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Case Report

A Rare Case of Malnutrition Hepatitis in a Patient with Anorexia Nervosa

Mumtaz O. Sanni*

Specialty Registrar, Gastroenterology, Lincoln County Hospital, United Kingdom.

***Corresponding Author:** Mumtaz O. Sanni, Specialty Registrar, Gastroenterology, Lincoln County Hospital, United Kingdom.*

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Abstract

Anorexia nervosa (AN) is a common eating disorder, particularly in women, with a lifetime prevalence estimated to be 0.3– 0.9%. This disorder is associated with numerous medical complications (cardiovascular, endocrine disorders, electrolyte and hematopoietic abnormalities, amenorrhea, and osteoporosis), among which changes in liver tests are frequent. Malnutrition-induced hepatitis is common among individuals with AN especially as body mass index decreases. The exact mechanism of liver damage has not been identified; however, some have hypothesized autophagy (programmed cell death) as a possible cause of hepatocyte damage. Starvation causes hepatocyte injury and death leading to a rise in aminotransferases. While the hepatitis of AN can reach severe levels, a supervised increase in caloric intake and a return to a healthy body weight often quickly lead to normalization of elevated aminotransferases caused by starvation. We report here, the case of a 58 year old lady with a background of anorexia nervosa who developed severe acute liver failure with histological evidence of starvation hepatitis while on admission for a right hip osteomyelitis, which was slowly reversed after careful and gradual nutritional replacement.

Keywords: *Anorexia nervosa (AN); Malnutrition Hepatitis; Chronic Starvation*

Introduction

Anorexia nervosa is an eating disorder that results in an individual's excessive restriction of food intake. According to the current edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), diagnostic criteria include

1. Intense fear of gaining weight: These individuals have a morbid fear of becoming "fat". The fear manifests itself through depriving the body of food.
2. Food intake restrictions: These individuals tend to eat less than the body needs to function optimally, leading to significantly low BMI.
3. Distorted body image: This has to do with the individual's perception of his/her body size. They have an over exaggerated image of themselves and think they are overweight even if they are dangerously underweight.

There are two subtypes of anorexia: the restricting type and the binge-eating/purging type.

People with the restricting subtype place severe restrictions on the amount and type of food they eat. Restrictive behaviors include counting calories, skipping meals, or eliminating certain foods (such as carbohydrates). These behaviors are sometimes coupled with excessive exercise.

Those with the binge-eating and/or purging subtype also restrict their food intake. In addition, they also regularly engage in binge eating or purging behaviors, such as self-induced vomiting or misuse of laxatives or diuretics, or both binge eating and purging. Anorexia nervosa has the highest mortality rate of all psychiatric illnesses due to the widespread organ dysfunction caused by the underlying severe malnutrition

There has been a documented relationship between patients with anorexia nervosa and severe hepatic injury. A mild increase in serum aminotransferase levels is indeed observed in up to 60% of these patients[1] leading the American Psychiatric Association to recommend a systematic assessment of liver tests for these patients[1]. Studies have shown an inverse relationship between body mass index (BMI) and liver enzymes such as aminotransferases. However, severe liver damage with a significant decrease in coagulation factors and encephalopathy appears to be uncommon in patients with anorexia nervosa, although some cases have been reported[1]. There could also be a significant increase in liver enzymes as part of the refeeding process due to hepatic steatosis and this could be distinguished from starvation hepatitis by ultrasound findings of a fatty liver which were hitherto not present in previous liver scans.

We present a case of a lady who developed severe derangements in her liver function test (LFT) and histological evidence of starvation induced hepatitis on a background of anorexia nervosa.

Case Presentation

A 58 year old lady, known to the specialist eating disorder services and psychiatric team with a history of anorexia nervosa diagnosed in 2007, admitted with abdominal pain, vomiting, right hip pain and swelling Other preexisting medical conditions included pelvic congestion syndrome, osteoporosis, previous deep venous thrombosis (DVT), lumbar disc herniation, bone necrosis, corneal oedema, keratitis. Her regular medications included mirtazapine, olanzapine, rivaroxaban and lactulose. She was not a smoker nor did she drink alcohol. Her only allergy was to sertraline.

On admission her weight was 50.45kg, height 1.78m, body mass index (BMI) 17, pulse was 54bpm, temperature 36.7 Celsius, blood pressure 111/72mmHg, saturations 100% on air, respiratory rate 18 breaths per minute.

