Metastatic Infections in Hemodialysis: An Analysis of 19 Cases

Hemodiyalizde Metastatik Enfeksiyonlar: 19 Olgunun Analizi

Aydın ÜNAL[1]
Tamer ARIKAN[2]
Murat Hayri SİPAHİOĞLU[1]
İsmail KOÇYİĞİT[1]
Bülent TOKGÖZ[1]
Güven KAHRİMAN[3]
Oktay OYMAK[1]

1 Erciyes University Faculty of Medicine, Department of Nephrology Kayseri, Turkey
2 Kayseri Education and Research Hospital, Department of Nephrology Kayseri, Turkey
3 Erciyes University Faculty of Medicine, Department of Radiology Kayseri, Turkey

ABSTRACT

OBJECTIVE: Metastatic infection is a rare but serious complication in patients undergoing hemodialysis (HD). In this retrospective study, we aimed to analyze the clinical aspects, responsible microorganisms, treatments, and clinical outcomes in HD patients with metastatic infection

MATERIAL and METHODS: Metastatic infection was defined as infection that occurs at a location physically separate from the portal of entry of the bacteria. We identified 21 metastatic infections in 19 HD patients at our hospital from December 2010 through November 2016.

RESULTS: The mean age was 66.4 ± 15.7 years. Twelve (63.2%) of the 19 patients were female whereas 7 (36.8%) patients were male. Type of vascular access was tunneled cuffed permanent catheter in 15 (78.9%) and arteriovenous fistula in 4 (21.1%) patients. The most common type of metastatic infection was spondylodiscitis. In the majority of these patients, the responsible infectious agents were Gram-positive microorganisms including *S. epidermidis* and *S. aureus*. The clinical outcome in the majority of the patients was complete recovery. Two patients died due to metastatic infection.

CONCLUSION: Metastatic infection in HD patients, especially those with a tunneled cuffed permanent catheter, is a serious complication, which may result in the patient's death. Gram-positive microorganisms are responsible for the majority of cases with metastatic infection.

KEY WORDS: Antibiotic therapy, Hemodialysis, Gram-positive microorganisms, Metastatic infection, Tunneled cuffed permanent catheter

ÖZ

AMAÇ: Metastatik enfeksiyon, hemodiyaliz (HD) uygulanan hastalarda nadir ama ciddi bir komplikasyondur. Bu geriye dönük çalışmada, biz metastatik enfeksiyonu olan HD hastalarında klinik görünümleri, sorumlu mikroorganizmaları, tedavileri ve klinik sonuçları analiz etmeyi amaçladık.

GEREÇ ve YÖNTEMLER: Metastatik enfeksiyon bakterinin giriş noktasından fiziksel olarak ayrı bir bölgede meydana gelen enfeksiyon olarak tanımlandı. Bizim hastanemizde Aralık 2010 ile Kasım 2016 tarihleri arasında 19 HD hastasında 21 metastatik enfeksiyon tespit edildi.

BULGULAR: Ortalama yaş 66.4 ± 15.7 yıldı. On dokuz hastanın 12'si (%63.2) kadın, 7'si (%36.8) erkekti. Damara ulaşım yolunun türü 15 (%78.9) hastada tünelli keçeli kalıcı kateter ve 4 (%21.1) hastada arteriyovenöz fistüldü. En sık görülen metastatik enfeksiyon türü spondilodiskitti. Hastaların çoğunda sorumlu enfeksiyon ajanları *S. epidermitis* and *S. aureus* gibi Gram-pozitif mikroorganizmalardı. Hastaların çoğunda klinik sonuç tam iyileşme idi. İki hasta metastatik enfeksiyon nedeniyle kaybedildi.

SONUÇ: Özellikle tünelli keçeli kalıcı kateteri olan HD hastalarında metastatik enfeksiyon ciddi bir komplikasyondur ve hastanın kaybedilmesine neden olabilir. Gram-pozitif mikroorganizmalar metastatik enfeksiyonlu olguların çoğundan sorumludur.

