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Acute oligo-anuric renal failure during the course of non-fulminant hepatitis A in a patient with anorexia nervosa

Anoreksiya nervosalı bir hastada non-fulminan hepatit A seyrinde gelişen akut oligoanürik böbrek yetmezliği

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Acute renal failure is a very rare complication seen during the course of non- fulminant hepatitis A. Several mechanisms have been postulated in the pathogenesis of renal failure. Firstly, there is insufficiency of renal blood flow due to developing endotoxemia or cryoglobulinemia, secondly mesangial proliferative glomerulonephritis or interstitial nephritis occurs due to immune complexes and finally there is acute tubular necrosis caused by the direct cytopathic effect of the virus or due to immune complexes.

The following case report describes a 17 year old male patient admitted with complaints of appetite loss and severe weight loss due to anorexia nervosa. During the second week of admission, he developed hepatitis A infection which was complicated by acute renal failure requiring hemodialysis therapy. Hepatorenal parameters returned to normal values by the fifth week of admission in this case of biopsy proven acute tubular necrosis.

In this case, the possible negative effects of malnutrition on the liver and kidneys were not observed. The present authors emphasize that during the course of non- fulminant hepatitis A, renal functions should be closely monitored and renal biopsy should be performed if acute renal failure occurs.

Key words: Hepatitis A , acute renal failure , anorexia nervosa

Akut böbrek yetersizliği, non-fulminant hepatit A seyrinde çok seyrek rastlanan bir komplikasyondur. Böbrek yetmezliğinin oluşumunda birkaç patogenetik mekanizma ileri sürülmektedir. Bunlar arasında; birinci olarak endotoksemi veya kriyoglobulinemiye bağlı renal kan akımındaki yetersizlik, ikinci olarak immün komplekslere bağlı mezangiyal proliferatif glomerulonefrit veya interstisyel nefrit gelişimi ve son olarak da virüsün yada immün komplekslerin doğrudan sitopatik etkilerine bağlı akut tübüler nekroz gelişmesi sayılabilir.

Burada, anoreksiya nervosa'ya bağlı iştahsızlık ve ileri derecede kilo kaybı ile başvurup, yatışının 2. haftasında akut nonfulminan hepatit A infeksiyonu gelişen 17 yaşında bir erkek hasta sunulmaktadır. Hepatit A infeksiyonu seyrine paralel olarak hastada, oligoanürik tipte akut böbrek yetersizliği gelişti ve hemodializ tedavisi gerektirdi. Yapılan renal biyopside, akut tübüler nekroz bulguları saptanan hastanın, yatışının 5. haftasında hepatorenal biyokimyasal parametreleri tümüyle normale döndü.

Anoreksiya nervosa'ya bağlı malnütrisyonun karaciğer ve böbrek üzerinde olası olumsuz etkilerinin gözlenmediği bu olgu sunumuyla, non-fulminan hepatit A seyrinde renal fonksiyonların yakından izlenmesinin gerektiği ve akut böbrek yetersizliği gelişirse, böbrek biyopsisinin yapılabileceği vurgulanmaktadır.

Anahtar kelimeler: Hepatit A, akut böbrek yetmezliği, anoreksia nervosa.

INTRODUCTION

Acute renal failure due to the development of hepatorenal syndrome is a very well known complication of acute fulminant viral hepatitis. However, it rarely develops during the course of non-fulminant hepatitis A (1,2).

In contrast to fulminant hepatitis A, hepatocellular reserve is mildly disturbed in these cases and acute oliguric or non oliguric renal failure develops by mechanisms other than those causing the so called functional hepatorenal syndrome.

In this report, a patient with anorexia nervosa who developed acute oligo-anuric renal failure requiring hemodialysis therapy during the course of acute viral hepatitis A is presented.

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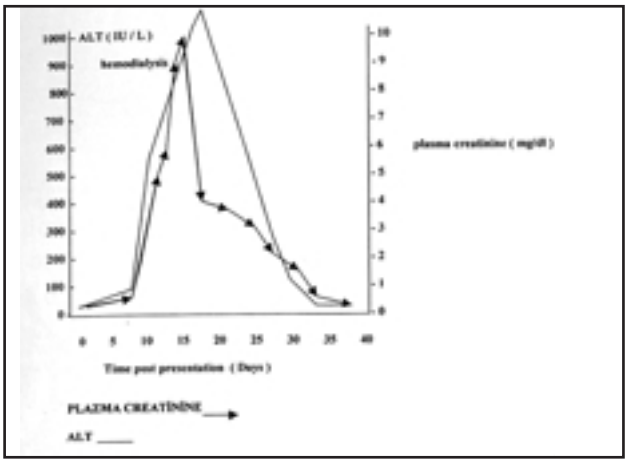

Figure 1. Temporal relationship between improvement in liver and renal function.

