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Case Report

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Hemodialysis Catheter-related Masses Case Report the Pro Inflammatory State in Chronic Kidney Disease

John D Rozich*, Jacob J Rozich, Thomas W Schultz and Noah S Rozich

Department of Medicine, Tuomey Hospital Sumter SC, USA

***Corresponding author**
Dr. John D Rozich, Department of Medicine, Tuomey Hospital Sumter, SC 29150, USA, Email: johnrozich@hotmail.com

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Abstract

Indwelling venous catheters provide essential functional vascular access for patients requiring emergent or urgent hemodialysis, though their long-term use is practically limited by known complications including increased rates of infection as compared with surgically created arteriovenous (AV) fistulas. Converging lines of evidence also support that chronic kidney disease (CKD) represents a pro-inflammatory state, an environment with active cellular and inflammatory pathobiology. Accordingly, implantation of catheters for even short-term use is associated with a fibrin-thrombin-cellular matrix often forming around the catheter. This "biomass" long considered innocuous, can cause occlusion of the catheter, contributing to reduced flow rates during dialysis. It may also result in embolic injury of downstream structures. This case report identifies a complex catheter-related biomass remaining after removal of the hemodialysis catheter and focuses on two concerns. First, intravenous masses associated with the catheter, or remaining after removal may provoke embolic and direct hemodynamic-related injury. But perhaps less obvious is their potential linkage to vascular immunoreactivity found in CKD. This latter potential may need to be part of the larger discussion surrounding the outcomes of such pathologic immunoresponsiveness in CKD patients on hemodialysis.

Introduction

A frequently encountered clinical challenge occurs when patients experience acute or chronic renal injury requiring hemodialysis in the setting of limited vascular access. Often, the setting is acute failure with hemodialysis indicated for volume overload, electrolyte abnormalities, acidosis or manifestations of uremia [1, 2]. This setting mandates time-sensitive vascular access most frequently accomplished via a two-port hemodialysis catheter allowing adequate flow rates [1]. Abundant literature details the many clinical issues encountered when hemodialysis is performed through use of venous catheters [3-8]. These include up to a seven-fold increase in rates of infection compared with surgically created arteriovenous (AV) fistulas and increased catheter-related thrombotic burden limiting flow rates and creating an embolic potential [9-12].

The increased thrombotic burden represents a spectrum of catheter-associated cellular matrix buildup that also consists of large bulky masses adherent to hemodialysis catheters [13-16]. These may not directly reduce flow rates but they are commonly detected within hours to days after catheter implant in the venous system. Such masses composed of fibrin-thrombin-cellular elements and may be sheared off or even remain attached to vascular structures once the hemodialysis catheter is removed [13, 15, 16]. They may then dislodge and directly injure downstream organ systems and nearby vasculature [6, 7]. We provide an example of a large catheter-associated "biomass" and its inherent pathological potential found on diagnostic Transesophageal echocardiography, present after the catheter was removed. The clinical concern at the time was its potential contribution to recurrent bacteremia.

But beyond the obvious infective, hemodynamic and anatomic injury potential, their linkage to vascular immunoreactivity found in CKD is of growing concern. This latter may be reflected in the noted pro-inflammatory state reported in CKD wherein immunoinflammatory activation could trigger or amplify formation of the biomass [17, 18]. This altered environment in CKD is thought to be important in the development of adverse cardiovascular (CV) outcomes, and we ask whether such vascular immunoreactivity ultimately contributes to characteristic vascular pathology in the form of accelerated coronary atherosclerotic disease found in hemodialysis patients [19-23].

Case

A 59 y.o. male undergoing hemodialysis for greater than 4 years had developed vascular access challenges 2 years into therapy, ultimately requiring prolonged use of an indwelling right subclavian venous catheter for maintenance hemodialysis. Despite rigorous sterility, 2 years into therapy, the patient developed 4 blood cultures positive for coagulation negative staphylococcus areas (CNSA) in the previous 3 weeks ultimately requiring removal of the dialysis catheter. Within 48 hours, 1 of 4 blood cultures was still positive for CNSA and a transthoracic followed by a trans esophageal echocardiogram were done showing a mass in the superior vena cava (SVC) extending

into the right atrium (Figures 1 & 2). This mass had the defining characteristic of a luminal echo lucent central area, compatible with this mass representing a fibrin thrombotic "wind sock" or "cast" that had formed (Figures 1&2) around the external surface of the hemodialysis catheter. Two cultures obtained shortly after catheter removal was positive, with four subsequent cultures negative for CNSA. Clinically the potential of this catheter associated biomass being the source of infection was entertained but cultures became negative and the patient improved clinically.