ANAHTAR SÖZCÜKLER: Antibiyotik tedavi, Hemodiyaliz, Gram-pozitif mikroorganizmalar, Metastatik enfeksiyon, Tünelli keçeli kalıcı kateter

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Correspondence Address:
Aydın ÜNAL
Erciyes Üniversitesi Tıp Fakültesi,
Nefroloji Bilim Dalı,
Kayseri, Turkey
Phone : + 90 352 437 93 49
E-mail : aydinunal2003@gmail.com

INTRODUCTION

Infection, a frequent complication, is the second leading cause of death in hemodialysis (HD) patients. HD patients have higher rates of bacteremia, whereas peritoneal dialysis patients have higher rates of peritonitis. The risk of bacteremia in the patient population is 26-fold higher than in the general population (1). The most important risk factor for bacteremia in HD patients is the use of central venous catheters. Use of a tunneled cuffed HD catheters for vascular access in the patients, especially the elderly and diabetics, is increasing (2, 3). Use of an HD catheter for vascular access is associated with a higher risk of bacteremia compared to use of an arteriovenous fistula (AVF) or graft (1).

HD-related bacteremia may be associated with metastatic complications, such as osteomyelitis, endocarditis, septic arthritis, or epidural abscess (4). Metastatic infections have been observed in approximately 5 to 10 percent of catheter-dependent HD patients (5). The increased frequency of the use of catheters has in turn led to an increasing incidence of such metastatic infections (6).

The aim of the present study was to evaluate the clinical aspects, etiological agents, treatments, and outcomes of metastatic infections among HD patients at our hospital.

PATIENTS and METHODS

The study included all HD patients with metastatic infection at our hospital (Erciyes University, Faculty of Medicine, Kayseri, Turkey) from December 2010 through November 2016.

We identified a total of 19 HD patients with a metastatic infection. This study was approved by the Clinical Research Ethics Committee of Erciyes University (2016/637). The hospital file of each patient was reviewed to assess the clinical and microbiological characteristics. Demographic data, clinical and microbiological findings, treatment of infection, and clinical outcomes were recorded.

Metastatic infection was defined as infection that occurs at a location physically separate from the portal of entry of the bacteria (7). Recurrent infection was defined as an episode that occurs within four weeks of completion of the treatment of a prior episode but with a different organism. Relapsing infection was defined as an episode that occurs within four weeks of completion of the treatment of a prior episode with the same organism.

Statistical Analysis

The SPSS 15.0 statistic software was used for the statistical analysis. The Kolmogorov-Smirnov test was used to determine normality of distributions of variables. Continuous variables with normal distribution were presented as mean ± standard deviation. The median value was used when a normal distribution was absent.

RESULTS

Table I shows the clinical and microbiological characteristics of 19 HD patients with metastatic infection. We identified 21 metastatic infections in 19 HD patients. The mean age was 66.4 ± 15.7 years. Twelve (63.2%) of the 19 patients were female whereas 7 (36.8%) patients were male. Median dialysis duration was 36 (2-145) months. Mean systolic and diastolic blood pressure was 134 ± 21 mm Hg and 75 ± 10 mm Hg, respectively. Mean albumin and hemoglobin values were 2.8 ± 0.8 g/dL and 9.6 ± 1.7 g/dL, respectively. Type of vascular access was a tunneled cuffed permanent HD catheter in 15 (78.9%) and AVF in 4 (21.1%) patients. The cause of end-stage renal disease was diabetes mellitus (DM) in 12 (63.2%), hypertension in 2 (10.5%), obstructive uropathy in 1 (5.3%), and unknown in 4 (21.1%) patients. The most common type of metastatic infection was spondylodiscitis. The clinical outcome in the majority of the patients was complete recovery. Metastatic infection relapsed in one patient with breast abscess. However, the relapsed infections ended in complete recovery with appropriate treatment. Similarly, the metastatic infection recurred in one patient with a hepatic abscess but the recurrent infection also ended in complete recovery with appropriate treatment. One patient with spondylodiscitis, who had clinical improvement in the metastatic infection, was voluntarily transferred to another hospital. One patient with spondylodiscitis self-discharged from the hospital and was lost to follow-up. Two patients died due to metastatic infection, in the form of pneumonia in one patient and septic arthritis in other patient.

The majority of the patients had co-morbid disorder(s), which was DM in seven (38.8%), coronary artery disease (CAD) in one (5.3%), and bladder cancer in one (5.3%), Coombs-positive hemolytic anemia in one (5.3%), chronic hepatitis C virus (HCV) infection in one (5.3%), DM plus CAD in one (5.3%), DM plus epilepsy plus valvular heart disease in one (5.3%), DM plus chronic obstructive pulmonary disease (COPD), DM plus asthma in one (5.3%), neurogenic bladder dysfunction in one (5.3%), and DM plus cerebrovascular disease (CVD) in one (5.3%) patient. Two (10.5%) patients had no co-morbid disease.

