



Case Report

Lessons from the success and failures of peritoneal Dialysis-Related Brucella Peritonitis in the last 16 years: Case report and Literature review

Muhammad Bukhari^{1,2*}, Azharuddin Mohammed¹, Abdullah Al-Guraibi², Ahmed Shahata¹ and Mansour Al-Ghamdi¹

¹Department of Nephrology and Kidney Transplantation, Armed Forces Hospital-Taif region, Saudi Arabia

²Department of Medicine, Taif University, Taif, Saudi Arabia

***Address for Correspondence:** Muhammad A Bukhari, ¹Department of Nephrology and Kidney Transplantation, Armed Forces Hospital-Taif region, 7100 Alwihdah St. Alawali, Makkah, Saudi Arabia, ²Department of Medicine, Taif University, Taif, Saudi Arabia, Tel: +966553502550; Email: bukhary5354@hotmail.com; drbukhari@tu.edu.sa

Submitted: 24 December 2018

Approved: 28 December 2018

Published: 31 December 2018

Copyright: © 2018 Bukhari MA, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Keywords: Peritoneal dialysis; Peritonitis; Brucella



Abstract

Brucellosis is a zoonotic infection that is endemic in some Mediterranean countries, North Africa and the Middle East. Brucella is a rare cause of peritonitis in Peritoneal Dialysis (PD) population and in non-dialysis patients alike. We report here a challenging case of PD-related Brucella peritonitis in a 45-year-old Saudi male with late peritonitis that delivered some key learning throughout its course from presentation, diagnosis and treatment to catheter salvage attempts so as to circumvent PD failure. We provide an in-depth review of limited published literature on PD-related Brucella peritonitis (seven cases, and present case) and summarized the data on key clinical characteristics, management and PD technique outcome to benefit nephrologists when encountered with this rare presentation.

Introduction

Brucellosis – or Malta fever- is a zoonotic infection that is transmitted by contact with infected animals and their products. Brucella infections are mainly reported in north and east Africa, the Middle East, South and Central Asia and Central and South America [1]. Worldwide, over 500,000 new cases of Brucella infections are reported annually. In Saudi Arabia the incidence of Brucella infections is around 137 cases per 100,000 per year [2]. Although Brucellosis typically presents with non-specific symptoms, in around 30% of cases, focal system involvement such as osteoarticular or gastro-intestinal involvement can be the initial manifestation [1,3].

Peritoneal Dialysis (PD) peritonitis remains one of the most important PD complications that can lead to PD catheter removal and failure in up to 18% necessitating modality change to Hemodialysis. In PD patients, peritonitis is usually caused by gram positive cocci [4]. To our knowledge, only 7 cases of Brucella PD peritonitis were reported to date. All of these cases were from the Middle East. In this article, we report the second case (eighth word wide) of Brucella PD peritonitis from Saudi Arabia and share some important diagnostic and therapeutic challenges faced by clinicians when encountered with this rare condition in light of available literature to-date.

Case

A 45-year-old male patient with Chronic Kidney Disease – stage 5D due to non-biopsy prove diabetic nephropathy on peritoneal dialysis (CCPD) for the past 3 years

presented to Emergency Room with fever, on-off vague generalized dull abdominal pain, vomiting and diarrhoea for 2-3 days. He reported that his son also developed similar symptoms. His past medical history included long standing Diabetes Mellitus for 16 years, hypertension, ischemic heart disease and moderate left ventricular systolic dysfunction. He was afebrile, haemodynamically stable with unremarkable general and systemic examination. Laboratory investigations showed normal white blood cells (WBC) count and a high CRP (Table 1). The peritoneal dialysate fluid WBC count was $32 \times 10^3/\text{mL}$, neutrophils 51% and did not support a diagnosis of PD peritonitis. Patient received supportive treatment for gastroenteritis in ER and discharged home.

Two days later, he re-presented to ER with non-resolving symptoms and fever. His temperature was high at 38 C° and blood pressure was 120/60 mmHg. On examination, his PD catheter exit site and tunnel were normal but abdomen was tender with turbid PD fluid. Laboratory investigations this time showed elevated inflammatory markers with normal AST 18(U/L), ALT 44 (U/L), amylase 8 (U/L), lipase 39 (U/L) and lactic acid 2.2 (mmol/L). PD fluid WBC count was high and consistent with neutrophilic PD peritonitis (neutrophils 86%) (Table 1).

Hospital course

Awaiting culture results, patient was started on treatment for PD peritonitis with protocol intraperitoneal antibiotics - cefazolin 1gm and ceftazidime 1gm daily. Abdominal X-Ray and ultrasound showed normal findings with no signs of tunnel infection. Further history now revealed that the patient consumed a popular locally processed 'Baladi' cheese (made from unpasteurized raw milk) days before his presentation.

