Chapter

Kidney Disease in Brucellosis

Shokoufeh Savaj

Abstract

Brucellosis, a prevalent zoonosis disease in different countries, can involve the kidney during infection and also present in the complicated form in hemodialysis (HD), peritoneal dialysis (PD), and kidney transplant (Tx) patient. In spite of few reports of kidney involvements in the literature, this infection can imitate a wide range of glomerular disease from minimal change, membranous glomeropathy, focal and diffuse proliferative glomerular disease to rapidly progressive glomerulonephritis. Cryoglobulinemia, thrombotic microangiopathy, and ANCA-associated glomerular disease are vasculitis form of the disease. Tubulointerstitial involvement, electrolyte disorder, renal abscess, and pyelonephritis can present the same as other Gram-negative infections. Moreover, peritonitis in PD patient, spondyloarthropathy in HD, and severe infection in kidney Tx patients have been reported. Infection recurrence and infection from kidney donors are another dilemma in renal recipients. Brucellosis as a multifaced disease can mimic a wide range of presentations in nephrology. Clinicians should keep in mind the diverse pictures of the disease, especially when they practice in the endemic area.

Keywords: kidney, brucellosis, glomerular disease, dialysis, kidney transplant

1. Introduction

Brucellosis, a prevalent zoonosis disease with a worldwide distribution, can involve the kidney during infection. In 1889, Bruce [1] firstly reported kidney disease in Malt fever. Since then, a wide range of kidney involvements from direct invasion of Brucella with abscess and tubulointerstitial nephritis, immune complex disease, vasculitis, and drug toxicity have been reported. Brucella infection in immunocompromised patient can induce a confusing picture with peritonitis in peritoneal dialysis (PD), spondylodiscitis in hemodialysis, and complicated form of the disease in kidney transplant (TX) patients. Immunosuppressive monitoring, drug side effects, and donor to recipient transmission or recurrence are great challenges in the management of organ recipients with brucellosis. In this chapter, different presentations of brucellosis in kidney including glomeruli, tubulointerstitial, and vasculature involvement are discussed. Secondly, the Brucella infection in PD, HD, and Tx patients are reviewed, and finally, the chance of infection transmission of Brucellosis in the donor and recipients and the challenging point of pretransplant evaluation in donors and recipients are discussed.

2. Glomerular disease in brucellosis

Glomerular disease is an uncommon presentation in brucellosis. It can present with hematuria, pyuria, proteinuria, increased blood pressure, edema, and renal

failure. Glomerular involvement from mild proteinuria, microscopic hematuria up to the severe presentations of glomerular disease including rapidly progressive glomerulitis resulted in end-stage kidney disease have been reported. Glomeruli affected by immune complexes or vasculitis during Brucella endocarditis. The usual glomerulopathy in cases with endocarditis is focal and diffuse proliferative glomerulonephritis which are presented in the literature as membranoproliferative [2] and rapidly progressive glomerulonephritis; IgA nephropathy reported in two patients [3, 4] with proteinuria and hematuria. Siegelmann et al. [4] reported a case with nephrotic range proteinuria (6.0–13.0 g/day) and focal and segmental glomerulonephritis with mesangial proliferation and heavy deposit of IgA. Proteinuria persisted 3 months after completion of therapy, which indicates a secondary form of IgA nephropathy. Minimal change disease is a rare presentation of brucellosis reported only in one case without endocarditis. The patient had massive proteinuria who received prednisolone and antimicrobial treatment with complete remission and no recurrence after 1 year [5]. Membranous nephropathy is also diagnosed in one case with proteinuria [6].

3. Vasculitis in brucellosis

Vasculitis is a lethal picture of brucellosis with systemic organ involvement. Turgay et al. [7] reported 52-year-old male with Brucella infection and ANCA-associated vasculitis that induced rapidly progressive glomerulitis. The patient had endocarditis with vegetation on the aortic valve and leukocytoclastic vasculitis. Serology showed a high titer of serum agglutinin for Brucella and positive P-ANCA test. The patient recovered with combination therapy of plasmapheresis, methylprednisolone pulse, and antibiotic therapy. The other vasculitis form of kidney disease is cryoglobulinemia. This systemic disease can happen in malignancy, autoimmune, and infectious disease. Mixed cryoglobulinemia in brucellosis has been reported in five cases (four from Peru and one from Spain). They had a high polyclonal cryoglobulin level (IgG, IgA, and IgM) with a female preponderance (4:1). Four cases had positive bone marrow culture and one diagnosed based on serology [8]. Thrombotic microangiopathy that presents with microangiopathic hemolytic anemia, thrombocytopenia, and variable signs of organ impairment due to platelet aggregation in the microcirculation has been reported in patients with brucellosis. Erdem et al. [9] reported a 51-year-old man with thrombotic microangiopathy, hematuria, diminished consciousness, and renal failure. The patient received combination therapy with antimicrobials and plasma exchange with a good response and no recurrence in 1.5 years follow-up.

4. Tubulointerstitial and parenchymal involvement in brucellosis

Direct invasion of parenchyma and abscess formation is a rare manifestation of Brucella, which has been reported in five cases in the literature. Li et al. [10] reported a 45-year-old man with fever and flank pain. CT scan showed a low-density lesion in the right kidney in CT scan and positive culture for Brucella. He received 8 weeks course of treatment and relapse after discontinuation of treatment, which needed another 16 weeks course of rifampin and moxifloxacin for the eradication of bacteria. There are reports of acute interstitial nephritis [11] and pyelonephritis [12] after Brucella infection. A perplexing point is antimicrobial therapy with rifampin, which can induce interstitial nephritis. Salih et al. reported a 52-year-old man with a diagnosis of Brucella. Patient referred with acute renal failure 2 weeks after treatment with rifampin. Renal failure recovered since the drug was discontinued [13].