Figure 1 shows subdiaphragmatic perihepatic bilobular abscess formation with a size of 98x58 mm (A) and a drainage catheter within the cavity of the abscess (B) (patient number 13). Figure 2 shows splenic abscess formation with a 3.5 mm diameter (patient number 14).

DISCUSSION

HD patients have high risk of infection from complications of bacteraemia, which usually originates from the vascular contamination by central venous catheters or routine skin penetration for blood access (8, 9). The frequency of bacteremia is greater in HD patients with indwelling tunneled catheters than in those with either AVF or synthetic graft (10). Similarly, the majority of our patients had a tunneled cuffed permanent catheter for vascular access.

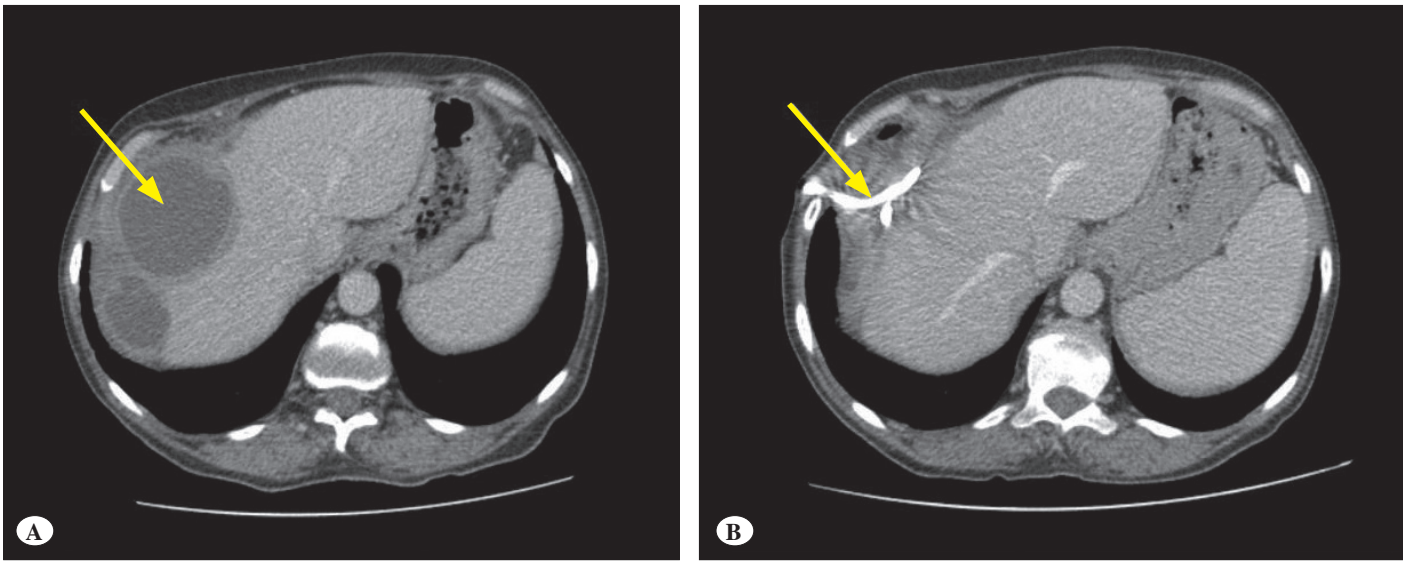

Figure 1: *Subdiaphragmatic perihepatic bilobular abscess formation with 98x58 mm diameter* ***(A)*** *and a drainage catheter within the abscess cavity* ***(B)****.*