On Day 4, blood cultures were still not back and a further sample sent to look for fungal peritonitis due to persistent symptoms. Later that day, laboratory reported positive cultures for Gram-negative coccobacillus and isolated heavy growth of *Brucella melitensis* from PD dialysate and blood, confirming *Brucella* PD peritonitis (Table 1).

Infectious diseases specialist was consulted who initiated treatment for focal Brucellosis with Rifampicin, Doxycycline and Ciprofloxacin. Patient developed diarrhoea and after 1 week of observation required discontinuing Rifampicin. Diarrhoea slowed with some initial improvement in general condition of the patient and infective markers. This was followed by anorexia, nausea, vomiting probably due to Doxycycline; it was switched to Minocycline after 2 weeks due to a better GI side-effect profile.

After 2 weeks into treatment, his symptoms and infective markers worsened again suggestive of poor response on dual therapy. Symptoms did not abate even after 15 days of admission and PD fluid culture isolated *Brucella melitensis* again, confirming a refractory disease. Patient wanted to remain on PD and this choice meant avoiding further injury to peritoneal membrane and preserving its function. PD catheter was removed and his modality switched to hemodialysis (HD) (Table 1).

Patient showed a steady clinical improvement subsequently with negative blood and PD catheter tip cultures. Patient received 12 weeks treatment and intended live related kidney transplantation instead of PD. At 6 months follow-up he was stable on HD.

An informed consent was obtained from the patient prior to case writing and this work received an ethical approval form the Research Ethics Board at Al-Hada Armed Forces Hospital.

Table 1: Clinical, biochemical and microbiological course of the patient following diagnosis.

	Symptoms	WBC Blood ($\times 10^9/\text{L}$)	WBC PD fluid ($\times 10^3/\text{mL}$)	CRP (mg/L)	Blood culture	PD Fluid culture
Day 1	+	4.2	32	94	B.Melitensis	B.Melitensis
Day 3	+++	15.9	2280	200	B.Melitensis	No growth
Day 8	++	8.8	445	109	-	-
Day 10	+++	9.5	1250	66	No growth	No growth
Day 15	+++	15.7	385	255	B.Melitensis	-

Discussion

Brucellosis manifesting with gastro-intestinal symptoms is uncommon; and Brucella peritonitis is even rare [3]. Only 3 cases of Brucella peritonitis were reported to-date in non-PD population including a previously healthy patient [5-7]. There are only 7 case reports of PD-related Brucella peritonitis excluding the present case - six from Turkey and one from Saudi Arabia [8-13]. The first reported case was by Taskapan et al. in 2002, while the majority is from 2008 onwards, probably reflecting an increased awareness and reporting from endemic areas. This may well be an underestimate given the worldwide annual reporting of half a million Brucellosis cases with high PD uptake rate (up to 75%) in some of these countries such as Mexico.

With globalization, boundaries of Brucella endemicity are getting faint as 'holiday PD' is now delivered to most of these favourite holiday destinations, some with high endemicity. Knowledge of local sources of Brucella is quite important as in our case; patient consumed a popular locally processed cheese (made from unpasteurized raw milk) days before his presentation.

Case reports analysis show that patient's were mostly males (except one) with a median age of 47.5 years (range 38 - 67), which probably reflect a high exposure due to lifestyle, dietary habits and occupational risk. PD vintage at the time of index peritonitis was variable between 2 months and 5 years. Brucella melitensis is the commonest species in humans and predictably reported in 5 out of 8 cases while the other 3 did not specify (Table 2).

Positive PD fluid culture for Brucella is diagnostic of PD-related Brucella peritonitis. Being a fastidious and intracellular organism, Brucellosis diagnosis requires longer culture time with conventional methods such as Castaneda. Brucella isolation on cultures is variably reported to be between 2 - 27 days depending on culture method and technique used locally and the disease duration; it typically takes between 4-14 days to grow, which may result in treating these patients initially as culture negative PD peritonitis [14-16]. Newer techniques can reduce this organism recovery time in cases with high index of suspicion. In our case, Brucella PD dialysate culture came back positive after 3 days using automated system BacT/Alert 3d system.

Table 2: Characteristics of reported cases of PD Brucellosis. F= Female; M= Male; R= Rifampicin; D= Doxycycline; Cef= Ceftriaxone; Mi= minocycline; A= Amikacin; Cip= Ciprofloxacin.

