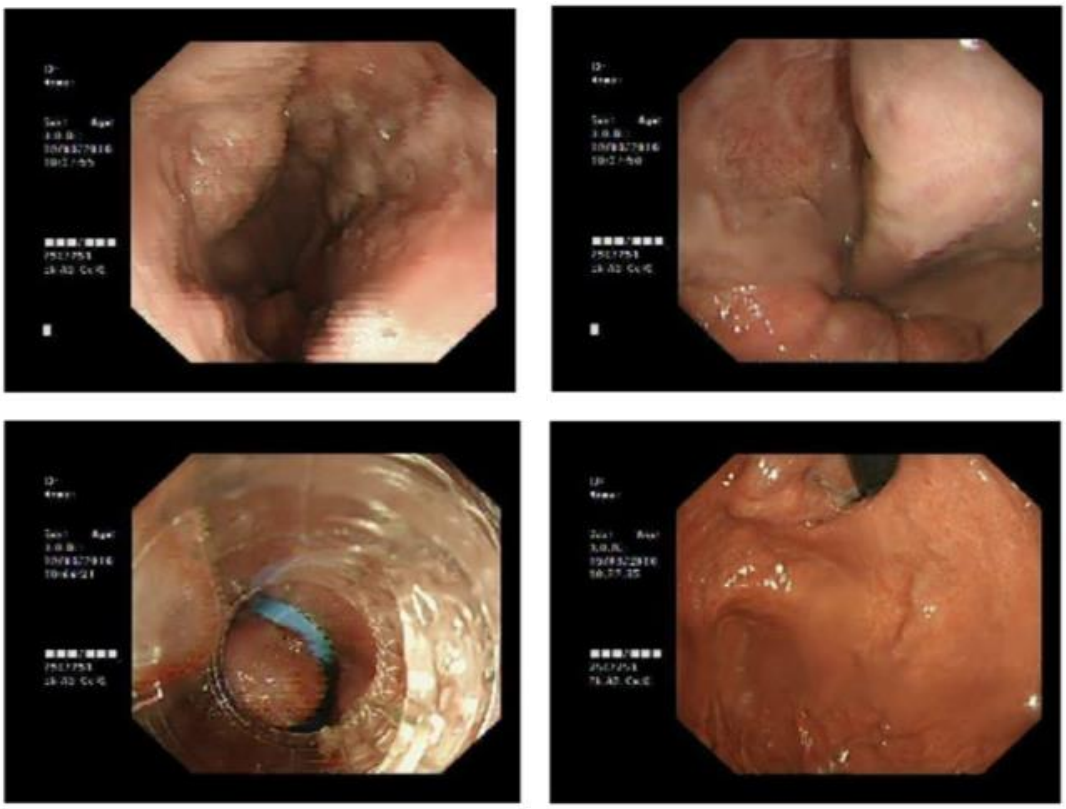

***Figure 1.*** *Patient's Endoscopic variceal ligation (EVL).*

***Table 2.*** *Biochemical indicators on 2020.08.19 and 2021.04.23.*

| Biochemical indicator | Before BMT | After BMT |
|---|---|---|
| Hemoglobin | 106 g/L | 146 g/L |
| Platelet | $79*10^9$/L | $177*10^9$/L |
| Leucocytes | $3.50*10^9$/L | $4.50*10^9$/L |
| Albumin | 26.4 g/L | 36.4 g/L |
| total bilirubin | 29.40 umol/L | 7.40 umol/L |
| Unconjugated bilirubin | 28.40 umol/L | 14.00 umol/L |
| Alkaline phosphatase | 133.00U/L | |

On August 25th, 2021, the patient underwent a Trans-gastroepiploic right portal vein catheterization allowing for access to the portal vein, a major blood vessel draining the digestive organs, through a small incision. Infusion port implantation, a port-a-cath, a small, implanted device, was placed to facilitate future BM-MSC administration. The patient's own bone marrow was extracted from the anterior superior iliac spine and processed to isolate BM-MSCs. These cells were then infused through the portal vein catheter. This BM-MSC transplantation procedure was repeated monthly.