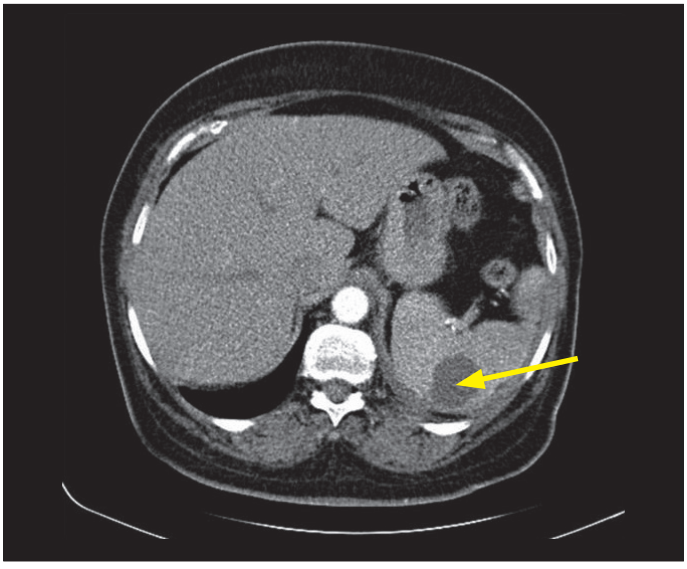

Figure 2: *Splenic abscess formation with a 3.5 mm diameter.*

HD patients may present with spondylodiscitis as a result of bacteraemia, since the thoracic spine is one of the most frequent locations of bacterial colonization (8, 11). Similarly, the type of metastatic infection in about half of our patients was spondylodiscitis. Early diagnosis of this spine infection and prompt initiation of the appropriate therapy are very important to reach successful treatment outcomes. Magnetic resonance image (MRI) is the main diagnostic method for prompt antibiotic treatment as blood or sample cultures may be negative. It can reveal discitis, bone destruction and abscess (8, 9). Similarly, spondylodiscitis was diagnosed by MRI imaging in all our patients suffering from it.

Spondylodiscitis as a metastatic infection can be generally treated successfully by appropriate antibiotic therapy. Surgical intervention may be necessary for patients who are unresponsive to antibiotic therapy and in those who have developed progressive spinal deformity or instability, epidural abscesses, or neurological impairment (9). Four of our nine patients with spondylodiscitis were treated successfully with antibiotic therapy and surgical intervention. Three patients, one of them transferred to another hospital, were treated successfully with only antibiotic therapy. One patient self-discharged from the hospital and was lost to follow-up. One patient, in whom surgical treatment was not performed because of his poor general health although there was an indication for it, died due to pneumonia.

Gram-positive microorganisms are the responsible agent for most HD catheter-related infections. Coagulase-negative staphylococci and *S. aureus* together account for 40 to 80 percent of cases (4). In the majority of our patients, the responsible infectious agents were these two skin-derived microorganisms. Gram-negative microorganisms were the responsible infectious agents in our patients with intraabdominal or hepatic abscess as expected. *S. aureus* infection is commonly associated with significant morbidity and mortality in HD catheter-related infections (4). Similarly, in our two patients who died, the responsible infectious agent was *S. aureus*.

HD patients, who have a catheter (temporary or permanent) for vascular access, are susceptible to infection. Some additional factors associated with chronic kidney failure such as malnutrition as well as comorbid conditions including DM make these patients more susceptible to infection (12). In accordance with this data, the majority of our patients with metastatic infection were diabetic.

Table I: Clinical and microbiological characteristics of hemodialysis patients with metastatic infection.

Number of patient	Age (years)	Sex	Co-morbid disorder	Vascular access type	Complaint	Type and location of infection	Duration of hospitalization (days)	Culture	Blood Culture	Treatment	Outcome
1	75	Female	DM	TCC	Back pain and inability to walk	Spondylodiscitis	76	Culture-negative	Culture-negative	Partial hemilaminectomy + flavectomy+ drainage of spinal epidural abscess + teicoplanin	Complete recovery
2	72	Female	DM	AVF	Back pain	Spondylodiscitis	26	Unable to obtain culture material	*S. epidermidis*	Ampicillin sulbactam	Complete recovery
3	74	Female	DM	TCC	Back pain	Spondylodiscitis	10	Unable to obtain culture material	Culture-negative	Ampicillin sulbactam	Complete recovery
4	45	Male	DM	TCC	Back pain	Spondylodiscitis	14	*S. epidermidis*	*S. epidermidis*	Posterior instrumentation and fusion + Partial hemilaminectomy + drainage of abscess + ampicillin sulbactam and rifampicin	Complete recovery
5	61	Male	DM	TCC	Back pain	Spondylodiscitis	11	Unable to obtain culture material	Culture-negative	Posterior instrumentation + Teicoplanin	Complete recovery
6	65	Female	DM	TCC	Back pain	Spondylodiscitis	36	Culture-negative	Culture-negative	Posterior instrumentation and fusion + hemilaminectomy + flavectomy + amoxicillin clavulanate and ciprofloxacin	Complete recovery
7	71	Female	Coombs-positive hemolytic anemia	TCC	Back pain	Spondylodiscitis	24	Unable to obtain culture material	*S. epidermidis*	Teicoplanin*	Self-discharge from hospital against medical advice
8	71	Female	DM + bronchial asthma	AVF	Pain + motor deficit in the right leg	Spondylodiscitis	18	Unable to obtain culture material	*S. epidermidis*	Vancomycin and meropenem	Transfer to another hospital

