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Case Report

Great Saphenous Vein Flow Pattern as a Simple Ultrasonographic Sign of Early Recanalization of Deep Vein Thrombosis: A Case Series Report

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We retrospectively examined patients with ultrasonographically occlusive acute proximal deep vein thrombosis (DVT). All patients were categorized into two groups on the basis of whether great saphenous vein (GSV) flow toward the common femoral vein was detected (flow [+]; n=10) or undetected (flow [–]; n=10). We investigated the relationship between the GSV flow pattern and DVT recanalization. Thrombus recanalization, which is defined as diameter reduction to lower than 40% of the vessel diameter, was confirmed in seven of the flow (+), and none of the flow (–). This study proposes that the GSV flow pattern may be a simple marker for the recanalization of proximal occlusive DVT.

Keywords: deep vein thrombosis, great saphenous vein, ultrasonography

Introduction

The frequency of incidence of deep vein thrombosis (DVT) has recently increased because of factors such as aging population, westernization of diet and lifestyle, and improvements in diagnostic techniques. Lately, ultrasonography (US) has become one of the leading reliable diagnostic techniques for DVT because of its noninvasiveness, convenience, and repeatability. Post-thrombotic syndrome (PTS) is the major chronic complication of DVT. Early recanalization of veins in occlusive DVT is imperative for the prevention of PTS because delayed thrombus regression could lead to the development of PTS.[1)]

In this case series report, we introduce an interesting case of a female patient with bilateral proximal DVT, whose left DVT was recanalized within 1 month, whereas the right DVT was not. Initial US findings revealed antegrade flow in the patient's left great saphenous vein (GSV), while retrograde flow was noted in the right GSV, which led us to focus on the relationship between the GSV flow pattern and DVT recanalization.

Case Report

An 85-year-old woman bedridden for spinocerebellar degeneration was transferred to our hospital with high fever and dyspnea. She was diagnosed with aspiration pneumonitis and, accordingly, antibiotics therapy was administered after emergent hospitalization. After 2 weeks, she presented edema in her bilateral lower limbs with an elevated D-dimer level (57.4 μg/mL). We suspected DVT since immobility is one of the risk factors associated with DVT.[2)] The subsequent US analysis revealed bilateral DVT from the inferior vena cava (IVC) to the popliteal vein (PopV), which filled the vessel lumen from the level of the common femoral vein (CFV) to the iliac vein (IV) (**Fig. 1**). **Figure 1** shows that the features of US appearance of thrombus such as echogenicity and mobility were equivalent in both limbs, except for the mode of the GSV flow pattern. While the patient's left GSV flow was antegrade, the right was retrograde. After 1-month heparinization, US analysis revealed recanalization in the left DVT but

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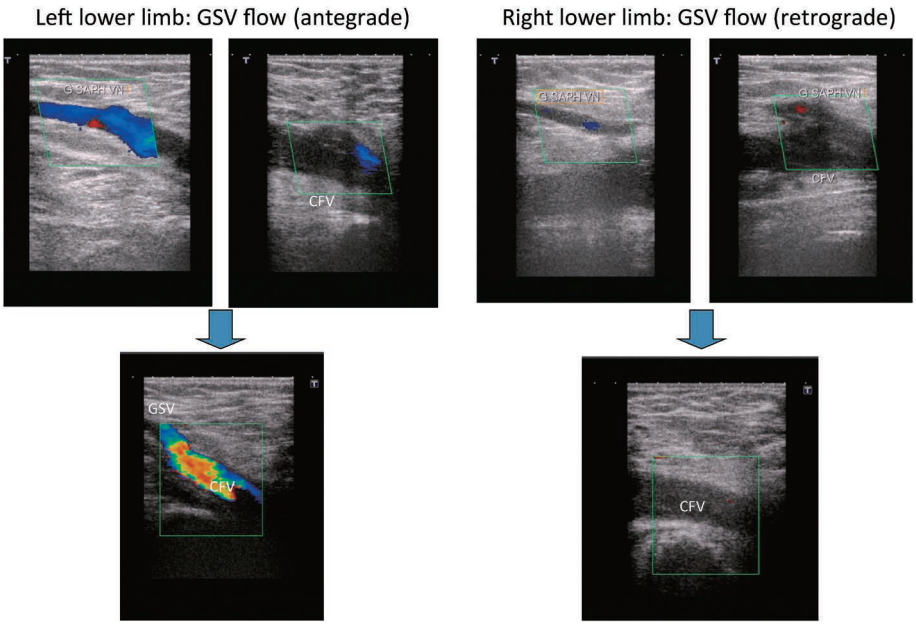

Fig. 1 Comparison of both lower limbs in the same patient. The patient had DVT in her bilateral lower limbs, with GSV flow (+) pattern on the left and GSV flow (−) pattern on the right. After 1 month, flow in the CFV was present on the left side, but not on the right side.