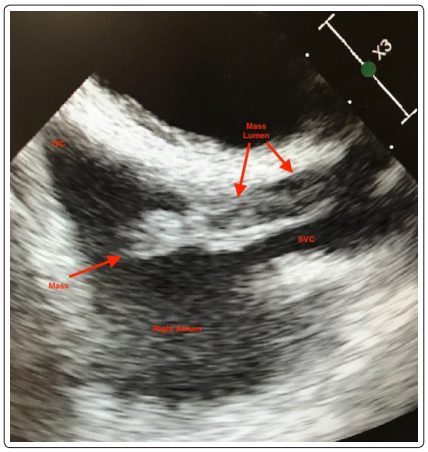

Figure 1: This thick-walled encasement on the longitudinal axis (Figure 1) showed the central echo lucent lumen likely formed around the external surface of the catheter. The distal end of the remnant cast is also striking for the multiple filamentous extensions. The biomass is in the superior vena cava and extends into the right atrium.

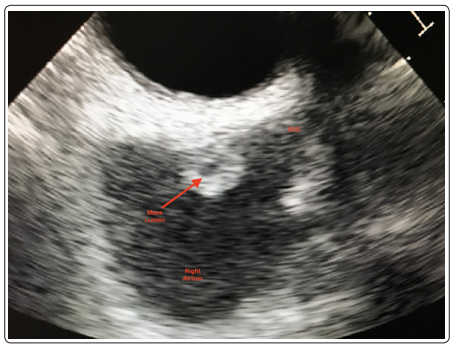

Figure 2: Same patient cross sectional short axis (Figure 2) showed the central circular lumen formed around the external surface of the catheter. The biomass is in the superior vena cava and extends into the right atrium.

Discussion

Acute or emergent hemodialysis is often accomplished by employing a 2-port catheter with access into the central venous system. Subsequent echocardiographic identification of the catheter-attached fibrin-thrombin-cellular matrix or biomass is so common as to be considered generally benign. It is reported that portions of the fibrin-thrombin biomass may remain adherent to the catheter or conversely may be sheared off and even remain in the venous system at the time of catheter removal through the skin [24-26]. As they are often identified in the subclavian veins, right atrium, superior vena cava (SVC) or right ventricle (RV), a knowledgeable echocardiographer will infer their presence and related etiology to a current or recently removed catheter [24-26].

Our patient demonstrated a remarkably intact residual encasement of what appears to be the entire longitudinal axis of the dialysis catheter attached to the SVC (Figures 1&2). This thick-walled encasement on the cross-sectional short axis (Figure 2) showed the circular lumen likely formed around the external surface of the catheter. The distal end of the remnant cast is also striking for the multiple filamentous extensions (Figure 1). It is unclear if these ribbon-like structures continue to change morphologically, either extending their length or thickening, however, there is likely a future/present embolic risk. Few reports identify specific variables that regulate the rate, amount or extent of catheter-related biomass formation, but our images support an extensive "coating" of the catheter possessing enough structural integrity to remain intact after the catheter itself was removed. It is also clear that embolization of part or all of this could have important clinical consequences [6, 7].

Anatomic Consequences and Beyond

While multiple reports document the direct injury potential of these catheter-related biomasses, including their potential for obstruction of flow and embolism, less is known about the cellular-fibrin matrix and its relationship to inflammation. Recent data supports both that CKD is a "proinflammatory state" and that nuanced biological communication from immune and inflammatory contribution cause vascular injury [27-31]. Although venous in location, growing evidence supports that heightened immunoinflammatory activity may "cross anatomic boundaries" and influence distant sites [21-23]. It is this resultant vascular damage mediated through heightened immune/inflammatory pathways that is suspected to have a primary role in the formation and propagation of coronary atherosclerosis. Of critical interest is whether such a proinflammatory state engenders a connection between arterial injury and subsequent adverse CV outcomes prevalent in CKD [21-23].