On physical examination, she was overtly underweight and cachectic, not jaundiced, tenderness in the right hip with fluid collection in the lower abdomen. Her liver was not enlarged.

Table 1: Blood results on admission.

Blood test on admission	Result	Reference range
Sodium (mmol/L)	131	133-146
Potassium (mmol/L)	2.8	3.5-5.3
Creatinine (mmol/L)	43	45-84
Urea (mmol/L)	4.2	2.5-7.8
eGFR (mL/min)	>90	
Glucose (mmol/L)	4.7	4-7
Magnesium (mmol/L)	0.79	0.70-1.00
Phosphate (mmol/L)	0.91	0.80-0.15
Bilirubin (umol/L)	7	0-21
Aspartate aminotransferase (AST) (U/L)	-	0-32
Alanine aminotransferase (ALT) (U/L)	44	0-33
Alkaline phosphatase (ALP) (U/L)	140	30-130
Gamma-glutamyltransferase (GGT) (U/L)	41	6-42
Calcium (mmol/L)	2.26	2.2-2.6
Adjusted Calcium (mmol/L)	2.43	2.20-2.60
Albumin (g/L)	28	35-50

International Normalised Ratio (INR)	1.2	0.9-1.1
Prothrombin Time (PT)	13.6	10.4-12.4
Activated Partial Thromboplastin Time (APTT)	33.2	26.9-34.5
C-reactive protein (mg/L)	123	0-5
Hemoglobin (g/L)	86	117-149
Mean Corpuscular Volume (MCV) (FL)	85	81-97
Mean Corpuscular Haemoglobin (MCH) (pg)	29.1	26.9-33.3
Mean Corpuscular Haemoglobin Concentration. (MCHC) (g/L)	344	320-359
White cell count (10^9/L)	5.7	4.3-11.2
Platelet count (10^9/L)	299	150-400
Neutrophils (10^9/L)	4.53	2.1-7.4
Lymphocytes (10^9/L)	0.83	1.0-3.6

A computed tomography scan of the abdomen and pelvis revealed features indicative of chronic osteomyelitis in the right pubic region with fluid collection extending from the right groin to the right symphysis pubis with further extension into the right lower anterior abdominal wall.

Magnetic resonance image of the pelvis confirmed erosion/destruction of symphysis and right superior and inferior rami-osteomyelitis, with abscess in the right adductor muscular plane and in the right lower anterior abdominal wall-likely abscesses.

She was admitted under the orthopaedic team and commenced on intravenous coamoxiclav and also had an ultrasound guided abdominal wall drain insertion done by the interventional radiographers and abscess was drained 9 days into admission. All the while on admission, her oral intake was very poor despite intervention by the nutrition team and the mental health team. Sometimes she went days without eating. She also routinely engaged in physical activities almost every hour and did two laps round the hospital frequently. This was due to her having compulsive thoughts to exercise.

Along with a graded and structured feeding plan, the dieticians encouraged her to minimize physical activity and recommended bed rest as she was at risk of having a cardiac arrest if she kept on exercising. Nasogastric feeding was also offered which she declined, but she agreed to a well spaced feeding regimen with oral supplements after much persuasion. All the while she had full capacity and was aware of risks of not eating and drinking.

On day 9 of admission routine bloods showed infection markers were almost back to normal with WBC in single digits but there was a significant elevation in LFTs especially the transaminases which were in the high thousands, but bilirubin remained normal. Due to the deranged LFTs, coamoxiclav was changed to Tiecoplanin after a discussion with the microbiologist. Her weight had also dropped to 39.3kg and BMI had dropped to 12.4. The LFT rise continued in significant fashion over the next 1 week before it gradually began to improve, but was still in the thousands. She was referred to the gastroenterology team about 2 weeks into the acute severe LFT derangement and an autoimmune liver screen, viral liver screen and a magnetic resonance cholangiopancreatography were requested. All these tests came back as normal. She was subsequently transferred to the gastroenterology ward.

On the gastroenterology ward, she still continued to refuse food. A multidisciplinary team meeting involving the dieticians, psychiatrists, gastroenterologist, and ward nurses was held and it was agreed that she would be managed under the mental health act section 3 after mental health assessment, which will enable restraint and also facilitate nasogastric tube placement and feeding as required.

On Day 18 of admission, she was detained in the hospital under section 3 of the mental health act (MHA), and a nasogastric tube was inserted for a structured feeding plan as recommended by the dieticians with daily refeeding bloods, while the gastroenterology team further continued to investigate and manage deranged LFTs and while still on antibiotics. She was also placed on strict bed rest.

