CASE REPORT

Renal Replacement Therapy

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Abstract

Background Non-cuffed hemodialysis (HD) catheters are often used for emergency or temporary vascular access. Its complications include thrombosis and catheter-related bloodstream infection (CRBSI); however, thrombophlebitis can also occur. Thrombophlebitis of the internal jugular vein (IJV) may present with symptoms, such as fever, lateral neck pain, and swelling, regardless of the presence or absence of infection; however, symptoms may be minor and easily overlooked. Sore throat is a well-known symptom of Lemierre's syndrome, but has not been reported in cases of thrombophlebitis without infection. We report two cases of HD catheter-associated IJV thrombophlebitis in patients that were diagnosed with sore throat.

Case presentation Case 1 included a 58-year-old woman with diabetic nephropathy on HD. She was admitted to our hospital due to the occlusion of an arteriovenous fistula (AVF) for dialysis. A temporary HD catheter was placed in the right IJV until an arteriovenous graft (AVG) was fabricated. After admission, CRBSI was suspected because she developed fever; however, bacteremia was ruled out and a sore throat gradually developed. Contrast-enhanced computed tomography (CT) revealed thrombophlebitis of the right IJV. Anticoagulation therapy was initiated and she was discharged due to an improvement of symptoms. Case 2 included an 83-year-old man with end-stage renal disease due to hypertensive nephrosclerosis. He was admitted to our hospital because of AVF occlusion. A temporary HD catheter was inserted into the right IJV and an AVG was created. He had elevated C-reactive protein levels after catheter placement but was asymptomatic. When removing the catheter, he complained of throat discomfort. Ultrasonography of the neck revealed thrombotic obstruction of the right IJV, and contrast-enhanced CT revealed thrombotic obstruction of the right IJV, and contrast-enhanced CT revealed thrombotic obstruction of the right IJV, and contrast-enhanced CT revealed thrombotic by the regative. He was discharged after anticoagulation therapy was started and symptoms improved.

Conclusions The presence of sore throat leads to the diagnosis of IJV thrombophlebitis. Pharyngeal symptoms that develop after central venous catheter (CVC) placement should be differentiated from thrombophlebitis using a minimally invasive vascular ultrasound.

Keywords Vascular access catheter, Dialysis catheter, Noninfectious thrombophlebitis, Catheter-related thrombosis, Phlebitis

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Background

Vascular access is essential for hemodialysis (HD). The vascular access used in emergency or temporary situations is a non-cuffed HD catheter. The use of HD catheters for dialysis initiation should be avoided whenever possible due to the increased length of hospital stay, higher cost, and risk of complications [1]. However, although HD catheters are used less frequently than in the past, they are still frequently used due to lack of patient awareness and unforeseen circumstances [2]. In addition, HD catheters are also mainly used in maintenance dialysis patients as a bridging use until permanent vascular access is created. Unlike other central venous catheters (CVCs), HD catheters have a route for the withdrawal of blood for dialysis treatment and a route for returning blood; therefore, it has a larger catheter diameter [3]. Complications associated with HD catheter placement include catheter-related bloodstream infections (CRBSI), catheter dysfunction, and thrombosis. Thrombosis associated with CVC placement is considered frequent [3–5], and venous thrombosis can rarely cause phlebitis. Herein, we report two cases of HD catheter-related thrombophlebitis of the internal jugular vein (IJV). The clinical courses of the two cases were different; however, in both cases, the diagnosis was prompted by pharyngeal symptoms that mimicked Lemierre's syndrome.

Case presentation

Case 1 A 58-year-old woman, who had started hemodialysis for end-stage renal disease (ESRD) caused by diabetic nephropathy 5 years prior, was admitted to our hospital due to an occluded arteriovenous fistula (AVF) in her left forearm, which was used for dialysis. She had undergone vascular access intervention therapy (VAIVT) for AVF stenosis several months earlier, and restenosis was observed on admission. She had a history of surgery for breast and endometrial cancer, but had no history of oropharyngeal infection. A non-cuffed HD catheter (double lumen, polyurethane, 12 French) was placed in the right IJV on day 2 of admission until an arteriovenous graft (AVG) in the left forearm was fabricated on day 8. As the patient had persistent fever after catheter placement, CRBSI was suspected. The catheter was removed on day 9 of admission and antimicrobial therapy with vancomycin was initiated. However, the blood culture results were negative, and antibiotics were administered for 1 week. The fever persisted and the patient developed sore throat after a few days. Contrast-enhanced computed tomography (CT) on day 16 revealed a complete occlusion of the right IJV due to thrombus formation and phlebitis (Fig. 1a, b). The fever and sore throat were considered to have been caused by right IJV thrombophlebitis, as no other etiology could explain the symptoms. Anticoagulation therapy (initially with heparin 12,000 units per 24 h, then switched to warfarin) was initiated on day 16 and the patient was discharged due to an improvement of symptoms on day 25. Heparin was volume-adjusted to achieve an activated partial thromboplastin time (APTT) value of 1.5 to 2.0 times and warfarin doses were adjusted for prothrombin time international normalized ratio (PT-INR) of approximately 2.0. After discharge from the hospital, anticoagulation therapy was discontinued as the thrombus disappeared on day 162; however, severe venous stenosis of the right IJV persisted (Fig. 1c).



