Journal of Regenerative Biology and Medicine

ISSN: 2582-385X
See KS Kris, et al.,2023- J Regn Bio Med
Case Report

Liver Regeneration: The Myth of Prometheus in Modern Medicine A Case Report

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Received date: 11-14-2023

Accepted Date: 11-30-2023

Published Date: 12-20-2023

Abstract

Liver regeneration is a complex process of tissue repair and regrowth that takes place in response to liver damage. The liver has the unique ability to regenerate itself after injury, allowing it to recover from a variety of insults including viral infections, drug-induced injury, or surgical resection. The process of liver regeneration involves a coordinated series of cellular and molecular events that ultimately lead to the restoration of liver function. The myth of Prometheus involves liver regeneration. In Greek mythology, Prometheus was a Titan who created humans and gave them fire, which he had stolen from the gods. As punishment for his actions, Zeus ordered Prometheus to be chained to a rock and have his liver eaten by an eagle every day, only for the liver to regenerate overnight and the cycle to repeat endlessly. This myth can be interpreted as a metaphor for the liver's remarkable ability to regenerate itself after injury. The liver has the ability to regenerate lost tissue and can even grow back to its full size and function after being partially removed, such as in a liver transplant or in cases of surgical resection for liver cancer.

The story of Prometheus and the regenerating liver has also been used in literature and art to symbolize themes such as endurance, resilience, and the power of the human spirit to overcome adversity. In this case report, Researcher report a patient that was initially presented with liver impairment, Osel Liver Regeneration Protocol was initiated and the subsequent resolution of the patient's ailment.

Keywords: Liver regeneration; Tissue repair; Prometheus; Hepatocyte growth factor; Epidermal growth factor; Transforming growth factor.

Introduction

Liver regeneration is a complex process of tissue repair and regrowth that takes place in response to liver damage. The liver has the unique ability to regenerate itself after injury, allowing it to recover from a variety of insults

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DOI: https://doi.org/10.37191/Mapsci-2582-385X-5(5)-140

including viral infections, drug-induced injury, or surgical resection.

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Case presentation

A 15-year-old patient with no known medical illness, presented initially to the outpatient clinic with complaints of lethargy, headache, myalgia, and mild itch.

The patient, a high schooler, is in the midst of examinations and was reported under stress. The patient has a history of taking traditional supplements from unknown sources and dosage for a few months prior to the symptoms.

Immediate laboratory tests were ordered. Liver profile revealed as follows:

11th February, 2023

	Liver Function			
	Total Protein	72	g/L	(57-80)
	Albumin	42	g/L	(33-47)
	Globulin	30	g/L	(20-39)
	Albumin/Globulin Ratio	1.4		(1.0-2.5)
	Alkaline Phosphatase	96	U/L	(30-450)
*	Total Bilirubin	26	umol/L	(<21)
*	GST	51	U/L	(<51)
*	AST	85	U/L	(<41)
**	ALT	191	U/L	(<51)

Table 1: Liver Profile.

After thorough evaluation, it was determined that it is best to harness the regenerative capability of the liver by initiating Osel Liver Regeneration Protocol.

Osel Liver Regeneration Protocol includes: IV alpha lipoic acid 1200mg+Extract of Human Placenta Derived Full-Term+IV Vitamin C 2000mg+IV Glutathione 1200mg,

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in 500 cc of normal saline and slow infusion over 1 hour.

It was determined that the patient would require 3 doses of infusion, once per month over a period of 3 months for the best outcome.

For donor of human placenta extract, in order to screen each donor, a complete medical history, interviewing such as a history of travel and serologic testing for viruses, bacteria and infection are performed, after nucleic-acid testing (NAT) to meet with requirements for HBV-DNA, HCV-RNA and HIV-1-RNA is carried out. In addition, it has been confirmed that high-pressure steam sterilization for 20 minutes at 121°C during the manufacturing process is effective in inactivating various viruses such as HIV etc. Furthermore, although in the product test, the nucleic-acid test meets with requirements for HBV-DNA, HCV-RNA, HIV-1-RNA, HTLV-DNA, and parvovirus B19-DNA, patients should be made aware of the following points during administration: To date, the transmission of infection, such as variant Creutzfeldt-Jakob disease (vCJD), by administration of this protocol has not been reported.

Post-infusion course

In the immediate first post-infusion period, the patient experienced expected lethargy, headache, and thirst. The patient also reported an episode of vomiting. No fever was recorded. These symptoms lasted for 5 to 7 days after the infusion.

In the immediate second post-infusion period, the patient reported reduced lethargy as compared to the first infusion. No other adverse events were reported.

In the immediate third post-infusion period, the patient did not experience any of her previous symptoms.

Follow-up examinations, including laboratory tests, were conducted to assess the progress of liver regeneration.

25th April, 2023

Liver Function			
Total Protein	71	g/L	(57-80)
Albumin	44	g/L	(33-47)
Globulin	27	g/L	(20-39)
Albumin/Globulin Ratio	1.6		(1.0-2.5)
Alkaline Phosphatase	77	U/L	(30-450)
Total Bilirubin	3	umol/L	(<21)
GST	14	U/L	(<51)
AST	15	U/L	(<41)
ALT	12	U/L	(<51)

Table 2: Progress of Liver Regeneration.

