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#33791 Summary

Summary | Review | Editing

Submission

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Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report

Lothar Matheus Manson Vanende Silalahi*[1,2], Justinus Agung Putranto[1]
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[2] Neurology Department, Siloam Hospitals, Yogyakarta Country

Abstract

Introduction: Cerebral venous thrombosis (CVT) is one type of uncommon stroke. CVT may be accompanied with hemorrhage. Anticoagulant remains the first-line treatment for CVT despite the presence of hemorrhage. We reported a hemorrhage CVT with favorably respond with anticoagulant without clinically bleeding complication. ***Case Presentation:*** We reported a 29-years-old Female, with acute onset headache, tingling and left-sided weakness. She had a history of preeclampsia, postpartum cardiomyopathy, and mitral regurgitation. On non-contrast head CT scan revealed right occipital subdural hemorrhage. During hospitalization, the neurological deficit worsened with new-onset seizure. Non-contrast head MRI MRA revealed occipital subacute hematoma and loss of right cerebral vein topography. The patient was treated with low-dose unfractionated heparin. After 5 days anticoagulation, neurological deficit improved with no bleeding complication. ***Conclusion :*** CVT may be accompanied with hemorrhage. Anticoagulation remains the first line treatment in CVT despite the hemorrhage. Clinician must consider the benefit and risk when treating hemorrhagic CVT with anticoagulant.

Keywords : anticoagulant, cerebral venous thrombosis, hemorrhage

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and reported annual incidence is about 5 per million.[1] CVT may be present with multiple signs and symptoms, mimicking other neurological disorder. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish.[2] Patients with CVT have a high mortality and morbidity, early recognition and of symptoms and treatment will improve outcome of these patients.[2,3]

On Imaging, CVT may be accompanied with hemorrhage.[4] One-third of CVT patients develop intracerebral hemorrhage or hemorrhagic venous infarct.[5] Presentation of hemorrhage in CVT make a diagnostic and therapeutic challenge.[4,6] There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factors in hemorrhagic CVT.[4]

Anticoagulation remains the first line treatment for CVT. Anticoagulation may prevent thrombus growth, to facilitate recanalization and to prevent deep vein thrombus.[5] In the managing CVT with hemorrhagic, physician must consider the benefit and risk of anticoagulation. Many literatures report that no adverse outcome when managing hemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of hemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established.[7] We reported a hemorrhagic CVT with favorably respond with anticoagulation.

CASE PRESENTATION

A 29-year-old Indonesian female, presented to the emergency department with 8 hours onset of weakness and tingling sensation in her left-side of body accompanied with progressive headache one day before admission. She denied any head trauma, fever, nausea, and vomiting. She had a history of postpartum cardiomyopathy with mitral regurgitation and severe preeclampsia 1 month before.

On examination, she was fully alert, mild headache (VAS Score: 3) and normal vital sign. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). Total NIHSS score were 3. Laboratory results were normal. Non-Contrast Head CT scan revealed a subdural hemorrhage on right occipital