Fig. 1 Findings of contrast-enhanced computed tomography (CT) of the neck in Case 1. **a** The coronal view shows thrombosed obstructions (arrowheads) of the right internal jugular vein (IJV). **b** The horizontal view shows a right IJV thrombosis (arrowhead) with phlebitis, surrounding soft tissue inflammation, and enlarged lymph nodes (arrows). The thyroid cartilage deviates to the left. **c** The horizontal view after 1 year shows severe stenosis of the right IJV (arrowhead)

Case 2 An 83-year-old man with ESRD due to hypertensive nephrosclerosis, who was on maintenance HD for months, was admitted to our hospital because of AVF occlusion in his right forearm. He was taking antiplatelet medications for ischemic heart disease. There were no specific symptoms or abnormal physical findings on admission. He had a thrombotic occlusion caused by shunt vein stenosis, and there was a large thrombus in the shunt vein. A non-cuffed HD catheter (triple lumen, polyurethane, 12 French) was inserted into the right IJV on day 2 of admission and an AVG was created on the right elbow region on day 11. The patient had elevated C-reactive protein (CRP) levels (0.235 mg/dL on admission, 6.92-10.93 mg/dL on days 8-12) after catheter placement but was asymptomatic, and blood culture results obtained on day 8 were negative. After catheter removal on day 17, the patient complained of throat discomfort especially during swallowing. Ultrasonography of the neck on the same day revealed thrombotic obstruction of the right IJV (Fig. 2a, b), and a subsequent contrastenhanced CT on day 18 revealed thrombophlebitis of the right IJV (Fig. 2c) but there was no pulmonary embolism (PE). Furthermore, repeated blood culture results were negative. The patient's symptoms improved after anticoagulation therapy (continuous intravenous heparin 10,000 units per 24 h on day 17 of admission, followed by oral warfarin on day 19) was commenced, and he was discharged from the hospital on day 23.

Discussion and conclusions

Thrombophlebitis is a condition characterized by the inflammation of veins associated with venous thrombosis. Thrombophlebitis has been reported to be caused by infections, CVC placement, hypercoagulability, malignancy, and collagen disease [6–9]. Septic thrombophlebitis, such as Lemierre's syndrome due to oropharyngeal infection, is the widely recognized form of thrombophlebitis of IJV [6]. There have also been reports of IJV thrombophlebitis associated with CVC placement that is mostly associated with CRBSI [5, 7, 10, 11]. However, there are few reported cases of IJV thrombophlebitis that are not associated with infection.

We searched PubMed using the keywords (internal jugular vein AND catheter AND thrombophlebitis OR thrombosis) and excluded reports with no description of symptoms, treatment, or complications. We retrieved 12 relevant articles (Table 1) [10-21]. These articles included 14 patients with catheter-related IJV thrombosis, but only three cases of thrombophlebitis [10, 11, 13].

All these reports of IJV thrombophlebitis were associated with infection and showed symptoms such as fever and lateral neck pain and swelling, similar to catheterrelated IJV thrombosis. The same is true in reports of IJV thrombophlebitis due to causes other than catheters, and fever, lateral neck pain, and swelling are thought to be the main symptoms, regardless of the presence or absence of infection [6–9]. Septic thrombophlebitis with pharyngeal infection, as in Lemierre's syndrome, is often accompanied by a sore throat [6, 7]. However, some cases such as IJV thrombosis may be asymptomatic and easily missed [6, 22].

Herein, we report two interesting cases of CVC-related non-pyogenic thrombophlebitis of the IJV that presented with pharyngeal symptoms mimicking Lemierre's syndrome. Case 1 was accompanied by fever; however, Case 2 initially showed only elevated CRP levels on blood tests and minimal symptoms.

Although the clinical course was different, the pharyngeal symptoms led to the diagnosis of IJV thrombophlebitis. Sore throat is mainly caused by pharyngeal infections, often due to respiratory viruses and group A Streptococcus (GAS), which are spread by droplet



Fig. 2 Ultrasonographic and contrast-enhanced CT images in Case 2. Ultrasonographic images of the neck (**a**: cross section, **b**: longitudinal section) showing dilation of the right IJV and a heterogeneous hyperechoic mass in the lumen (arrowheads). Coronal CT image **c** showing a right IJV thrombus with surrounding soft tissue inflammation. The thrombus reaches the superior vena cava (arrowheads).