At the eight-week follow-up, the patient demonstrated a substantial reduction in liver enzyme levels, with normalization of bilirubin, GGT, AST and ALT and improved liver function. The patient reported that the patient felt back to the old self with renewed

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energy and vigor, being happy and cheerful. The patient was discharged from the clinic with instructions for outpatient monitoring.

Discussion

Liver regeneration is a complex process involving multiple cellular and molecular mechanisms [1]. In this case, successful liver regeneration was observed following initiation of our liver regeneration protocol.

The initiation of liver regeneration involves the activation of various growth factors and signaling pathways, promoting hepatocyte proliferation and the restoration of liver tissue [2].

Although the precise mechanisms governing liver regeneration remain the subject of ongoing research, the remarkable regenerative capacity of the liver offers promising opportunities for the treatment of liver diseases and the potential for novel therapeutic interventions [3].

Process of liver regeneration

The process of liver regeneration begins with the activation of hepatic progenitor cells, which are present in the liver and have the capacity to differentiate into hepatocytes or cholangiocytes [4].

Following liver injury, these cells proliferate rapidly and migrate to the site of damage. Once there, they differentiate into mature hepatocytes or cholangiocytes, depending on the nature and severity of the injury.

The proliferation of hepatic progenitor cells is regulated by a number of growth factors, including hepatocyte growth factor (HGF), epidermal growth factor (EGF), and transforming growth factor-alpha (TGF-α). These growth factors bind to receptors on the surface of hepatic progenitor cells, triggering a cascade of intracellular signaling events that ultimately result in cell division.

The newly formed hepatocytes and cholangiocytes then begin to reestablish the liver architecture by forming new hepatic cords and bile ducts. This process is mediated by cell-cell interactions and the secretion of extracellular matrix proteins, such as collagen and fibronectin.

Underlying mechanisms

The mechanisms underlying liver regeneration are complex and involve a variety of signaling pathways and molecular interactions. One of the key drivers of liver regeneration is the activation of the Wnt/β-catenin pathway, which regulates the proliferation and differentiation of hepatic progenitor cells [5]. The activation of this pathway is triggered by the release of Wnt ligands from the extracellular matrix, which bind to receptors on the surface of hepatic progenitor cells.

Another important pathway involved in liver regeneration is the Notch signaling pathway. This pathway is activated by the interaction between Notch receptors on hepatic progenitor cells and their ligands on neighboring cells [6]. Activation of the Notch pathway promotes the differentiation of hepatic progenitor cells into cholangiocytes [7].

Alpha-lipoic Acid

Alpha-lipoic acid (ALA) has been investigated for its potential role in liver health and

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regeneration. Although research on this specific topic is limited, ALA's antioxidant and anti-inflammatory properties suggest that it may have beneficial effects on liver regeneration. Here are some ways in which ALA could potentially impact liver regeneration:

1. Antioxidant Activity: ALA functions as a potent antioxidant and can scavenge free radicals, reducing oxidative stress in the liver. Oxidative stress is known to contribute to liver damage and impede the regenerative process. By neutralizing free radicals, ALA may support a favorable environment for liver cell regeneration [8].
2. Anti-inflammatory Effects: Chronic inflammation can hinder liver regeneration. ALA has been shown to possess anti-inflammatory properties by inhibiting the activation of pro-inflammatory signaling pathways. By reducing inflammation, ALA may promote a more conducive environment for liver tissue repair and regeneration [9].
3. Cellular Energy Metabolism: ALA plays a crucial role in energy metabolism by acting as a cofactor for enzymes involved in mitochondrial function.
4. Enhanced mitochondrial activity can support the energy demands of rapidly dividing liver cells during the regenerative process.
5. Insulin Sensitivity: ALA has been studied for its effects on insulin sensitivity and glucose metabolism. Improved insulin sensitivity can contribute to better metabolic regulation, potentially benefiting liver health and regeneration [10].

While the mechanisms by which ALA may directly influence liver regeneration are not yet fully understood, the above properties suggest that ALA may have a positive impact on the regenerative capacity of the liver.

Vitamin C

Vitamin C, also known as ascorbic acid, is an essential nutrient with numerous physiological functions in the body.

While its specific role in liver regeneration is not as extensively studied as other aspects of liver health, vitamin C does play several important roles that may contribute to liver regeneration. Here are some ways in which vitamin C may impact liver regeneration:

1. Collagen Synthesis: Vitamin C is essential for collagen synthesis, a critical component of the extracellular matrix that provides structural support to tissues. During liver regeneration, the synthesis and remodeling of collagen are necessary for the restoration of liver tissue architecture. Adequate vitamin C levels can support collagen production, contributing to the regenerative process [11].
2. Antioxidant Activity: Vitamin C acts as an antioxidant and can scavenge free radicals, protecting liver cells from oxidative stress. Liver regeneration involves a cascade of events that can generate reactive oxygen species (ROS), leading to

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oxidative damage. By neutralizing free radicals, vitamin C helps to reduce oxidative stress and create a favorable environment for liver tissue repair.