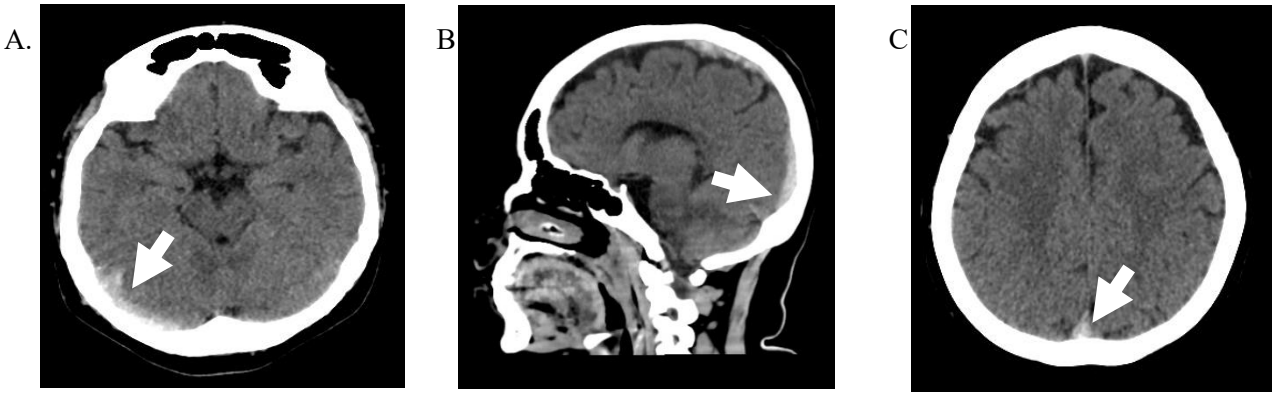

Figure 1. Non-Contrast Head CT scan
A and C. Axial view of subdural hemorrhage especially on right occipital (arrow) B. Subdural hemorrhage on sagittal view (arrow)

We assessed the patient as acute subdural hemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and continue the drugs for her cardiomyopathy and mitral regurgitation with candesartan, furosemide, spironolactone and bisoprolol.

Six hours after admission, focal-aware seizure occurred on her left side of body last for 2 minutes and spontaneously resolved. After the seizure, the left body weakness worsened and especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. During waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, last for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

Head MRI showed a subacute hemorrhagic lesion in occipital and revealed no subdural hemorrhage. On Head MRA revealed loss of normal cerebral vein topography on the right side. We found high blood D-dimer levels (4300 ng/mL)

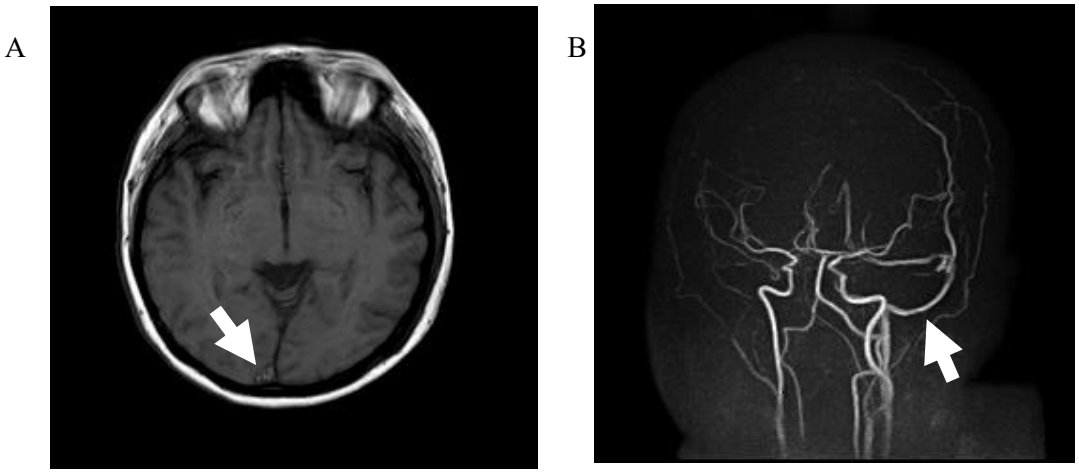

Figure 2. Non-Contrast Head MRI and MRA
A.Occipital Hemorrhage (arrow) B. Left Sigmoid Sinus (arrow) with loss off normal vein signal ont the rigt

Based in this result, we assessed the patient with cerebral venous thrombosis with hemorrhage. We stop the tranexamic acid and plan for anticoagulation with low dose unfractionated heparin, initial bolus dose 60 U/kgBW continued with 12 U/kg/BW/hour. We targeted for APTT 1,5-2 x control with fast bridging with oral warfarin 1 x 2 mg.

Six hours after anticoagulation, there was no seizure and the neurological deficit improved with NIHSS score 5. After 4 days anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3 and no bleeding complication. After 5 days anticoagulation, we stop the anticoagulant then the patient discharged with 2 mg oral warfarin for anticoagulation.

