A CASE OF LEPTOSPIROSIS PRESENTING WITH NEPHROTIC SYNDROME, ACUTE RENAL FAILURE AND THROMBOCYTOPENIA

NEFROTİK SENDROM, AKUT BÖBREK YETERSİZLİĞİ VE TROMBOSİTOPENİ İLE PREZENTE OLAN BİR LEPTOSPIROZ OLGUSU

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ABSTRACT

Leptospirosis is a disease caused by the spirochete of the group Leptospirae. Its clinical presentations are mostly subtle. We present a case of leptospirosis presenting with nephrotic syndrome, acute renal failure (ARF) and thrombocytopenia.

A 50-year-old male patient was admitted for abdominal pain and swelling. He had painful fingers, elbows, knees and the fever five days ago. However, arthralgia and fever regressed with ampicillin treatment. On the admission physical examination, edema, hypotension, bilateral pleural effusion and ascites were present. The characteristics of the ascites was compatible with the nephrotic syndrome. Abnormal laboratory findings were; thrombocyte: 35000/mm³, proteinuria: 9 g/day, serum albumin: 2.4 g/dL, CPK: 1526 U/L, AST: 134 U/L, ALT: 58 U/L. Intra sedimintinde bol dismorfik eritrosit görüldü. Ertesi gün trombosit sayısı 24000/mm³ oldu. İdrar miktarı giderek azaldı ve 4. günde kreatinin düzeyi 6.2 mg/dL oldu. Hepatit belirteçleri negatifti. İzlemi boyunca ateş ve sağlik görülmendi. Orta derecede AST, ALT yüksekliği, yüksek CPK, trombositopeni ve ABY ile komplike olan nefrotik sendrom olması nedenile leptospiroz düşünüldü. Doksisiklin 2x100 mg/gün ve seftriakson 1x2 g/gün başlandı. Tedavinin 3. gününde diürezi 6 L/gün'e kadar yükseldi. Trombosit, CPK ve serum kreatinin düzeyleri sırasıyla tedavinin 3., 5. ve 6. günlerinde normale döndü. Proteinüri giderek azaldı ve 15. günde tamamen kayboldu. Anti-mikrobiyal tedaviye 20 gün devam edildi. Bu arada ELISA ile çok yüksek leptospira IgM ve orta derecede yüksek leptospira IgG saptandı.

Sonuç olarak, her ne kadar leptosomal nefropatide temel lezyon tubulointerstisyal nefrit ise de nadiren ABY ile komplike olmuş nefrotik sendrom ile de prezente olabilir. Hipotansiyon, trombositopeni ve CPK artışını tanıyan destekleyici sonuçlardır. Genellikle, nefrotik sendrom ve ABY diyализe gerek kalmadan uygun antimikrobiyal tedavi ile iyileşir.

Anahtar kelimeler: Leptospiroz, nefrotik sendrom, trombositopeni.
Nephrotic syndrome, ARF and thrombocytopenia in leptospirosis

L/day on the 3rd day of treatment. Thrombocyte, CPK, and serum creatinine levels returned to normal on 3rd, 5th and 6th days of the treatment, respectively. Proteinuria gradually decreased and totally disappeared on the 15th day. Antimicrobial therapy was continued for 20 days. Meanwhile a very high titer of leptospira IgM and a mild increase in the titer of leptospira IgG was observed in the ELISA test for leptospira antibodies. In conclusion, while the principal lesion of leptospiral nephropathy is tubulointerstitial nephritis, it may rarely present as nephrotic syndrome complicated with acute renal failure. Hypotension, thrombocytopenia, and elevated CPK were the pointers for the correct diagnosis. Nephrotic syndrome and ARF improved with the appropriate antimicrobial therapy without need for dialysis.

Key words: Leptospirosis, nephrotic syndrome, thrombocytopenia.