3. Immune Function: Vitamin C plays a vital role in immune system function, including the production and function of immune cells. A well-functioning immune system is essential for tissue repair and regeneration, as it helps combat infections and promote a healthy environment for regeneration to occur [12].
4. Iron Absorption and Storage: Vitamin C enhances the absorption of iron from the diet and promotes its storage in the body. Iron is a crucial nutrient for red blood cell production and oxygen transport, which are essential for tissue healing and regeneration.

While these mechanisms suggest that vitamin C may support liver regeneration, it's important to note that additional research specifically focused on vitamin C's role in liver regeneration is warranted.

Human placenta

The use of human placenta in liver regeneration is an area of ongoing research and exploration. Placental tissue contains a variety of growth factors, cytokines, and stem cells that have the potential to promote tissue repair and regeneration. While research on the specific application of human placenta in liver regeneration is limited, there have been some studies and preliminary findings that suggest potential benefits. Here are a few key points:

1. Growth Factors and Cytokines: Human placenta is a rich source of growth factors and cytokines that are involved in various cellular processes, including tissue regeneration. These factors, such as hepatocyte growth factor (HGF) and transforming growth factor-beta (TGF-β), have been shown to promote liver cell proliferation and regeneration.
2. Anti-inflammatory and Immunomodulatory Properties: The placenta contains immune-modulating factors that can help regulate inflammation and immune responses. Modulating the inflammatory environment during liver regeneration is crucial for optimal healing and tissue repair [13].
3. Stem Cells and Progenitor Cells: Placental tissue contains various types of stem cells and progenitor cells that have the potential to differentiate into liver cells or support liver regeneration indirectly by secreting growth factors and promoting tissue healing [14].
4. Extracellular Matrix Components: The extracellular matrix (ECM) of the placenta contains structural proteins and growth factors that play a role in tissue regeneration. These components may aid in providing a supportive environment for liver cell growth and regeneration [15].

While these factors suggest the potential of human placenta in liver regeneration, it is important to note that further research is needed to fully understand its effectiveness, safety, and optimal application.

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Additionally, the ethical considerations surrounding the use of human placenta should be carefully evaluated and regulated.

Glutathione

Glutathione plays a significant role in liver regeneration due to its involvement in various cellular processes. Here are some key points about the role of glutathione in liver regeneration:

1. Antioxidant Defense: Glutathione is a powerful antioxidant that helps protect liver cells from oxidative stress, which can occur during liver injury or damage. It scavenges free radicals and reduces reactive oxygen species (ROS), preventing oxidative damage and promoting a favorable environment for liver regeneration [16].
2. Detoxification: The liver is responsible for detoxifying various substances, including drugs, toxins, and harmful compounds. Glutathione plays a crucial role in the detoxification process by participating in the conjugation and elimination of toxic substances. This detoxification capacity is important for liver regeneration as it helps clear harmful metabolites and supports the regeneration of healthy liver tissue [17].
3. Cell Signaling and Proliferation: Glutathione is involved in cellular signaling pathways that regulate cell proliferation and survival. It helps modulate the redox balance within cells, which influences cell growth and differentiation. Proper glutathione levels are essential for promoting hepatocyte proliferation and facilitating liver tissue regeneration.
4. Immune System Modulation: Glutathione has immunomodulatory properties that can influence the immune response during liver regeneration.

It helps regulate the activity of immune cells, such as Kupffer cells and T cells, which play crucial roles in tissue repair and inflammation resolution. By modulating immune cell function, glutathione can promote a favorable environment for liver regeneration [18].

Overall, glutathione's antioxidant properties, involvement in detoxification processes, regulation of cell signaling, and modulation of the immune system contribute to its role in liver regeneration. However, the precise mechanisms through which glutathione influences liver regeneration are still an area of ongoing research.

Factors influencing liver regeneration

The efficiency of liver regeneration can be influenced by a number of factors, including the extent and nature of the liver injury, the age and health of the individual, and the presence of underlying liver disease. For example, individuals with chronic liver disease or cirrhosis may have impaired liver regeneration due to the accumulation of scar tissue and the loss of functional liver tissue [19].

Advancements in the understanding of liver regeneration have opened up potential

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therapeutic avenues for liver diseases. Current and emerging therapeutic approaches, including the use of growth factors, stem cell-based therapies, tissue engineering, and regenerative medicine techniques could be further enhanced.

It also highlights ongoing research and future directions in the field of liver regeneration.

Conclusion

Liver regeneration is a complex and dynamic process that holds immense clinical significance. Further research is required to unravel the intricate mechanisms governing liver regeneration and to develop targeted therapeutic interventions.

The story of Prometheus and his regenerating liver symbolize the regenerative capabilities of our bodily organs, something which clinical medicine could leverage on.

Advancements in the understanding of liver regeneration have opened up potential therapeutic avenues for liver diseases including the use of growth factors, stem cell-based therapies, tissue engineering, and regenerative medicine techniques could be further enhanced. Harnessing the regenerative potential of the liver has the potential to revolutionize the treatment of liver diseases and improve patient outcomes.

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