Following BM-MSC treatment, the patient exhibited significant improvement in various biochemical parameters, as illustrated in Figure 2. Notably: Albumin levels, a marker of liver function and nutritional status, increased from 25.6 to 35.6 g/L within 6 months and remained stable thereafter. Platelet levels, essential for blood clotting, also improved. Liver enzyme levels, including alanine aminotransferase (ALT), serum glutamic-oxaloacetic transaminase (SGOT), and bilirubin, all decreased, indicating reduced liver injury. Prothrombin time, a measure of blood clotting function, normalized.

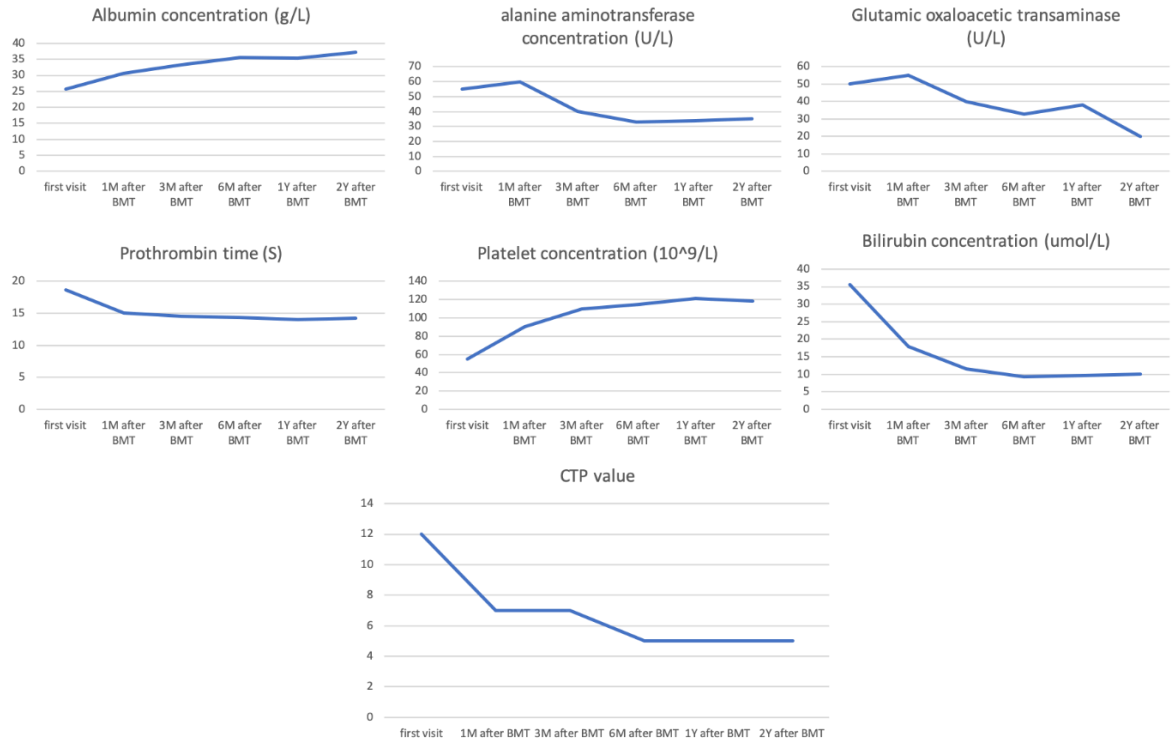


***Figure 2.*** *Improvement in biochemical indicators of the patient.*

The Child-Turcotte-Pugh (CTP) demonstrated a significant improvement. The patient's initial CTP score of 12 (indicating moderate-to-severe disease) decreased to 5 after 6 months of BM-MSC treatment (indicating mild disease and improved self-care capabilities). Furthermore, the patient did not experience any further episodes of upper gastrointestinal bleeding for at least one year following the last documented follow-up. These findings suggest a potential therapeutic benefit of BM-MSC transplantation in this case of decompensated post-hepatitis B cirrhosis.