INTRODUCTION

Leptospirosis is an infection caused by pathogenic leptospires. Traditionally, the genus Leptospira comprised two species: the pathogenic L. interrogans and the free-living L. biflexa. Although seven species of pathogenic leptospires are now recognized on the basis of their DNA relatedness, it is more practical clinically and epidemiologically to use a classification based on serologic differences. The pathogenic leptospires are divided into serovars according to their antigenic composition. It is a frequently encountered disease which is transmitted from animals to humans and generally can not be diagnosed. It can be seen endemically in tropical and warm climates. Clinical characteristics vary from a mild flu-like illness to a disease of acute and life threatening features. It is characterized by signs and symptoms such as: fever, icterus, nausea, vomiting, abdominal pain, headache, myalgia, oliguria, respiratory and circulatory failure, hemorrhagic diathesis, rhabdomyolysis, and pancreatitis (9). In this case report, a leptospirosis case presenting with nephrotic syndrome, ARF and thrombocytopenia was presented.

CASE

A 50-year-old male was admitted to hospital for abdominal pain and swelling. Onset of the disease was with pain in both of his interphalangeal joints, elbows, and knees. He had been treated with metamizol sodium and lincomycin for two days without any improvement. Five days prior to admission, fever increasing to 40°C, bloodless mucoid defecation with inguinal and perianal pain, headache, myalgia, oliguria, respiratory and circulatory failure, hemorrhagic diathesis, rhabdomyolysis, and pancreatitis was suspected. Because of the patient’s poor overall health, a nephrotic syndrome, hypotension, thrombocytopenia, and high levels of AST, ALT, CPK on admission, and an oliguric ARF development within 4 days of follow up, leptospirosis was suspected. Due to nephrotic syndrome, ARF, and thrombocytopenia, disseminated intravascular coagulation secondary to infection was suspected. However, due to absence of fragmented erythrocytes on blood smears, normal fibrinogen level (405 mg/dL), and normal coagulation tests ruled this diagnosis out. Urine output decreased to 300 mL/day in spite of adequate hydration and diuretic and serum creatinine level increased to 6.2 mg/dL on the 4th day. Serum calcium and phosphore levels were 6.5 mg/dL and 6.0 mg/dL, respectively. Acute renal failure was diagnosed. However, due to development of oliguria and creatinine increase in spite of hydration of the patient with hypoalbuminemia, renal vein thrombosis was also thought in the differential diagnosis but renal vein doppler ultrasound was normal.

Diagnostic and therapeutic paracentesis was done upon aggravation of abdominal pain, ascites, and leukocytosis. Levels of albumin, LDH, and leukocyte in the ascitic fluid were 1.6 g/dL, 346 U/L, 400/mL, respectively. Serum-ascitic fluid albumin difference was lower than 1.1. Ascites was compatible with nephrotic syndrome.

Fecal analysis for colonic diarrhea was normal. C. difficile toxin was A+B negative. Abdominal ultrasound and CT were normal. Kidney sizes were within normal ranges. Due to nephrotic syndrome, hypotension, thrombocytopenia, and high levels of AST, ALT, CPK on admission, and an oliguric ARF development within 4 days of follow up, leptospirosis was suspected. Because of the patient’s poor overall health, a
treatment of 2x100 mg doxycycline and 1x2 g ceftriaxone was started without waiting serological examination results. Clinical and laboratory results rapidly improved without a need for the dialysis. Three days later, urine output was elevated to 6 L/d. At the 3rd day of treatment, sodium and thrombocyte levels were 139 mmol/L and 165,000/mm³, respectively; CPK was 160 U/L on the 5th day; creatinine, AST, and ALT were 1.4 mg/dL, 34 U/L, 46 U/L, respectively, on the 6th day; Ca was 7.6 mg/dL and P was 2.6 mg/dL on the 12th day; and albumin was 3.2 g/dL on the 15th day. Proteinuria gradually decreased and disappeared. Leptospira IgM antibody and IgG antibody were both positive by ELISA. Treatment continued for 20 days.

DISCUSSION

Leptospirosis is a spirochete disease. It is the most common zoonosis in domestic or wild animals. Animals excrete infected urine in soil or water and may cause human infections through abraded wound, mucosa, conjunctiva, or by drinking contaminated water. Leptospirosis is mostly asymptomatic (15). But sometimes, it can present with fever, headache, abdominal pain, myalgia, icterus, hemorrhagic diathesis, hypotension and clouding of consciousness (3). Moreover, circulatory failure, rhabdomyolysis, and pancreatitis may also be seen. Five factors are described to be associated with mortality: respiratory failure, hemoptysis, oliguria, metabolic acidosis, and tubulointerstitial nephritis (11). Renal failure has been reported to be a cause of death for 1/3 of all cases.