Study	Age, Gender	Time to Peritonitis	Blood		PD Dialysate			Brucella agglutination test		Treatment regimen	Treatment Duration	PD Outcome (Catheter removal)
			WBC count ($\times 10^3/L$)	Culture	WBC count ($\times 10^3/mL$)	WBC Predominance	Culture	Serum	Dialysate			
Taskapan et al. 2002	47, M	12 m	6.2	Brucella Melitensis	300	Neutrophils	Brucella Melitensis	1/2560	Unknown	R, D	Unknown	Yes
Ozsisik et al. 2006	39, F	5 y	14.5	No growth	3,140	Neutrophils	Brucella Melitensis	Negative	1/60	R, D	6 weeks	Yes
Alothman et al. 2008	67, M	4 m	8.1	Unknown	3,356	Neutrophils	Brucella Spp	1/2560	Unknown	R, D	12 weeks	Yes
Unal et al. Case 1, 2009	38, M	2 m	4.08	Brucella Melitensis	1,600	Neutrophils, lymphocytes	Brucella Melitensis	1/640	Negative	R, D	6 weeks	No
Unal et al. Case 2, 2009	52, M	6 m	8.1	Brucella melitensis	5,100	Neutrophils	Brucella Melitensis	1/640	1/20	R, D	6 weeks	No
Solak et al. 2012	48, M	3 y	7.16	No growth	820	Lymphocytes	Brucella Spp	1/5120	Unknown	R, D and Cef	6.5 weeks	No
Koz et al. 2014	49, M	Unknown	7.10	No growth	1300	Lymphocytes	Brucella Spp	1/1280	1/80	R, D and A	6 weeks	No
Presented Case, 2018	45, M	3 y	15.9	Brucella melitensis	2280	Neutrophils	Brucella Melitensis	N/A	Unknown	R, D and Cip then Mi and Cip	12 weeks	Yes

All cases of PD-related Brucella peritonitis reported high Brucella titer on serum agglutination test (SAT) ranging from 1/640 to 1/5120 except Ozisik et al., which was negative [10]. High serum titers were not associated with positive blood cultures; SAT titers in PD fluid were significantly lower as compared to serum. Once a blood, tissue or fluid culture isolates Brucella, value of testing for titers may not be well justified. However, if initial SAT is positive, looking for persistent infection with appropriate cultures is mandated. Although Brucellosis cases provoke lymphocytic reaction, 5/8 (62.5%) cases of PD-related Brucella peritonitis presented with neutrophilic predominance on PD fluid WBC differential count.

All reported cases were treated as per standard focal brucellosis therapy consisting of oral doxycycline and rifampicin. Doxycycline was substituted with IV ceftriaxone in one case and with Minocycline in our case due to GI intolerance [11]. Another case was treated successfully with the addition of intraperitoneal (IP) Amikacin that obviated the need for PD catheter removal [9]. It is hard to decipher from a single case report that additional efficacy of IP aminoglycoside could salvage PD catheters due to many unreported confounders.

The duration of antibiotics therapy ranged from 6-12 weeks; all 4 patients with preserved PD catheter received only 6 – 6.5 weeks treatment indicating no clear benefit of longer treatment durations on catheter salvage.

Overall catheter removal and PD failure was high at 50%, which stands higher than those reported for fungal peritonitis [17]. Catheter removals were performed due to either treatment refractory Brucellosis or recurrent disease [8,10,12]. Case-series data analysis shows that patient's age, presence of fever, PD vintage, duration of therapy, serum Brucella titer or blood culture positivity do not predict catheter survival.

In summary, Brucella is a rare cause of dialysis-related peritonitis but limited data could be due to under-reporting and missed diagnoses given its high endemicity and annual incidence worldwide. It can lead to a very high PD failure rate despite modern antimicrobials. With globalization and holiday PD, a high index of suspicion with thorough clinical history is vital for its early diagnosis particularly in non-endemic areas. Newer Brucella culture techniques are now available for rapid recovery of organism that would have previously been classed culture negative. Factors favoring early removal of PD catheter are not yet clear, and we suggest PD catheter removal decisions in these cases are to be based on the current international guidelines for catheter removal and patient choice [18].

Conclusion

We reported this case to share our experience of this rare condition with our Nephrology community. Moreover, we summarized the previously reported cases of this disease. With the limited data on Brucella PD peritonitis, following learning points may be concluded

Brucella species can rarely cause peritonitis in PD and Non-PD patients.

PD Brucellosis can be treated successfully with conventional oral anti-biotic therapy.

Additional IP aminoglycoside may have a role in treating PD Brucellosis to avoid catheter removal although it is hard to reach a solid conclusion based on current evidence.