## 4. Discussion

Mesenchymal stem cells (MSCs) derived from bone marrow possess unique biological properties that may contribute to their therapeutic potential in liver disease. Studies have demonstrated the inherent ability of MSCs to self-replicate and proliferate extensively [12]. This characteristic allows for the generation of a sufficient cell population for therapeutic purposes. MSCs exhibit the capacity to differentiate into various cell lineages under specific conditions [1]. While in vitro and animal studies suggest the possibility of MSC differentiation into hepatocytes [3, 4], further research is needed to definitively confirm this in humans. Regardless of their differentiation potential, MSCs can secrete a diverse array of cytokines and growth factors [9]. These paracrine signals can modulate the microenvironment within the liver, promoting tissue repair and regeneration.

Emerging clinical data support the potential benefits of BM-MSC transplantation for patients with liver disease. Studies have reported improvements in liver function and regeneration following BM-MSC administration [14]. The presented case aligns with these observations. Following BM-MSC transplantation, the patient experienced significant clinical improvement, including: Enhanced appetite and physical strength, Resolution of fatigue and poor appetite, Reduction of ascites, Increased serum albumin levels, Improved coagulation function, Enhanced liver reserve function at 12 weeks post-transplantation These findings suggest that autologous BM-MSC transplantation has the potential to Ameliorate clinical symptoms in patients with end-stage liver disease Improve liver function, coagulation function, and liver reserve function, Enhance patient quality of life.

Furthermore, the patient tolerated the BM-MSC therapy well, with no reported adverse reactions. This case adds to the growing body of evidence suggesting the safety and potential feasibility of autologous BM-MSC transplantation for patients with end-stage liver disease. It is crucial to acknowledge that further well-designed clinical trials are necessary to definitively establish the efficacy and long-term safety of BM-MSC therapy for liver disease.

Autologous bone marrow-derived mesenchymal stem cell (BM-MSC) transplantation offers several advantages over alternative cell sources. Bone marrow collection is a minimally invasive procedure, readily accessible for autologous transplantation. By utilizing the patient's own cells, the risk of immune rejection (GVHD) is virtually eliminated, overcoming a major limitation of allogeneic (donor-derived) cell therapy. Autologous BM-MSC transplantation closely re-

sembles autologous blood transfusion, exhibiting a high safety profile with minimal risk of adverse reactions. Furthermore, the use of autologous cells avoids the potential for transmission of infectious diseases associated with allogeneic sources. Compared to some other therapeutic options, BM-MSC transplantation is a less invasive procedure, potentially reducing associated costs and patient discomfort.

## 5. Conclusion

The field of autologous BM-MSC transplantation has witnessed significant progress in recent years, emerging as a promising therapeutic approach for end-stage liver disease. While challenges remain regarding large-scale clinical application, ongoing research and refinement of techniques hold promise for the development of safe and effective BM-MSC therapy for this debilitating condition. Further well-designed clinical trials are warranted to definitively establish the efficacy and long-term safety of this approach.

## Abbreviations

| | |
|---|---|
| CTP | Child-Turcotte-Pugh |
| ESLD | End Stage Liver Disease |
| EGD | Esophagogastroduodenoscopy |
| EVL | Endoscopic Variceal Ligation |
| BM-MSC | Bone Marrow Derived Mesenchymal Stem Cells |
| SGOT | Serum Glutamic-oxaloacetic Transaminase |

## Author Contributions

**Muhammad Saeed:** Conceptualization
**Siyab Aamir:** Data curation
**Karrar Shaaban Imran:** Investigation
**Gulnaz Bahtiyarova:** Methodology
**Younes Nabgouri:** Resources
**Nida Hassan:** Project administration
**Nnamdi Cletus Opara:** Validation
**Zhang Ming:** Writing – original draft, Writing – review & editing

## Conflicts of Interest

Authors declare no competing conflict of interest.