On admission, our patient had nephrotic syndrome, hypotension, hyponatremia, thrombocytopenia, and had high levels of AST, ALT, CPK. Jaundice or fever were not observed during the follow-up period. Clinical symptoms in leptospiral nephropathy can vary from urine sediment changes to ARF. Renal failure has been reported to occur in 44-67% of the symptomatic cases (8). Clinically, non-oliguric acute renal failure, hypokalemia and sodium wasting appear frequently in leptospirosis. Causes of acute renal failure are hemodynamic changes, immune response, and probably direct nephrotoxicity. The outer membrane protein from leptospira has been thought to be responsible for renal dysfunction. However, the exact mechanisms of renal involvement are still unclear (14).

The kidneys are invariably involved in leptospirosis. Related findings range from urinary sediment changes (leukocytes, erythrocytes and hyaline or granular casts) and mild proteinuria in anicteric leptospirosis to renal failure and azotemia in severe disease (9). Leptospiral ARF may be oliguric or nonoliguric (1). Principal lesion is tubulointerstitial nephritis. In most of the cases, only proximal tubules are affected. Proximal (type I) renal tubular acidosis and tubular necrosis may be seen (15). Hyponatremia and hypokalemia associated with renal tubular dysfunction, are commonly observed (4, 8). Vasculitis may be observed during the acute phase of the disease. However, glomerular changes are rare (8). Hematuria and mild proteinuria have been rarely reported (3). Our case presented with nephrotic syndrome, hypotension, and hyponatremia and 4 days later oliguric ARF developed. Acute renal failure regressed without need for dialysis therapy, only by antimicrobial treatment on 6th day. But, nephrotic syndrome was regressed on 15th day. Leptospirosis can be diagnosed by serology or by isolating the organism from the patient (9). Serologic method used is mostly ELISA, microscopic agglutination test or PCR (15). In the present study, serological diagnosis was accomplished by ELISA.

Acute renal failure is an adverse prognostic factor in leptospirosis. It is generally associated with cholestasis icterus (12). However, in our patient jaundice was not present. Severe hypotension is the most important sign of renal and pulmonary complications (3, 6, 8) and our patient had hypotension on admission. However, with the development of renal failure, blood pressure gradually increased. The pulmonary complications observed in leptospirosis are as follows: pulmonary hemorrhage, pulmonary edema, interstitial pneumonia, and ARDS. However, no pulmonary complication was observed in our patient. The myalgia and high level of CPK seen on admission, regressed by the 5th day of the treatment.

In severe cases of leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin or erythromycin is recommended. In milder cases, oral treatment with tetracycline, doxycycline, ampicillin or amoxicillin should be considered. Although several other antibiotics, including newer cephalosporins are highly active against leptospires in vitro, no clinical experience has yet been gained with these drugs (5, 7, 9, 10). While doxycycline is preferred for chemoprophylaxis and early treatment, IV penicillin (1.5 million units, every 6 hour) and ceftriaxone (1 g/day) are used later in the disease and in severe cases (5, 13). A successful combined therapy with ciprofloxacin has been reported for uveitis (5). We used doxycycline and ceftriaxone combination in the treatment of our patient. Starting from the 3rd day of the treatment, clinical and laboratory results improved significantly. Antimicrobial therapy is often given for 7-8 days (5, 7, 10). However, we applied the treatment for 20 days.

Recovery after leptospiral nephropathy is generally without sequelae (12). Long-term follow-up studies of leptospiral ARF cases have revealed a rapid renal recovery but complete recovery may take about 6 months (2, 4). In our case, a complete recovery was observed on the 15th day of antibiotic therapy. The patient’s renal functions were normal at 2 months follow up. Renal dysfunction may rarely become permanent, leaving the patient dependent on regular hemodialysis (11).

CONCLUSION

Although the principal lesion in leptospiral nephropathy is tubulointerstitial nephritis, glomerular pathology may also be observed. Thus, in nephrotic syndrome cases complicated with ARF, leptospirosis should be considered. Hypotension, thrombocytopenia, and low CPK, are the signs supporting the diagnosis. Nephrotic syndrome and ARF, generally heal with appropriate antimicrobial therapy without a need for dialysis.

REFERENCES