On day 19, she was found to barely responsive in acute severe hypoglycaemia and she had to be urgently resuscitated with intravenous glucose. Over the next 10 days (up to day 28), she kept having episodes of early morning hypoglycaemia and her enteral feeds had to be adjusted severally to manage this. Eventually her blood glucose levels normalized.

Table 2: Blood glucose readings showing persistent hypoglycaemia on admission.

Days	19	20	21	22	23	23	25	26	27	28	29	30
Blood Glucose (mmol/L)	3.1	5.2	3.8	2.7	2.5	3.4	3.1	2.7	3.9	2.6	7.1	5.0

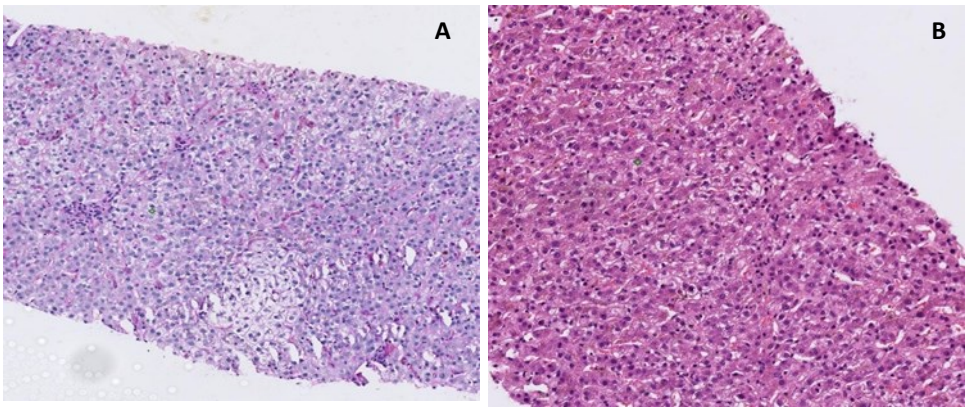
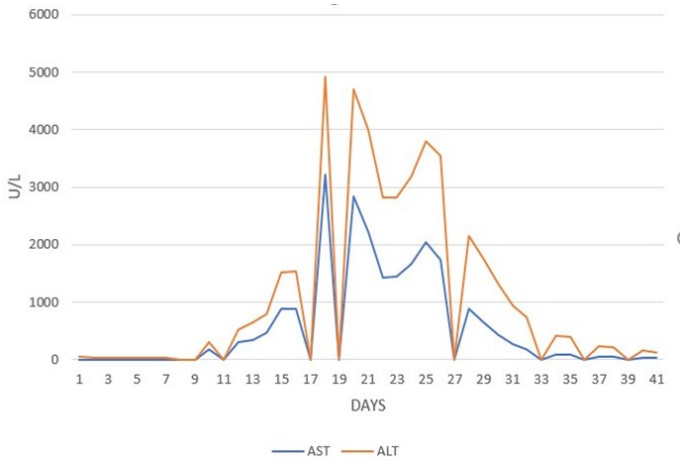
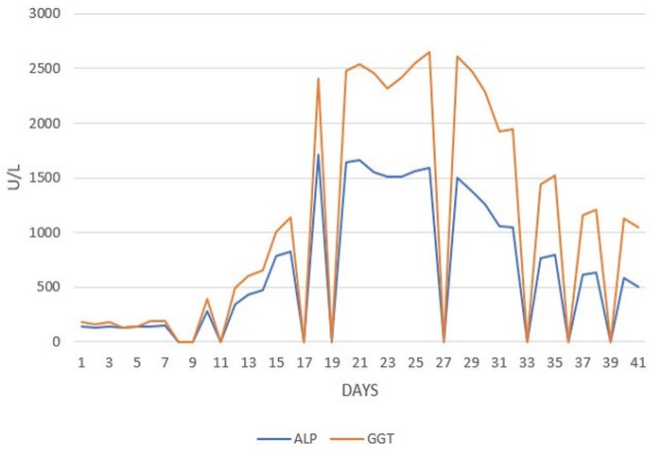


Figure 1. *Histology a & b. H&E and PAS stains showing hepatocyte pallor and mild lobular inflammation.*

She was more cooperative while under section 3 of the MHA and her feeds were more regular. LFTs improved, episodes of hypoglycaemia became less frequent and gradually her LFTs (especially her transaminases returned to normal levels. She was subsequently discharged from the gastroenterology ward for further follow up by the mental health and eating disorder units, and to have her LFTs monitored to ensure further resolution of cholestatic LFTs which takes longer than the transaminases.