DISCUSSION

The main target of CVT therapy are initiating anticoagulant therapy, treating underlying causes such as sepsis, dehydration, prothrombotic drugs, and risk factors that trigger CVT, while ensuring patient stability by stopping seizures and managing elevated intracranial pressure if necessary [8,9]. Hemorrhage is one of the clinical features that occur in CVT patients, either naturally or associated with anticoagulation drugs [10]. In this case the bleeding was present at the time of admission, which created a dilemma in anticoagulation administration. Anticoagulant therapy is still recommended despite hemorrhage features in CVT [11,12]

Evidence for for choosing anticoagulation in treating cases of CVT remains weak because of the rarity of CVT. Therapy for CVT is guided by consensus and not from high-quality trials. Treatment with Unfractionated Heparin (UFH) or Low-Molecular-Weight Heparin (LMWH) is recommended in acute phase of CVT [13]. In the previous report, it was found that cases of death were found to be higher following the administration of UFH compared to LMWH but in general, clinician must balance the risks and benefits of anticoagulation depending on the clinical situatuion [11,14].

The choice of therapy recommendations in cases of pregnancy and puerperium is not different from cases of acute CVT in adults in general, the choice of therapy in pregnant women remains with LMWH because it has lower side effects such as osteoporosis, although both are safe because they do not cross the placenta. In lactating mothers and in the puerperium, LMWH and UFH and warfarin may be used [10]. In this case report, we use UFH because of the readiness of protamine sulfate as antidote and short-acting feature so that we may control the bleeding complication during anticoagulation.

The duration of oral anticoagulant therapy for CVT will depend on the patient's condition. The evidence whether long-term (>6 months) anticoagulation improve outcome in CVT remains weak. Long-term therapy is required for life in recurrent CVT, CVT followed by VTE, CVT with thrombophilia with INR target 2-3 [15]. It is suggested that using oral anticoagulant therapy with Vitamin K Antagonist (VKA) for 3-12 month to prevent reccurent CVT and other thromboembolic events [16]. Pregnant women and during the puerperium period can be given oral anticoagulant therapy for up to 6 weeks postpartum. It also recommended to replace all hormonal contraceptives to become non-hormonal [15].

CONCLUSION

Cerebral venous thrombosis is one type of uncommon stroke type. The manifestation of cerebral venous thrombosis may mimic the other neurological disease. The most common manifestation of cerebral venous thrombosis are headache and seizure. Cerebral venous thrombosis may be a diagnostic challenge, the recognition of risk factor and the clinical manifestation are important for the suspicion of cerebral venous thrombosis. Brain imaging combined with blood D-dimer levels may lead to confirm the cerebral venous thrombosis.

Imaging of cerebral venous thrombosis may accompanied with hemorrhage. Anticoagulation remains the first line treatment for cerebral venous thrombosis. Anticoagulation is beneficial in cerebral venous thrombosis with hemorrhage because of favorable outcome compared with if not anticoagulated. The evidence regarding anticoagulant type, dose, and optimal timing for hemorrhagic CVT remains unclear. Clinician must consider the benefit and risk when treating hemorrhage cerebral venous thrombosis with anticoagulant.

REFERENCES

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5. Ghandehari, K. *et al. Safety assessment of anticoagulation therapy in patients with hemorrhagic cerebral venous thrombosis*. *Ir J neurol* vol. 12 http://ijnl.tums.ac.ir (2013).
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14. Misra, U. K., Kalita, J., Chandra, S., Kumar, B. & Bansal, V. Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: A randomized controlled trial. *European Journal of Neurology* **19**, 1030–1036 (2012).
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Correspondence

Section Editor
2023-11-20 05:13 PM

Subject: [JKS] Editor Decision DELETE

lothar Lothar Matheus Manson Vanende Silalahi:

We have reached a decision regarding your submission to Jurnal Kedokteran Syiah Kuala, "Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report".

Our decision is: Revisions Required

Azzam Faiz Mutawakkil
Jurnal Kedokteran Syiah Kuala Unit, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh
Azzamfm_00@yahoo.com

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Author
2023-11-23 03:35 PM

Subject: Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report DELETE

I have revised and attached the full text and the description of the revision version.