## References

[1] Aydin, S., Sağraç, D., & Şahin, F. Differentiation Potential of Mesenchymal Stem Cells into Pancreatic β-Cells. (0065-2598 (Print)). https://doi.org/10.1007/5584_2019_476

[2] Fox, R. K. When to consider liver transplant during the management of chronic liver disease. (1557-9859 (Electronic)). https://doi.org/10.1016/j.mcna.2013.09.007

[3] Hernández, R., Jiménez-Luna, C., Perales-Adán, J., Perazzoli, G., Melguizo, C., & Prados, J. Differentiation of Human Mesenchymal Stem Cells towards Neuronal Lineage: Clinical Trials in Nervous System Disorders. (1976-9148 (Print)).

[4] Jopling, C., Boue S Fau - Izpisua Belmonte, J. C., & Izpisua Belmonte, J. C. Dedifferentiation, transdifferentiation and reprogramming: three routes to regeneration. (1471-0080 (Electronic)). https://doi.org/10.1038/nrm3043

[5] Karagiannakis, D. A.-O. X., & Stefanaki, K. Spleen stiffness: a predictive factor of dismal prognosis in liver cirrhosis. (1865-7265 (Electronic)). https://doi.org/10.1007/s12328-022-01752-z

[6] Kim, T. S., & Choi, D. A.-O. Liver Dysfunction in Sepsis. (2233-6869 (Electronic)). https://doi.org/10.4166/kjg.2020.75.4.182

[7] Liu, J. A.-O., Yuan, Z., & Wang, Q. Pluripotent Stem Cell-derived Strategies to Treat Acute Liver Failure: Current Status and Future Directions. (2225-0719 (Print)). https://doi.org/10.14218/JCTH.2021.00353

[8] Miró, J. M., Laguno M Fau - Moreno, A., Moreno A Fau - Rimola, A., & Rimola, A. Management of end stage liver disease (ESLD): what is the current role of orthotopic liver transplantation (OLT)? (0168-8278 (Print)). https://doi.org/10.1016/j.jhep.2005.11.028

[9] Park, C. W., Kim, K. S., Bae, S., Son, H. K., Myung, P. K., Hong, H. J., & Kim, H. Cytokine secretion profiling of human mesenchymal stem cells by antibody array. (2005-3606 (Print)). https://doi.org/10.15283/ijsc.2009.2.1.59

[10] Philips, C. A., & Kedarisetty, C. K. Palliative Care for Patients with End-Stage Liver Disease. (0973-6883 (Print)). https://doi.org/10.1016/j.jceh.2022.08.003

[11] Tekin, A., Beduschi, T., Vianna, R., & Mangus, R. S. Multivisceral transplant as an option to transplant cirrhotic patients with severe portal vein thrombosis. (1743-9159 (Electronic)). https://doi.org/10.1016/j.ijsu.2020.07.010

[12] Uccelli, A., Moretta, L., & Pistoia, V. (2008). Mesenchymal stem cells in health and disease. *Nature Reviews Immunology*, *8*(9), 726-736. https://doi.org/10.1038/nri2395

[13] Xu, M., Chen, Y., & Artru, F. A.-O. Acute decompensation of cirrhosis versus acute-on-chronic liver failure: What are the clinical implications? (2050-6414 (Electronic)). https://doi.org/10.1002/ueg2.12538

[14] Yu, S., Yu, S., Liu, H., Liao, N., & Liu, X. (2023). Enhancing mesenchymal stem cell survival and homing capability to improve cell engraftment efficacy for liver diseases. *Stem Cell Research & Therapy*, *14*(1), 235. https://doi.org/10.1186/s13287-023-03476-4