Recent findings show that "distant" vascular territories are impacted by stress from local bacterial infections [22, 32]. Thus, native vascular or immunoactive cells geographically removed from an initial bacterial pneumonia or diabetic foot infections may be activated and amplified in their expressive responses [32, 33]. This has been termed an "echo" effect and supports the observation that pneumonia is linked to increased thrombotic and adverse CV outcomes [22]. Therefore suggesting that a venous catheter may trigger immunologic and inflammatory activity that impacts distant arterial beds is consistent with reported observations. Systemic bacterial endotoxin can also activate a more reactive inflammatory biochemical profile in atherosclerotic arteries than in normal arteries [32]. This may hint at a responsible mechanism whereby periodontal or gram-negative bacteria are associated with increased CV ischemic outcomes [34].

Catheter use in hemodialysis provides fertile ground for vascular bacterial release [10, 12, 34]. But suggesting that catheter use is the sole or even critical proximate cause for immunoinflammatory vascular atheromatous damage in patients with CKD is almost assuredly an oversimplification. However, for many years nephrologists have observed that albumin levels inversely correlate with hemodialysis catheter use and may result from heightened inflammation [19, 35]. In fact, implanting a dialysis catheter has been demonstrated to be significantly correlated to higher C-reactive protein levels, while after catheter removal, these elevations return to baseline levels [19, 35]. These results concluded that the presence of a hemodialysis catheter is an independent determinant of an exaggerated inflammatory response in CKD requiring hemodialysis.

But patients requiring hemodialysis present with an etiologic spectrum of end stage CKD accompanied by multiple comorbidities each contributing to their CKD etiology and phenotype. These factors likely underwrite the "proinflammatory" state found in CKD, perhaps independently of subsequent modes of hemodialysis. A diverse source of bacterial products including endotoxins and heat-shock proteins that may cross epithelial barriers and generate local and systemic inflammatory injury from gastrointestinal microflora may also be an important contributor [36, 37]. Microbial pathogen associated molecular patterns (PAMPs), small molecular motifs conserved within a class of microbes, are hypothesized to activate innate immune receptors [38, 39]. These conserved molecular motifs are found within bacterial lipopolysaccharides, endotoxins located on the cell membranes of gram-negative bacteria, flagellum and lipoteichoic acid from gram-positive bacteria [40, 41]. When these PAMPs activate cellular immunity through toll-like receptors (TLRs), formyl-peptide receptors (FPRs) or C-type lectin receptors (CLRs), and Nod-like receptors (NLRs) for example, they are hypothesized to be responsible for leukocyte and vascular cell activation within atheromata [39, 42, 43]. This linkage of the inflammatory/immune systems to the development of atheroma likely support the disease progression to coronary artery disease and probably underwrite to a variable extent, the adverse CV outcomes witnessed in CKD [19, 44].

CKD Pro-Inflammation and Catheter "Biomass": Consequences?

While a variety of subtle immunologic-driven modulators may be active in patients with CKD and are believed to influence this proinflammatory microenvironment. A central focus of the present case is whether clinicians have underestimated the role of the catheter as it may serve as a "trip wire" in effect to boost both the local and perhaps also the systemic pre-existing inflammatory cascade harming downstream structures [45-49]. At the very least, this type of data have required reexamination of long held views that previously regarded catheter associated biomass as relatively benign as long as either the infective, embolic or thrombotic consequences were held in check. But the embolic and thrombotic consequences can be devastating and the frequency and cumulative impact may still be underappreciated [50-53]. The critical variables of this "perfect storm" in CKD remain speculative and largely unstudied, but the spectrum of pathology is tangible. Our concern is that catheter-related fibrin/thrombotic biomass volume in this environment can no longer be ignored or treated as innocuous.

Conclusion

There is recognition that indwelling venous dialysis catheters are associated with multiple adverse clinical events. These include a higher likelihood of bacterial infection and uncommon but not rare direct catheter-related erosive or embolic vascular injury. Our hypothesis further proposes that attached or residual fibrin/thrombotic biomasses occur more frequently, perhaps even after explantation of the catheter, and that they may carry additional complications related to proinflammatory disease pathophysiology and extending beyond the obvious embolic risk. These additional complications likely are mechanistically expressed within a sensitized or vulnerable host. Their potential role in recurrent vascular injury may be indirect, inconsequential or determinative. However, such venous catheter-biomass volume and/or related residua must be accounted for and investigated more fully if we are to improve the safety of catheter use in this vulnerable population.

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