Regards,

Lothar

JKS Jurnal Kedokteran Syiah Kuala

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Website: http://jurnal.usk.ac.id/JKS, e-mail: jks@usk.ac.id

REVIEWER SUMMARY

Article Code	:	JKS-33791
Title	:	Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report
First Author	:	Lothar Matheus Manson Vanende Silalahi, Justinus Agung Putranto

Editor Decision: Accept with revision

Comments for the author

Reviewer 1

1. Its better if in abstract and discussion the writers can discuss more detail the effect of post partum cardiomyopathy.
2. Its better if the treatment and the progress therapy can more detail day by day (can precented in table).
3. Is the publication ethics not available?
4. Please make the references using Harvard style.

Reviewer 2

1. Please make sure the case presentation as suggestion.
2. Please answer the question in the discussion about how is the therapy in breastfeeding woman.
3. Please add some references (if available) about the reccurent CVT.

Regard,
Fitra Fitra, Azzam Faiz Mutawakkil
JKS Editor
Faculty of Medicine, Universitas Syiah Kuala
Banda Aceh - Indonesia

Jurnal Kedokteran Syiah Kuala
Volume XX, Issue XX, Date (MM-YYYY)
Pages: XX

Case Report

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Lothar Matheus Manson Vanende Silalahi*[1,2], Justinus Agung Putranto[1]
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Abstract

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Keywords : anticoagulant, cerebral venous thrombosis, hemorrhage

Commented [Ma1]: Reviewer 1:
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INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and reported annual incidence is about 5 per million.[1] CVT may be present with multiple signs and symptoms, mimicking other neurological disorder. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish.[2] Patients with CVT have a high mortality and morbidity, early recognition and of symptoms and treatment will improve outcome of these patients.[2,3]

On Imaging, CVT may be accompanied with hemorrhage.[4] One-third of CVT patients develop intracerebral hemorrhage or hemorrhagic venous infarct.[5] Presentation of hemorrhage in CVT make a diagnostic and therapeutic challenge.[4,6] There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factors in hemorrhagic CVT.[4]

Anticoagulation remains the first line treatment for CVT. Anticoagulation may prevent thrombus growth, to facilitate recanalization and to prevent deep vein thrombus.[5] In the managing CVT with hemorrhagic, physician must consider the benefit and risk of anticoagulation. Many literatures report that no adverse outcome when managing hemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of hemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established.[7] We reported a hemorrhagic CVT with favorably respond with anticoagulation.

CASE PRESENTATION

A 29-year-old Indonesian female, presented to the emergency department with 8 hours onset of weakness and tingling sensation in her left-side of body accompanied with progressive headache one day before admission. She denied any head trauma, fever, nausea, and vomiting. She had a history of postpartum cardiomyopathy with mitral regurgitation and severe preeclampsia 1 month before.

On examination, she was fully alert, mild headache (VAS Score: 3) and normal vital sign. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). Total NIHSS score were 3. Laboratory results were normal. Non-Contrast Head CT scan revealed a subdural hemorrhage on right occipital

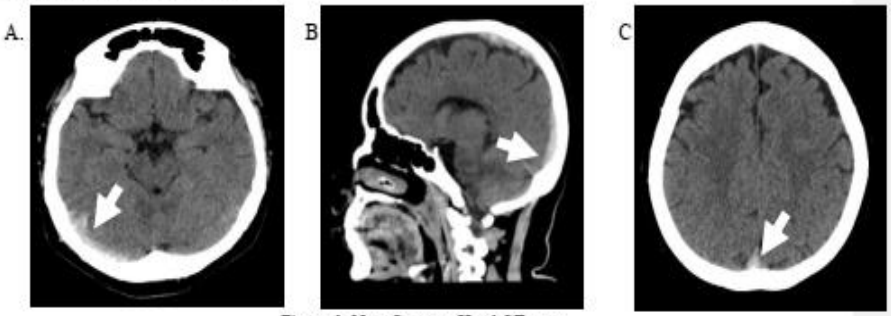

Figure 1. Non-Contrast Head CT scan
A and C. Axial view of subdural hemorrhage especially on right occipital (arrow) B. Subdural hemorrhage on sagittal view (arrow)

We assessed the patient as acute subdural hemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and continue the drugs for her cardiomyopathy and mitral regurgitation with candesartan, furosemide, spironolactone and bisoprolol.