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| Table 1 | Case reports | and case s (| eries of IJV | ' thrombo | isis or thror | nbophleb | itis associat | ed with CVC | insertion | | | | | |
|----------------------|---------------------|-------------------------|--------------------------|----------------|---------------|--|---|---|---|--------------------------|---------------------------------|--|--------------------------|------------|
| Authors | Publication year | Country | Number of patients | Age (years) | Sex (M/F) | Catheter type | Insertion site | Thrombus location | Symptoms | Bloodstream infection | Associated factors | Treatment | Complications | References |
| Harter et al | 2002 | Germany | 4/233 | 40-64 | all F | CVC | N | <u>∼</u> | Erythema (122/233) and edema/ purulence (10/233) at entry site | Only one case | Malignancy | Not describe | None | 12 |
| et al | 2006 | USA | _ | 49 | Σ | CVC | Right JJV | Right UV | low grade fever, right-sided neck swell- ing and erythema, mandibular pain, and limitation of mouth opening | + | Testicular neoplasm | Antibiotics and surgical interven- tion | Thrombophle- bitis | m |
| Lee et al | 2006 | USA | - | 25 | Σ | HD cath- eter (tun- neled catheter) | Right JJV (previous left JJV cath- eter place- ment) | Right JJV, left subcla- vian vein, innominate vein and SVC | Left-sided neck and arm pain and swell- ing | 1 | ESRD | Intravenous anticoagu- lation, anti- biotics and thrombec- tomy | Chylous pericar- dium | 4 |
| Pratap et al | 2007 | India | - | 68 | Σ | HD cath- eter | Right JJV | Right JJV, subclavian vein and SVC | Fever and right-sided neck well- ing | I | ESRD and multiple myeloma | LMWH and warfarin | None | 15 |
| Saran- teas et al | 2009 | Greece | - | 30 | ≥ | CVC | Right JJV | Right JJV, brachio- cephalic vein, and persistent left SVC | No symp- tom | 1 | Multiple trauma | Heparin | 1 | 16 |
| Di Cocco et al | 2010 | Italy | _ | 52 | ш | U C C C | Right JV | Right JJV and SVC | Swelling of her face, upper chest, and arms, and distended veins over her chest wall | 1 | SdA | LMWH (90 U/kg every 12 h), warfarin (target PT- INR value 2.0–3.0, 6-month treatment course planned) | SVC syndrome | 11 |

| Authors | Publication year | Country | Number of patients | Age (years) | Sex (M/F) | Catheter type | Insertion site | Thrombus location | Symptoms | Bloodstream infection | Associated factors | Treatment | Complications | References |
|------------------|---------------------|-----------------|--|----------------|--------------|--|-------------------|---------------------------------------|---|--------------------------|-----------------------|--|---|---------------|
| Smith et al | 2012 | USA | | 58 | ш | HD cath- eter (tun- neled catheter) | Right IJV | Right IJV and sigmoid sinus | Headache and neck pain | 1 | ESRD | Heparin (weight- based pro- tocol) and warfarin | None | 18 |
| Minami et al | 2012 | Japan | - | 76 | ш | CVC | Right IJV | Right JJV | No symptom (external jugular vein dilatation) | I | Prone posi- tion | Catheter removal only | None | 6 |
| Caccese et al | 2012 | Italy | - | 68 | Σ | CVC | Right JJV | Right IJV and subcla- vian vein | Fever | + | Multiple trauma | Antifungal therapy and debride- ment of right JJV | Thrombophle- bitis | 10 |
| Binnani et al | 2012 | India | . | 21 | Z | HD cath- eter | Right JJV | Right JV and dural sinus | Fever, right-sided neck swell- ing, and generalized weakness | 1 | T | Heparin, antibiotics, thrombec- tomy and craniotomy | Hemorrhagic cerebral venous infarct | 20 |
| Hagiya et al | 2013 | Japan | . | 85 | Щ | CVC | Right IJV | RIGHT IJV and SVC | Fever and edema of right upper extremity | + | I | Antifungal therapy | Thrombophle- bitis | 1 |
| Ma et al | 2019 | China | - | 66 | × | CVC | Right JV | Right JV | Slight pain- ful swelling of his neck | I | CVC malpo- sition | LMWH (weight- adjusted doses) and rivaroxaban (long-term) | Pue | 21 |
| CVC; centra | I venous cathete | r, IJV; interna | l jugular vein | 1, LMWH; low | -molecular-v | veight hepar | rin, HD; hemo | idialysis, ESRD; e | ind-stage renal c | lisease, SVC; super | ior vena cava, Af | ⁵ 5; antiphospho | ipid syndrome, PT-I | NR; prothrom- |