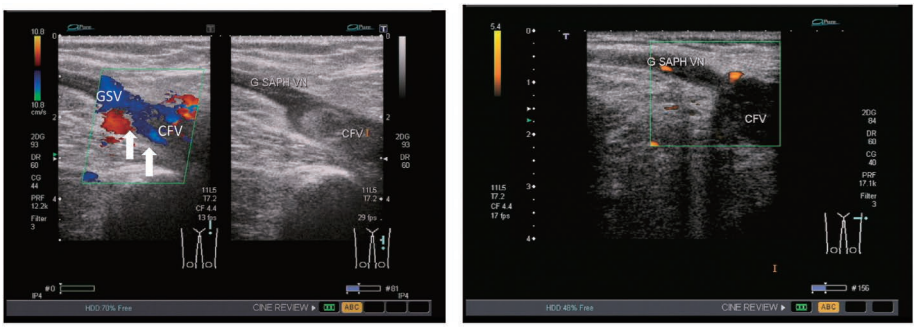

Fig. 2 The GSV flow patterns as on the US. Left, the GSV flow (+) pattern was defined as flow from the GSV to the CFV through the thrombosed segment, even if it was minuscule. Right, the GSV flow (−) pattern was defined as no flow from the GSV to the CFV, even if no thrombus was detected in the GSV (in such cases, the GSV flow entered collateral veins rather than the CFV). Note that the right panel showed an ultrasonogram of power Doppler mode, indicating no significant inflow to the CFV.

not in the right.

This finding led us to focus on the GSV flow pattern in patients with acute occlusive proximal DVT and to investigate whether the GSV flow into the CFV could be an essential sign of DVT recanalization.

We retrospectively evaluated patients with acute DVT that was considered ultrasonographically occlusive, and who presented from May 2006 to March 2017. The inclusion criteria were as follows: (a) DVT at a site from the superficial femoral vein (SFV)/PopV to the CFV/IV; and (b) the conduction of a follow-up examination by US at approximately 2 months after initial diagnosis. We excluded patients who had no follow-up US, had no thrombus at sites from the CFV to the SFV, or absence of data on the GSV flow pattern in the medical record. This study was approved by the Institutional Ethical Committee and was performed in accordance with the guidelines present in the Declaration of Helsinki version 2008.

To semiquantify thrombus echogenicity, we graded low, intermediate, or high echogenic appearance as 0, 1, or 2, respectively. While low-to-intermediate echogenicity was graded as 0.5, intermediate-to-high was graded as 1.5.

Table 1 The background characteristics and DVT change

	Inflow (+) (n=10)	Inflow (−) (n=10)	
Age (years)	77.0±10.1	70.7±10.0	N.S.
Male/female	4/6	6/4	N.S.
BMI (kg/m^2)	24.1±3.3	23.3±2.5	N.S.
Left limb/right limb	9/1	7/3	N.S.
Mobile thrombus (%)	0	0	N.A.
Echogenicity	0.6±0.6	0.9±0.5	N.S.
Cancer (%)	30.0	50.0	N.S.
Steroid (%)	30.0	10.0	N.S.
Immobility (%)	20.0	20.0	N.S.
D-dimer (μg/mL)	18.2 (13.4–27.1)	32.1 (11.0–38.3)	N.S.
APTT (sec)	65.4±29.4	59.6±22.0	N.S.
PT-INR	1.99±0.34	1.97±0.43	N.S.
IVC filter (%)	60.0	50.0	N.S.
PTE (%)	20.0	30.0	N.S.
Follow-up duration (weeks)	7.3±1.9	7.6±1.5	N.S.
D-dimer at US follow-up (μg/mL)	2.8 (1.1–4.7)	5.5 (1.1–6.2)	N.S.
Recanalization of thrombus (%)	70.0	0.0	P<0.01
PTS after 6 months (%)	25.0	50.0	N.S.

BMI: body mass index; APTT: activated partial thromboplastin time; PT-INR: prothrombin time-international normalization ratio; IVC: inferior vena cava; PTE: pulmonary thromboembolism; US: ultrasonography; PTS: post-thrombotic syndrome; N.S.: not significant; N.A.: not assessed

The recanalization of thrombus was defined as diameter reduction to lower than 40% of the vessel diameter by US, which is similar to the definition for residual vein thrombosis, a known risk factor associated with recurrent thrombotic events.[3] The assessment of the thrombus recanalization covered the entire scannable area from the IVC to the PopV as long as possible.