Six hours after admission, focal-aware seizure occurred on her left side of body last for 2 minutes and spontaneously resolved. After the seizure, the left body weakness worsened and especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. During waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, last for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

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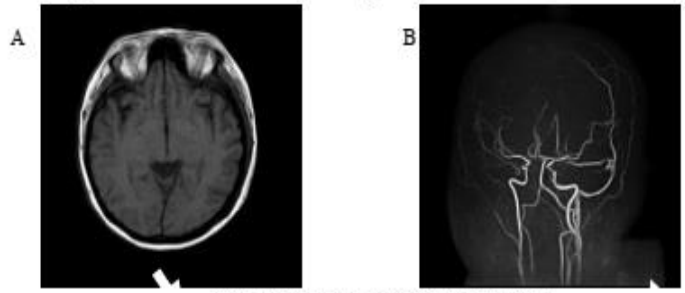

Figure 2. Non-Contrast Head MRI and MRA
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Commented [Ma2]: Reviewer 1:
Its better if the treatment and the progress therapy can more detail day by day (can precented in table).

Commented [Ma3]: Reviewer 2:
Any consultation with cardiologist for postpartum cardiomyopathy with mitral regurgitation at ward?

Please make it clear. Its CVT following witf SDH, or SDH following with CVT? Because the title is CVT

Based in this result, we assessed the patient with cerebral venous thrombosis with hemorrhage. We stop the tranexamic acid and plan for anticoagulation with low dose unfractionated heparin, initial bolus dose 60 U/kgBW continued with 12 U/kg/BW/hour. We targeted for APTT 1,5-2 x control with fast bridging with oral warfarin 1 x 2 mg.

Six hours after anticoagulation, there was no seizure and the neurological deficit improved with NIHSS score 5. After 4 days anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3 and no bleeding complication. After 5 days anticoagulation, we stop the anticoagulant then the patient discharged with 2 mg oral warfarin for anticoagulation.

Commented [Ma4]: Reviewer 2:
Patient condition at discharge?

DISCUSSION

The main target of CVT therapy are initiating anticoagulant therapy, treating underlying causes such as sepsis, dehydration, prothrombotic drugs, and risk factors that trigger CVT, while ensuring patient stability by stopping seizures and managing elevated intracranial pressure if necessary [8,9]. Hemorrhage is one of the clinical features that occur in CVT patients, either naturally or associated with anticoagulation drugs [10]. In this case the bleeding was present at the time of admission, which created a dilemma in anticoagulation administration. Anticoagulant therapy is still recommended despite hemorrhage features in CVT [11,12]

Evidence for for choosing anticoagulation in treating cases of CVT remains weak because of the rarity of CVT. Therapy for CVT is guided by consensus and not from high-quality trials. Treatment with Unfractionated Heparin (UFH) or Low-Molecular-Weight Heparin (LMWH) is recommended in acute phase of CVT [13]. In the previous report, it was found that cases of death were found to be higher following the administration of UFH compared to LMWH but in general, clinician must balance the risks and benefits of anticoagulation depending on the clinical situatuion [11,14].

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Commented [Ma5]: Reviewer 2:
How about breastfeeding woman?

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Commented [Ma6]: Reviewer 2:
Please add some references (if available) about the reccurent CVT

CONCLUSION

Cerebral venous thrombosis is one type of uncommon stroke type. The manifestation of cerebral venous thrombosis may mimic the other neurological disease. The most common manifestation of cerebral venous thrombosis are headache and seizure. Cerebral venous thrombosis may be a diagnostic challenge, the recognition of risk factor and the clinical manifestation are important for the suspicion of cerebral venous thrombosis. Brain imaging combined with blood D-dimer levels may lead to confirm the cerebral venous thrombosis.