Factors favoring removal of the catheter are not yet clear and we suggest PD catheter should be removed as indicated by the international guidelines for catheter removal [18].



References

1. Corbel MJ, Alton GG, Ariza J, et al. Brucellosis in humans and animals. Who Press. 2006; 1–102. **Ref.:** <https://goo.gl/JMgboN>
2. Dean AS, Crump L, Greter H, Schelling E, Zinsstag J. Global Burden of Human Brucellosis: A Systematic Review of Disease Frequency. *PLoS Negl Trop Dis.* 2012; 6: e1865. **Ref.:** <https://goo.gl/3FwJdf>
3. Colmenero JD, Reguera JM, Martos F, Sánchez-De-Mora D, Delgado M, et al. Complications Associated with Brucella melitensis Infection. *Medicine.* 1996; 75: 195–211. **Ref.:** <https://goo.gl/mhtprN>
4. Abe S, Obata Y, Sato S, Muta K, Kitamura M, et al. Causative bacteria and risk factors for peritoneal dialysis-related peritonitis: A retrospective study. *Acta Med Nagasaki.* 2016; 60: 145–151. **Ref.:** <https://goo.gl/BNGygY>
5. Gencer S, Ozer S. Spontaneous Bacterial Peritonitis Caused by Brucella melitensis. *Scand J Infect Dis.* 2003; 35: 341-343. **Ref.:** <https://goo.gl/kL3xcA>
6. Javeri H, Jamieson S, Sehgal R, Cadena J. Brucella canis peritonitis. *Infection.* 2014; 42: 195-197. **Ref.:** <https://goo.gl/ZgF3Ld>
7. Makaritsis KP, Liaskos C, Papadamou G, Dalekos GN. Spontaneous bacterial peritonitis : an unusual manifestation of brucellosis in a previous healthy male patient. *BMJ Case Reports.* 2015; 2015: pii: bcr2015209387. **Ref.:** <https://goo.gl/5FZjqV>
8. Allothman A, Khurmi A. Al, Sadoon S, AlHejaili F. Brucella Peritonitis in a Patient on Peritoneal Dialysis. *Saudi journal of kidney diseases and transplantation.* 2008; 19: 428-430. **Ref.:** <https://goo.gl/chU7WS>
9. Koz S, Sahin I, Kayabas U, Kuzucu C. Brucella and peritoneal dialysis related peritonitis : case report and review of literature. *Clinical nephrology.* 2014; 82: 283-286. **Ref.:** <https://goo.gl/PZ2cyW>
10. Ozisik L, Akman B, Huddam B, Azap OK, Bilgic A, et al. Isolated Brucella Peritonitis in a CAPD Patient. *Am J Kidney Dis.* 2006; 47: e65-66. **Ref.:** <https://goo.gl/vbsrHL>
11. Solak Y, Biyik Z, Demircioglu S, Polat I, Genc N, et al. Brucella Peritonitis in Peritoneal Dialysis: A Cases report and Review of The Literature. *Perit Dial Int* 2012; 32: 126–130. **Ref.:** <https://goo.gl/Kaw9uE>
12. Taskapan H, Oymak O, Sümerkan B, Tokgoz B, Utas C. Brucella peritonitis in a patient on continuous ambulatory peritoneal dialysis with acute brucellosis. *Nephron.* 2002; 91: 156–158. **Ref.:** <https://goo.gl/bNSxGs>
13. Unal A, Sipahioglu MH, Kavuncuoğlu F, Tokgoz B, Oymak O, et al. Peritoneal dialysis-related peritonitis caused by Brucella melitensis. *Dial Transplant.* 2009; 38: 515–516. **Ref.:** <https://goo.gl/RJccgQ>
14. Yagupsky P. Detection of brucellae in blood cultures. *J Clin Microbiol.* 1999; 37: 3437–3442. **Ref.:** <https://goo.gl/jSrbUP>
15. Mangalgi S, Sajjan A. Comparison of three blood culture techniques in the diagnosis of human Brucellosis. *J Lab Physicians.* 2014; 6: 14-17. **Ref.:** <https://goo.gl/E61cbs>
16. Rodriguez-Torres A, Feroso J LR. Brucellosis. *Medicine* 1983; 48: 3126-3136.
17. Prasad N, Gupta A. Fungal peritonitis in patients on continuous ambulatory peritoneal dialysis: A single centre Indian experience. *Perit Dial Int.* 2005; 25: 207-222 **Ref.:** <https://goo.gl/JHqJd5>
18. Li PK, Szeto CC, Piraino B, de Arteaga J, Fan S, et al. ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment. *Ispd.* 2016; 36: 481–508. **Ref.:** <https://goo.gl/UegCt2>