Table 1 (continued)

Yoshida et al. Renal Replacement Therapy (2023) 9:4 Page 5 of 7

bin time international normalized ratio

infection [23]. The possibility that viral pharyngitis, a self-limiting condition, may have existed cannot be ruled out, because detailed observation of the pharynx was not performed in these cases. However, since there was no patient with similar symptoms in the same room, it is unlikely that acute pharyngitis was caused by inhaling infectious droplet; moreover, based on the clinical course, it is more reasonable to consider that the symptoms were associated with IJV thrombophlebitis. It may be a clinical manifestation of IJV thrombophlebitis due to the anatomically dense nature of this region, which would make it conducive to the spread of infection to adjacent structures, including the pharynx. CVC placement is a risk factor for venous thrombosis and thrombophlebitis [4, 5, 22]; therefore, pharyngeal symptoms in patients, after the placement of indwelling CVCs in the IJV, should be differentiated from thrombophlebitis; moreover, these symptoms should first be assessed for venous thrombus using a minimally invasive vascular ultrasound.

Our patients were later evaluated for thrombogenic predisposition; however, no previous thrombosis, new malignancy, or other causes, such as antiphospholipid syndrome or protein C and S deficiency were identified. However, Case 1 had a history of catheter placement, and repeated venous endothelial injury may have caused thrombophlebitis. Among CVCs, HD catheters are considered more prone to complications than other CVCs because of their larger diameter; therefore, special care should be taken when using HD catheters.

PE and infection were ruled out in our patients. However, PE, which can be fatal, is known to occur more frequently in patients with infectious thrombophlebitis [6, 7]. There were no cases of PE in catheter-related thrombosis, including catheter-related septic thrombophlebitis, as shown in Table 1. However, cases of serious complications such as SVC syndrome and the development of dural sinus thrombosis have been reported [17, 20]. Therefore, if a thrombus is found in the IJV on vascular ultrasound and thrombophlebitis is strongly suspected based on the clinical situation, infectious complications, PE, and extension of the IJV thrombus to other sites should be excluded, and CT scans would be useful to evaluate these complications.

In the treatment of infectious thrombophlebitis, appropriate treatment of the underlying infection is important, and anticoagulation therapy for the prevention of complications such as PE and post-thrombotic syndrome is considered on an individual basis [6, 7]. Thrombophlebitis without infection is considered equivalent to the treatment of venous thrombosis, but the indication for anticoagulation in venous thrombosis of the IJV is controversial [4, 24]. This is because the risk of developing PE or post-thrombotic syndrome,

which is a serious complication, varies in frequency depending on the venous site and literature [22, 24]. Most patients reported in Table 1 were treated with anticoagulants for venous thrombosis. Although it is difficult to explain the absence of PE in all cases as an effect of anticoagulation therapy, the absence of bleeding complications indicates a certain level of safety. We considered that the thrombus in our cases posed a high risk of PE because it was large and partially suspended; therefore, we administered antithrombotic therapy. No pulmonary embolization occurred and we confirmed that the thrombus had disappeared. However, in Case 1, the right IJV atrophied, and severe venous stenosis occurred after the thrombus disappeared. Similarly, in Case 2, the right IJV was atrophic and organic, and the collateral tract developed accordingly. There have been no detailed reports on the treatment and outcomes of non-infectious thrombophlebitis associated with CVC placement, and it would be desirable to accumulate more cases in the future to clarify the necessity of treatment.

In conclusion, the symptoms of IJV thrombophlebitis associated with CVC placement may be minimal; however, the presence of sore throat may lead to the diagnosis of IJV thrombophlebitis. Pharyngeal symptoms that develop after CVC placement should be differentiated from thrombophlebitis using a minimally invasive vascular ultrasound.

Abbreviations

| HD | Hemodialysis |
|--------|---|
| CVC | Central venous catheter |
| CRBSI | Central venous catheter-related bloodstream infection |
| IJV | Internal jugular vein |
| ESRD | End-stage renal disease |
| AVF | Arteriovenous fistula |
| AVG | Arteriovenous graft |
| CT | Computed tomography |
| APTT | Activated partial thromboplastin time |
| PT-INR | Prothrombin time international normalized ratio |
| CRP | C-reactive protein |
| PE | Pulmonary embolism |
| GAS | Group A Streptococcus |

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SY wrote the initial draft. SY, KU, TN, IN, and MW participated in the discussion and treatment of the patients. TN, IN, and MW reviewed and revised the manuscript accordingly. All authors have read and approved the final manuscript.

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All data and materials have been included in the manuscript.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Written informed consent was obtained from the patients for the publication of this article.

Competing interests

The authors declare that they have no competing interests.

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