Imaging of cerebral venous thrombosis may accompanied with hemorrhage. Anticoagulation remains the first line treatment for cerebral venous thrombosis. Anticoagulation is beneficial in cerebral venous thrombosis with hemorrhage because of favorable outcome compared with if not anticoagulated. The evidence regarding anticoagulant type, dose, and optimal timing for hemorrhagic CVT remains unclear. Clinician must consider the benefit and risk when treating hemorrhage cerebral venous thrombosis with anticoagulant.

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Commented [Ma7]: Reviewer 1: Harvard style

RESPONSE TO REVIEWERS COMMENT

Article Code	:	JKS-33791
Title	:	Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report
Author	:	Lothar Matheus Manson Vanende Silalahi, Justinus Agung Putranto

REVIEWER 1

Comment 1 :

Its better if in abstract and discussion the writers can discuss more detail the effect of post partum cardiomyopathy.

Answer : I add the effect of post partum cardiomyopathy in introduction section of abstract (green highlight, page 1, row 10-12) and in the first paragraph of discussion (green highlight, page 5, row 3-8)

Comment 2 :

Its better if the treatment and the progress therapy can more detail day by day (can precented in table).

Answer : I add the table on case report section (table 1, highlighted green, page 4) to show the clinical improvement and therapy during anticoagulation

Comment 3 :

Is the publication ethics not available?

Answer : The case report had been passed the publication ethics review by Health Research Ethics Comission of Siloam Hospitals Yogyakarta. I have declared the publication ethics in the fulltext, Introduction section (green highlight, page 2, row 22-24)

Comment 4 :

Please make the references using Harvard style.

Answer : I revised the references citation using Harvard Style (in the pararagraph and reference section) (green highlight, page 7-8)

Please mention the addition or revision part in the manuscript in page and line number with highlight or font color

REVIEWER 2

Comment 1 :

Please make sure the case presentation as suggestion.

Answer : I revised this case presentation as suggestion to clinician while treating hemorrhagic CVT with anticoagulant (yellow highlight on conclusion section of abstract, page 2, row 25-26 and on conclusion section, page 6, row 23-24)

Comment 2 :

Please answer the question in the discussion about how is the therapy in breastfeeding woman.

Answer : I add the explanation about therapy of CVT in breastfeeding woman in discussion section page 5 (yellow highlight, row 34-38)

Comment 3 :

Please add some references (if available) about the reccurent CVT.

Answer : I add some references about reccurent CVT on discussion section on page 6 (yellow highlight, row 6-9)

Please mention the addition or revision part in the manuscript in page and line number with highlight or font color

Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis with Post-Partum Cardiomyopathy: Case Report

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Abstract

Introduction

Cerebral venous thrombosis (CVT) is one type of uncommon stroke. The postpartum period is a risk factor for CVT. Cardiomyopathy increases the risk of CVT because of prothrombotic state. CVT may be accompanied with hemorrhage. Anticoagulant remains the first-line treatment for CVT despite the presence of hemorrhage. We reported a hemorrhage CVT with favorably responded with anticoagulant.

Case Report

We reported a 29-year-old Female, with acute onset headache, tingling, and left-sided weakness. She had a history of preeclampsia, postpartum cardiomyopathy, and mitral regurgitation. On non-contrast head CT scan revealed right occipital subdural hemorrhage. During hospitalization, the neurological deficit worsened with new-onset seizures. Non-contrast head MRI MRA revealed occipital subacute hematoma and loss of right cerebral vein topography. The patient was treated with low-dose unfractionated heparin. After 5 days of anticoagulation, the neurological deficit improved with no bleeding complication.

Conclusion

CVT may accompanied with hemorrhage. Anticoagulation remains the first-line treatment in CVT. We suggest clinicians to treat CVT with anticoagulant despite the presence of hemorrhage while considering the benefits and risks of the anticoagulant.

Keywords: cerebral venous thrombosis, anticoagulant, hemorrhage

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and the reported annual incidence is about 5 per million (Al-Sulaiman, 2019). CVT may be present with multiple signs and symptoms, mimicking other neurological disorders. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish (Idiculla et al., 2020). Patients with CVT have a high mortality and morbidity, early recognition of symptoms and treatment will improve the outcome of these patients (Bose et al., 2019; Idiculla et al., 2020).

