

Critical study of alcohol and hepatocytes cell necrosis

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Introduction

The tissue shows vast inflammation, there are large gaps in between the hepatocytes due to cell necrosis and the hepatocytes remaining are large and swollen. There are fatty deposits throughout the tissue and fibrous structures present which are most likely collagen. The hepatocytes themselves are not only swollen but have the presence of globular material within. This is identified as Mallory bodies, seen in cases of alcoholic hepatitis. These globules are aggregates of intermediate filaments in the cytoplasm which have resulted from hepatocyte injury. Neutrophils can be seen in the sample which is the likely cause of inflammation. These would have been called to the tissue due to the necrosis of the hepatocytes and the presence of cellular debris within the lobules [1]. An infiltration of macrophages can be seen which would also be due to the debris present.

The first stage of alcoholic liver disease is the increase of fatty deposits in the liver. Heavy alcohol consumption causes the production of large fatty globules a process known as macrovesicular steatosis collecting in the liver cells. Ethanol consumed is metabolised by alcohol dehydrogenase in the mitochondria into toxic acetaldehyde which is metabolised by aldehyde dehydrogenase into acetic acid [1][2][3]. The production of acetaldehyde causes a higher NADH: NAD ratio which is the main mechanism in the development of this condition. This NADH production causes increase in lipogenesis and a decrease in fatty acid oxidation. The higher levels of fatty acids signal the hepatocytes to compound glycerol into triglycerides [3]. This is seen in the first stage of liver damage known as alcoholic hepatitis [2].

Excess alcohol intake can also cause hepatocyte injury via oxidative stress from increased NADH production in which free radicals damage the hepatocytes (increased production by the Kupffer cells); and from lipid peroxidation where acetylhyde binds to proteins forming adducts [1]. This binding triggers humoral and cellular immune responses resulting in tissue injury. There is an increase in pro inflammatory cytokines such as tumour necrosis factor and interleukin -6 and a decrease in anti inflammatory cytokines such as interleukin -4 [1]. These cytokines in particular TNF are secreted by the Kupffer cells (macrophages) located in the liver. They're activated by the increased levels of endotoxin released from the breakdown of alcohol by intestinal bacteria; this binds to the CD14 receptor on their surface initiating response. The release of these cytokines leads to the hepatic stellate cells producing increased levels of collagen which leads to liver fibrosis and also causes destructive damage to the hepatocytes. This leads to the last stage of liver disease known as cirrhosis which can occur in prolonged alcoholic hepatitis, seen in 40% of cases [1][4].

Individuals suffering with alcoholic hepatitis have an increase in serum bilirubin due to the inability of the damaged liver to process it. Bilirubin is normally removed from the blood by the liver, processed by it and released into the bile [4][5]. They'll also have prolonged prothrombin time which reflects decreased hepatic synthetic function [4][5]. A number of clotting factor proteins are produced in the liver so an increase in coagulation time suggests a decrease in these factors indicating dysfunction of the liver.

Decreased serum albumin can be observed in cases of liver injury as this is

the main protein produced in the liver. Thyroid tests can indicate liver dysfunction such as testing for T3- triiodothyronine which appears decreased in individuals with alcoholic hepatitis and is proportional to the level of damage[6][4]. There is also a decrease in serum cholesterol level seen in this condition.

In cases where excessive alcohol consumption is not the cause of hepatitis further testing should be done. Individuals can develop hepatitis due to drug use as currently 1000 drugs are seen to be hepatotoxic [7]. There must be a chronic correlation seen between when the medicine was first taken and the observation of hepatitis. There must also be a correlation between the removal of medication and the recession of the condition [4].

Other causes of hepatitis must also be tested for such as viral hepatitis. There are 5 subsets of viral hepatitis A, B, C, and the less common D and E forms. Hepatitis A is the most common form and is passed on by the faecal-oral route. It's tested for by the presence of the anti-HAV IgM antibody which tests positive before the development of clinical hepatitis and remains positive for at least 4 months. Hepatitis B is tested for by the presence of surface antigen HBsAg. Anti HBC total and Anti - HBC IgM is also tested for. A soluble protein HBeAg is produced by the virus in acute and early chronic stages of hepatitis B so positivity of this indicates infection. Hepatitis C infection has the presentation of Anti-HCV seen in 90% of individuals with this infection [7].

The possibility of autoimmune hepatitis can be ruled out by testing of HLA class II expression on the surface of the hepatocytes. There is also an increase seen in IgG antibody and a variety of other antibodies such as SLA/LP (anti soluble liver protein) [8].

References

- [1] Hopkins. J. Alcoholic liver disease – Introduction, gastroenterology and hepatology. Baltimore M. D 2010
- [2] [www. britishlivertrust. org](http://www.britishlivertrust.org) . Accessed 28. 11. 10
- [3] Drriad. Pathogenesis of hepatitis infection from chronic alcoholism, Figure 1. 2007
- [4] [www. hepatitis. org](http://www.hepatitis.org). Phillipe. L, Hepatogastroenterology department, Brugmann University Hospital Brussels Accessed 28. 11. 10
- [5] [http://www. gastro. com/Gastro/liverdisease/liver_function. aspx](http://www.gastro.com/Gastro/liverdisease/liver_function.aspx), Gardner. P. W and Waldstreicher. W, American Liver Foundation 1995 Accessed 28. 11. 10
- [6] Borzio. M et al, Thyroid function tests in chronic liver disease: evidence for multiple abnormalities despite clinical euthyroidism. GUT Journal of gastroenterology and hepatology, Vol 24(7), Jul 1983. [http://www. ncbi. nlm. nih. gov/pmc/articles/PMC1420033/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1420033/). Accessed 28/11/10
- [7] [http://www. oaml. com/PDF/CLP012. pdf](http://www.oaml.com/PDF/CLP012.pdf). Guidelines for clinical laboratory practice, revised March 2000, Accessed 28. 11. 10

[8]Krawitt. E. L Autoimmune hepatitis: classification, heterogeneity, and treatment, January 1994. Am. J. Med. Vol 96 (1A): 23S-26S.