CASE PRESENTATION

A 17 year old male patient was admitted with a five month history of appetite loss and severe weight loss (15 kg/ 5 months) and malaise. He had not used any nephrotoxic or hepatotoxic medications or any other toxic substance either before or during his present complaints.

On physical examination, he appeared ill and cachectic (body mass index : 15.5 kg/m^2). He was conscious and cooperative. There was no edema, jaundice or cyanosis. Initial examination findings were as follows: blood pressure: 100/50 mmHg, heart rate: 80/min., respiratory rate: 14/min., body temperature 36.5 °C. He had no hepatosplenomegaly and showed no peripheral signs of chronic liver disease. There was no lymphoadenopathy and his subcutaneous fatty tissue, skin turgor and muscle tone were significantly decreased. There was no other pathological finding on physical examination of other body systems including the urogenital system.

Initial laboratory findings disclosed the following values: Hb: 12.7 g/dl, Hct: 37.3% WBC: 6700 /mm^3, Plt: 215000/mm^3. There was hyponatremia, hypopotasemia or hypochloridemia (133 mEq/ l, 2.7 mEq/ l, 82 mEq/l respectively). Urinanalysis demonstrated no glucose, protein or myoglobin in the urine. In microscopy, there were 3-4 erythrocytes per high power field. Urinary Na was 47 mEq/ l. ESR, glucose, urea, creatinine, uric acid, Ca, P, transaminases, bilirubin, GGT, ALP, LDH, CPK, prothrombin time and activity, aPTT, free T3, free T4, TSH and tumor markers were all within normal limits. The initial imaging studies were found to be normal (teleradiography, abdominal ultrasonography (USG) and abdominal computed tomography (CT)).

In the first seven days of admission, fluid and electrolyte replacement therapy resulted in blood pressure and volume status returning to normal limits. Meanwhile, a differential diagnosis was made among malignancy, metabolic causes, chronic infection and finally anorexia nervosa.

After psychiatric evaluation of the patient, a diagnosis of anorexia nervosa was made even though this disorder is rarely seen in men.

On the ninth day of admission, BUN, creatinine, AST and ALT values started to increase while the patient was receiving only supportive vitamin, fluid and electrolyte therapy but no psychotropic drug therapy related with his diagnosis (Figure 1). There was a mild prolongation of prothrombin time. Oliguria, which did not respond to diuretic therapy turned to anuria in one-two days and there was an increase in the following : BUN 80 mg/dl, creatinine: 10.57 mg/dl, AST: 534 IU/L, ALT: 1241 IU/L, LDH: 392 IU/L, total bilirubin: 2.05 mg/dl. Serological markers were as follows: HBsAg (-), anti HBc IgM and anti HBc IgG (-), anti HCV (-), anti Leptospira IgM (-), EBV, HSV; CMV was were found to be negative. Anti HAV IgM was positive. There was no growth in urine and blood cultures.

Abdominal USG was performed: liver length was 157 mm, parenchymal echogenity was increased and intrahepatic bile ducts were found to be normal. Spleen length was 138 mm. Both kidneys were of normal size. Parenchymal echogenity was increased and there was no sign of urinary obstruction. Renal biopsy showed focal tubular necrosis and there was also a mild diffuse increase in mesangial matrix and cell component. IgM deposits were not demonstrated in immunohistochemical analysis (Figure 2,3).

On the 14 th day of admission, hemodialysis was performed for the first time (BUN was 80 mg/dl and creatinine 10.57 mg/dl). After a total of three hemodialysis sessions, diuresis started and BUN and creatinine levels decreased. AST and ALT values improved parallel to the correction of the patient's renal functions.

The patient was discharged on the 37 th day, and

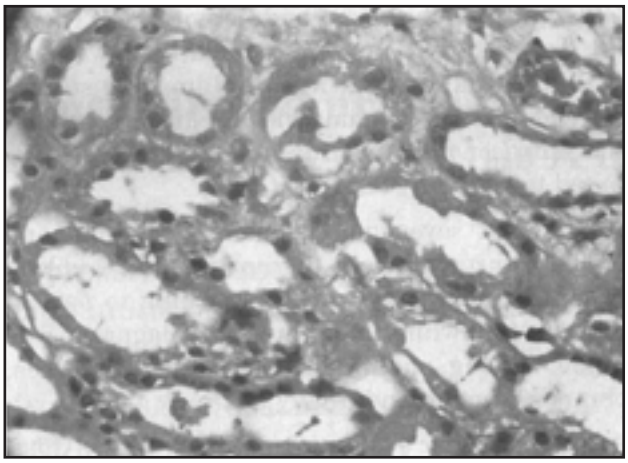

Figure 2. Photomicrograph of patient 's kidney. (H&E x 200) Degenerative changes of tubular epithelium and necrosis of proximal tubulus.