Graph 1: *Trend of transaminases.*



Graph 2: *Trend of cholestatic LFTs.*

Discussion

We have presented a case of a female who is known to have anorexia nervosa, who was admitted and managed for osteomyelitis, but developed malnutrition hepatitis while on admission due to very poor oral intake and rapidly worsening BMI. This lady, despite being aware of her worsening clinical state due to her poor nutrition, initially remained largely uncooperative with most of the plans instituted by the gastroenterology, nutrition and mental health team. She had to be eventually sectioned under the mental health act so she could be adequately managed and fed enterally till LFTs normalized.

Elevations in aminotransferases, specifically aspartate aminotransferases (AST) and alanine aminotransferase (ALT), are the most common laboratory abnormalities seen in patients with liver dysfunction due to AN[4]. Over 50% of patients with AN develop mild liver injury with abnormally increased AST and ALT due to starvation[4]. AST and ALT elevations are generally mild to moderate with values in the hundreds U/L but can rise to markedly elevated levels in the thousand's U/L, particularly as body weight decreases, just as seen in this patient. A median peak value of ALT of 56 times of normal has been reported in a recent case series[1]. Furthermore, just as seen in this patient, ALT characteristically tends to be elevated disproportionately more than AST in AN, similar to non-alcoholic liver disease and in contrast to other common forms of liver disease such as that due to alcohol. However, from day 18 when this patient was sectioned and more compliant with NG feeds, a downward trend in transaminases was observed. Interestingly, these biochemical signs of acute liver injury are devoid of corresponding liver cell necrosis, which we would expect with such an elevation in liver enzymes[5]. Cholestatic LFTS were also severely deranged and though improvements in them were also observed, it was not as rapid as those of the transaminases and though they remained deranged till discharge, the downward trend is expected to continue.

As BMI falls to values near 12 kg/m2 or less, the risk of marked elevations of aminotransferases increases[4]. In this patient, BMI went to as low as 12.4Kg/m^2 and expectedly, LFT derangements worsened. In one study, patients with AN admitted to a medical stabilization unit for eating disorders at less than 50% of their ideal body weight (IBW) had 12 times the risk of having severely elevated liver enzymes, defined as greater than three times the upper limit of normal, compared to those patients at 70% of their IBW[4]. In this study of 181 total patients, the average BMI was 12.8 kg/m2. Over 35% of the patients had severely elevated AST or ALT levels, thereby substantiating the fact that more severe elevations in liver enzymes are common in individuals in individuals with more severe degrees of malnutrition from AN.

This patient also had repeated episodes of hypoglycaemia requiring frequent modifications to her feeding regimen. Hypoglycaemia is recognized as potentially one of the most fatal conditions that may arise in AN as hepatic failure worsens and transaminases rise[4]. Hypoglycemia is associated with a poor prognosis in AN[6] with depleted liver glycogen stores and impaired gluconeogenesis as the proposed mechanisms for hypoglycemia[7]. Hepatic biopsies done on 12 patients in a 2008 study with a BMI < 13 kg/m^2 showed significant glycogenic depletion along with numerous autophagosomes involved in autophagy[2]. A recent study has suggested an almost five times increased risk of hypoglycemia in AN, independent of body weight, when aminotransferases are severely elevated to levels greater than three times the upper limit of laboratory normal values. This patient at some point had transaminases greater than 30 times the upper limit of normal, and this was most likely the reason for her recurrent severe hypoglycaemic episodes. Increases in bilirubin and alkaline phosphatase, however, are much less common and have been sited in one study to occur in less than 15% of patients with AN[4]. This is likely due to the underlying pathophysiology of the liver injury in AN. In this patient however, though bilirubin was largely normal throughout admission, ALP was severely deranged, with accompanying derangement in GGT, with these cholestatic liver enzymes also improving as transaminases also improved.

Conclusion

Chronic starvation or malnutrition has been established as a cause of hepatitis, with severe derangements in transaminases, profound glycogen depletion and histological evidence of hepatocyte autophagy. The severity of LFT derangement is inversely proportional to body weight and this almost always reversible with improved nutrition. While the treatment might appear straight forward, the management as seen in this case could be quite complicated depending on the underlying circumstances.

Conflicts of Interest

The author has not provided a conflict of interest declaration.

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