Table I continue: Clinical and microbiological characteristics of hemodialysis patients with metastatic infection.

9	60	Male	DM + CAD	TCC	Chills, fever, back pain	Spondylodiscitis + pneumonia	11	Culture-negative	*S. aureus*	Vancomycin and piperacillin/ tazobactam	Exitus
10	18	Female	Neurogenic bladder dysfunction	TCC	Fever and hypotension	Intraabdominal abscess	18	*E.coli* + *Morganella morganii*	Culture-negative	Drainage of abscess + ciprofloxacin and clindamycin	Complete recovery
11	75	Female	DM + epilepsy + valvular heart disease	TCC	Abdominal pain and dyspnea	Intraabdominal abscess	13	ESBL positive *K. pneumonia*	Culture-negative	Drainage of abscess + imipenem/cilastatin	Complete recovery
12	73	Female	DM + COPD	TCC	Abdominal pain	Intraabdominal abscess	33	Alpha-hemolytic streptococci + Diphtheroid bacilli**	Culture-negative	İmipenem/cilastatin	Complete recovery
13	57	Female	None	TCC	Abdominal pain	Hepatic abscess	39	ESBL positive *E.coli*	Culture-negative	Drainage of abscess + imipenem/cilastatin and metronidazole	Recurring***
13				TCC	Abdominal pain	Hepatic abscess	16	*Serratia marcescens*	Culture-negative	Drainage of abscess + sulperazone	Complete recovery
14	60	Female	DM	TCC	Abdominal pain and coughing	Splenic abscess	21	Culture-negative	Culture-negative	Drainage of abscesses + ampicillin sulbactam and metronidazole	Complete recovery
15	64	Male	Bladder cancer in remission	TCC	Lump in the breast	Breast abscess	15	*S. aureus*	Culture-negative	Drainage of abscess + ampicillin sulbactam	Relapsing****
15				TCC	Lump in the breast and pain and swelling in the knee	Breast abscess and septic arthritis	23	*S. aureus* in both cultures	Culture-negative	Drainage of abscess + arthroscopic lavage + amoxicillin clavulanate and rifampicin	Complete recovery
16	66	Male	None	TCC	Swelling and pain in the left knee	Septic arthritis	23	*S. aureus*	*S. aureus*	Drainage of abscess + arthroscopic lavage + cephazolin	Complete recovery
17	88	Male	CAD	AVF	Swelling and pain in the left knee	Septic arthritis	39	*S. aureus*	*S. aureus*	Drainage of abscess + arthroscopic lavage + vancomycin	Exitus
18	77	Male	DM + CVD	AVF	Fever and bilateral thigh pain	Multiple abscess in bilateral thigh	46	*Methicillin-resistant S. epidermidis*	Culture-negative	Drainage of abscesses + vancomycin	Complete recovery
19	89	Female	Chronic hepatitis C virus infection	TCC	Pain in the knees and swelling of the left foot	Osteomyelitis in the left foot	35	Unable to obtain culture material	*Methicillin-resistant S. epidermidis*	Vancomycin	Complete recovery

* Surgery was planned, but the patient refused it, ** Possibility of contamination, *** Hepatic abscess recurred 14 days later, **** Breast abscess relapsed 15 days later

DM: Diabetes mellitus, **TCC:** Tunneled cuffed permanent catheter, **AVF:** Arteriovenous fistula, **CAD:** Coronary artery disease, **COPD:** Chronic obstructive pulmonary disease, **ESBL:** Extended spectrum beta lactamase, **CVD:** Cerebrovascular disease

In conclusion, metastatic infection in HD patients, especially those with a tunneled cuffed HD catheter, is a serious complication, which may result in the patient's death. Gram-positive microorganisms are responsible for the majority of cases with metastatic infection.

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