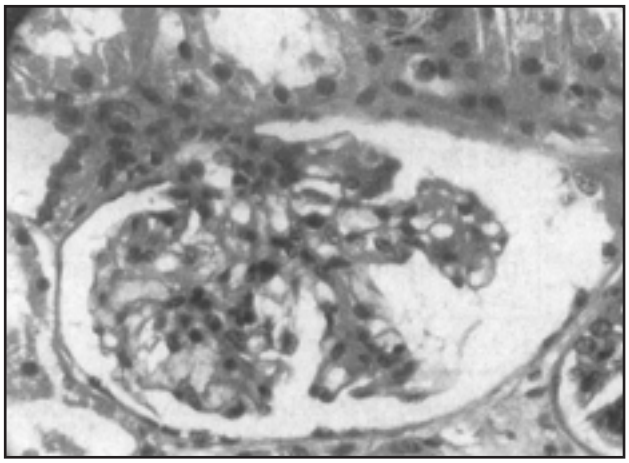

Figure 3. (H&E x 200). Mildly diffuse increase in mesangial matrix and cell.

his general condition was satisfactory with hepatorenal parameters within normal ranges. (BUN: 17 mg/dl, creatinine: 0.93 mg/dl, AST: 27 IU/L, ALT: 45 IU/L)

DISCUSSION

In the literature, various mechanisms have been suggested in the pathogenesis of acute renal failure seen during the course of the non- fulminant hepatitis A. Cryoglobulinemia or dysfunction of reticuloendothelial system is said to result in endotoxemia which causes defects in renal blood flow (3). However, it has not been qualitatively or quantitatively researched whether or not endotoxemia occurs during mild cases of acute hepatitis A (4). Secondly it has been emphasized that the development of mesangial proliferative glomerulonephritis or interstitial nephritis due to the precipitation of circulating immune complexes causes acute renal failure (5,6). In the literature, acute tubular necrosis is the most common histopathologic finding among cases in which renal biopsies are performed and a third mechanism is suggested to be the development of acute tubular necrosis due to the possible direct cytopathic effect of the virus on the tubular cells or indirectly by immune complexes. It has also been suggested that hyperbilirubinemia, hyperuricemia and drugs can increase this damage (3,7). Increase in serum levels of bilirubin and bile acids are known to cause renal hypoperfusion by a decrease in total peripheral resistance and left ventricle dysfunction (8) which can increase sensitivity to ischemic damage in renal tissues (9).

The presence of hypovolemia for any reason during the course of acute hepatitis A can be a sole cause of renal failure and can also be the contributing factor in the previously mentioned mechanisms.

In the present case, there was a borderline hypotension and hypovolemia. Normovolemic and normotensive status was achieved by aggressive fluid and electrolyte replacement in the days before renal failure developed. Urinary Na value was greater than 10 mEq/l prior to the development of renal failure. This finding suggests that initial hypovolemia was not a contributing factor in the renal failure developing later on during the course of acute hepatitis A.

In renal biopsy, there were findings of focal tubular necrosis but immune deposits could not be demonstrated. This clearly shows that acute tubular necrosis is responsible for the development of acute renal failure. The mild diffuse increase in mesangial matrix and cells was a coincidental finding and it was not a component of tubular necrosis. This lesion may be evaluated to be a result of likely immunopathological processes in the past.

Significiant increases in bilirubin levels are seen in most cases reported in the literature and this increase is markedly higher in patients requiring hemodialysis than those who do not (4). However,

bilirubin values were not over 3 mg/dl in either the few reported cases or ours (10-12). Thus we can suggest that the minimal bilirubin increase in our case could not have had an effect on the progression of tubular necrosis. However, it can still be speculated that the hypovolemia present before the development of hepatitis A and also the severe loss of appetite and weight (which was confirmed to be due to anorexia nervosa at psychiatric evaluation and not to any organic cause) may have created a predisposition to development of acute renal failure, even though this was not supported by the urine Na levels. In such patients, we suggest that renal functions should be closely monitored and that if acute renal failure occurs, renal biopsy should be performed for the differential diagnosis.

There were no clinical, biochemical or radiological findings indicative of possible liver and kidney damage due to severe malnutrition.

In the literature, cases of acute renal failure due to rhabdomyolisis induced by severe hypophosphotemia during the course of anorexia nervosa have been reported (13,14). However, in the present case, due to the normal blood phosphate and CPK levels and absence of myoglobinuria, this possibility was excluded. When the relationship between anorexia nervosa and the immune system is considered, it is likely that the course of hepatitis A, which is a viral infection, can also be affected. Although a marked predisposition to infections is surprisingly not seen in anorexia nervosa, high cortisole levels and significiant decreases in leucocyte counts, especially in CD2 and CD4 lymphocytes, have been found (15). However, the non-fulminant course of hepatitis A infection in our case does not make such an interaction possible.

In conclusion, renal functions should be closely observed during the course of hepatitis A infection and renal biopsy should be performed if acute renal failure occurs, in order to contribute to the understanding of the pathogenesis of acute renal failure, about which there remain many unknown factors.

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