In this study, all patients were categorized into two groups based on whether or not the GSV flow toward the CFV across the thrombus was detected by color Doppler imaging. **Figure 2** shows representative GSV ultrasonograms. The presence/absence of the GSV flow into the CFV was determined using US; the GSV flow into the CFV (flow [+] pattern) was defined as the detection of flow from the GSV toward the CFV across the DVT site, even if it was diminutive. In contrast, the flow (−) pattern signified absence of flow from the GSV into the CFV or reversed from the CFV to the GSV, even if no thrombus was detected in the GSV (in such cases, the GSV flow entered the collateral veins rather than the CFV). All patients were treated with anticoagulants and were fitted with compression stockings. The standard regimen of anticoagulation therapy includes an intravenous bolus injection with 5,000 U of unfractionated heparin (UFH), followed by continuous intravenous infusion targeting 1.5–2.5 times the upper limit of activated partial thromboplastin time (APTT). Then, we replaced UFH with warfarin targeting prothrombin time-international normalization ratio (PT-INR) of 1.5–2.5 or direct oral anticoagulants.[4]

Data were summarized as mean ± standard deviation or median (interquartile range) for continuous variables or percentages. The two groups were compared using the unpaired two-sided Student t-test for continuous variables or the χ^2 test (Fisher's exact test) for categorical variables. We used EZR software for statistical analysis.[5]

In this study, we included 10 flow (+) limbs and 10 flow (−) limbs. **Table 1** presents the comparisons of characteristics between the two groups. The rate of IVC filter implantation was high because of the background characteristics of proximal DVT. We did not find any differences in background factors (e.g., age, sex, lesion site, thrombus echogenicity, follow-up period, or cancer prevalence) or laboratory data (e.g., D-dimer levels at the initial diagnosis or APTT on treatment). However, we determined that DVT demonstrated recanalization in seven limbs of the flow (+) group, whereas recanalization of DVT was not observed in any limb of the flow (−) group. Notably, the comparison of D-dimer levels at 2 months did not present significant differences between the two groups (5.5 μg/mL for the flow (−) group vs. 2.8 μg/mL for the flow (+) group, respectively; P = 0.32). The incidence rate of PTS during the first 6-month period was 50% (3 of 6) for the flow (−) group and 25% (2 of 8) for the flow (+) group, although the difference was not noted to be statistically significant.

Discussion

Caprini et al.[6] investigated the recanalization of acute DVT based on US findings and reported that the recanalization rates of DVT affecting the CFV at 1, 4, 12, and 24 weeks after the diagnosis were 6%, 20%, 54%, and 78%, respectively. In addition, they found similar rates of DVT recanalization at other sites.[6]

Regarding the US findings of the recanalization process, Puskás et al.[1] reported two main patterns of recanalization. However, these US findings can be challenging to detect.[1] This study highlighted that the antegrade GSV flow could be an easily visualizable sign of DVT recanalization.

The determination of the mechanisms of the antegrade GSV flow can be challenging. Several patients in this cohort had a massive thrombus that was connected with soleus muscle vein thrombosis, indicating that they may have propagated into the CFV and the IV. If so, the propagating thrombus could have gaps between the thrombus and the vein wall at the proximal region. In some cases, computed tomography (CT) findings revealed a ring-like enhancement around the thrombus, even though the venous flow could not be detected using Doppler study. Overall, in our opinion, gaps between the thrombus and the venous wall may be candidates for the drainage route of the GSV flow. In addition, reportedly, the flow itself could further enhance the recanalization process.[7,8]

This study has some limitations. First, owing to the retrospective study design, contrast-enhanced CT imaging was performed only in 40% of patients and the diagnosis was confirmed based on US findings. It is possible that some patients could benefit from avoiding the repeated exposure to a contrast medium in clinical settings. Second, the number of patients in this cohort is too small to derive a definitive conclusion. Hence, further large-scale, extensive, multicenter, and prospectively designed studies are warranted to overcome the limitations of this study. Finally, this study has a limitation in the GSV flow assessment. In the flow (+) group, three cases resulted in no recanalization. Of these, two cases exhibited a substantial reduction in the thrombus area at the site of the CFV close to the GSV inflow, although residual ultrasonographically occlusive thrombi at the further proximal site of the CFV or IV were detected. In these cases, we identified the development of collateral circulation that bypassed the thrombus of the upper site. The GSV flow assessment could not avoid such collateral cases, which is the limitation of this method. Hence, assessment using additional modalities, such as CT, is required for overcoming this limitation.

Conclusion

This study infers that the GSV flow into the CFV may be a simple marker of early recanalization of proximal ultrasonographically occlusive DVT. Thus, attention paid to the GSV flow using US could provide valuable information.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

Study conception and design: AO
Data collection: AO, IY
Data analysis: AO, YO
Writing: AO, YO
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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