5. Electrolyte abnormality in Brucella infection

Syndrome of inappropriate secretion of ADH (SIADH), which presented with hyponatremia in a euvolemic patient without other electrolyte abnormality has been reported in patients with brucellosis. Bala et al. [14] in a study of 160 children and adolescent with SIADH reported 21.9% prevalence of SIADH. Urinary sodium (>25 mmol/L) with normal dietary salt intake, low uric acid (<2 mg/dL), the absence of kidney, thyroid or adrenal disease, and history of diuretic use were the criteria for diagnosis. Hyponatremia had a correlation to the severity of disease and managed with fluid restriction. Renal tubular disorder presented in 31 patients with active brucellosis [15]. They had phosphorus, potassium, and sodium handling abnormality in 31 patients. These patients were not malnourished, received fluid therapy, or hospitalized. They proposed that besides glomerular damage, tubular dysfunction is another presentation of Brucella infection.

6. Brucellosis in hemodialysis patients

Musculoskeletal problem is a prevalent feature in hemodialysis (HD) patients, which presents due to renal osteodystrophy and amyloidosis resulted from beta 2 microglobulin deposition in the joints. These symptoms can mislead the clinician to overlook Brucella diagnosis. Inversely, fever as a common presentation of the infectious disease is missing in those ill patients. Most of the reported cases of brucellosis in HD patients presented with musculoskeletal pain, arthralgia, low back pain, and malaise in the acute form of brucellosis. Paravertebral and epidural abscess with spondylodiscitis in thoracic and lumbar vertebra and neurobrucellosis with a headache, diplopia, and cranial nerve involvement were reported as the complicated chronic form brucellosis in HD patients [16]. There is also a report of fatal septicemia and endocarditis [17, 18] in HD patients. Blood cultures should be performed in HD patients when typical symptoms of brucellosis exist even when the patient has no fever. Drug toxicity and dose adjustment are the other obstacles in the treatment of these patients. Rifampin and doxycycline with a hepatic metabolism do not need any dose adjustment; however, aminoglycosides, cephalosporins, and fluoroquinolones should be prescribed based on patient's eGFR and patient needs a supplement dose after dialysis course.

7. Brucellosis in peritoneal dialysis (PD) patients

Peritoneal dialysis patients are at risk of peritonitis. Gram-positive organisms are the common cause of infections in 80% of the episodes. There are few reports of peritonitis due to Brucella infection in the literature. All of the cases presented with a typical peritoneal infection with neutrophil predominance with a positive culture in 5–21 days [19]. Organ involvement is hematogenous in most of the studies; however, Osizik et al. [20] showed a positive peritoneal fluid culture with a negative blood culture and serology. They proposed a direct inoculation of bacteria from the catheter to peritoneum based on the patient's occupation. The other issue in Brucella peritonitis in PD patients is any need for catheter removal after Brucella infection. Taskapan et al. [21] and Alothman et al. [22] reported two cases with a recurrence of infection in 6–8 weeks after treatment that resulted in catheter removal for complete eradication of bacteria. On the other hand, Unal et al. [23] and Solak et al. [19] in two different reports showed the complete cure of infection despite keeping peritoneal catheter. Drug regimen in these studies was 6 weeks course of rifampin and doxycycline.

8. Brucellosis in renal transplant recipients

However, the prevalence of brucellosis is around 1 in 500,000 population, and there are few reports in renal transplant recipients. In another view, these patients are at risk of different opportunistic infections. Most of the time, diagnosis of brucellosis was lately with the complicated form of the disease. There were two reports of neurobrucellosis in renal Tx patients in the literature, one with loss of consciousness and encephalitis [24] and the other one with a seizure and headache [25]. Endocarditis [26], pulmonary involvement [27], hepatobiliary and hematologic [28], pyelonephritis and dysuria [29], and arthritis [30] were other presentations of the disease. They were diagnosed based on serology or fluid culture that finally guided to the diagnosis of brucellosis. In addition to the complicated form of the disease and late diagnosis, drug interferences, especially calcineurin inhibitors, are another challenging point in the treatment of disease. Rifampin decreases drug level and inversely clarithromycin increases drug level that induces calcineurin toxicity. Hence, streptomycin with nephrotoxic nature cannot be the first choice in renal Tx patient. Ting et al. suggested tigecycline as an alternative drug in renal Tx patient. Triple antibacterial treatment has experienced in these immunocompromised patients with a complicated form of the disease [26, 30]. In these six reports, all of the patients completed the 6–12 weeks course of treatment with a good outcome and no recurrence; however, they experienced a serum creatinine rise.

9. Kidney donor evaluation before transplant

Evaluation for Brucella infection is suggested before organ transplantation in donors and recipients, especially in endemic areas. There are some reports of Brucella transmission and recurrence after liver [31], bone marrow transplantation [32, 33]. Serologic tests including serum agglutination and ELISA should be performed before organ transplant. Positive titers consisted of 1:80 in the non-endemic area and 1:160 in the endemic area are suspicious and needs further evaluation. Serologic tests are not enough to distinguish active and past infection, which needs more evaluation by infectious disease specialist.

10. Conclusion

In this chapter, a wide range of Brucella presentations was discussed. Brucellosis as a multifaced disease can imitate a large group of non-infectious causes of kidney disease. Hence, the misdiagnosis could be hazardous and end to the patient's morbidity and mortality. Clinicians should keep in mind the diverse pictures of the disease, especially when they practice in the endemic area.

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