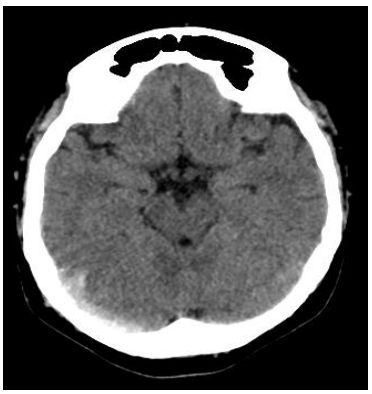
On Imaging, CVT may be accompanied with hemorrhage (Pongmoragot & Saposnik, 2012). One-third of CVT patients develop intracerebral hemorrhage or hemorrhagic venous infarct (Ghandehari et al., 2013). Presentation of hemorrhage in CVT makes a diagnostic and therapeutic challenge (Pongmoragot & Saposnik, 2012a; Shrestha et al., 2016). There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factor in hemorrhagic CVT (Pongmoragot & Saposnik, 2012).

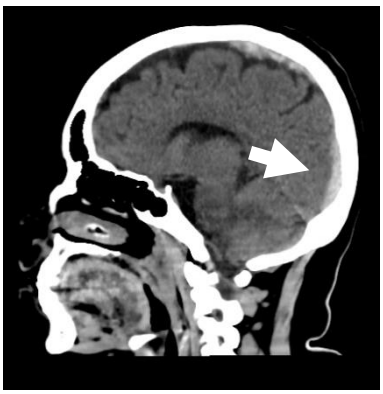
Anticoagulation remains the first-line treatment for CVT. Anticoagulation may prevent thrombus growth, facilitate recanalization, and prevent deep vein thrombus (Ghandehari et al., 2013). When managing CVT with hemorrhagic, physicians must consider the benefits and risks of anticoagulation. Many literatures report no adverse outcome when managing hemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of hemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established (Hegazi et al., 2009). We reported a hemorrhagic CVT with favorably responded with anticoagulation. This case report has passed the research ethics review from the Health Research Ethics Comission of Siloam Hospitals Yogyakarta.

CASE REPORT

A 29-year-old Indonesian female, presented to the emergency department with 8 hours onset of weakness and tingling sensation in her left side of body accompanied with progressive headache one day before admission. She denied any head trauma, fever, nausea, and vomiting. She had a history of postpartum cardiomyopathy with mitral regurgitation and severe preeclampsia 1 month before.

On examination, she was fully alert, mild headache (VAS Score: 3), and had normal vital signs. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). The total NIHSS score was 3. Laboratory results were normal. A non-contrast Head CT scan revealed a subdural hemorrhage on the right occipital.

A. 

B 

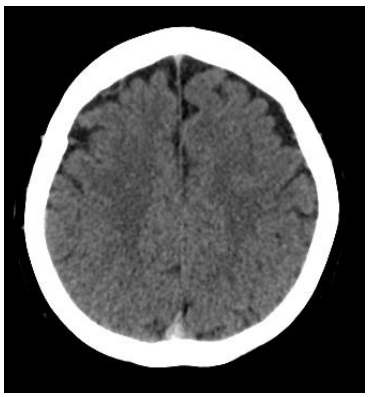
C 

Figure 1. Non-contrast Head CT scan

A and C. Axial view of subdural hemorrhage especially on right occipital B. Subdural Hemorrhage on sagittal view

We assessed the patient as acute subdural hemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and mecobalamin. Oral candesartan, furosemide, spironolactone, and bisoprolol were given after consultation with cardiologist for her cardiomyopathy and mitral regurgitation condition.

Six hours after admission, a focal-aware seizure occurred on the left side of body lasted for 2 minutes, and spontaneously resolved. After the seizure, the left body weakness worsened especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. While waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, lasting for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

Head MRI showed a subacute hemorrhagic lesion in the occipital and revealed no subdural hemorrhage. On Head MRA revealed loss of normal cerebral vein topography on the right side. The blood D-dimer level was 4300 ng/mL.

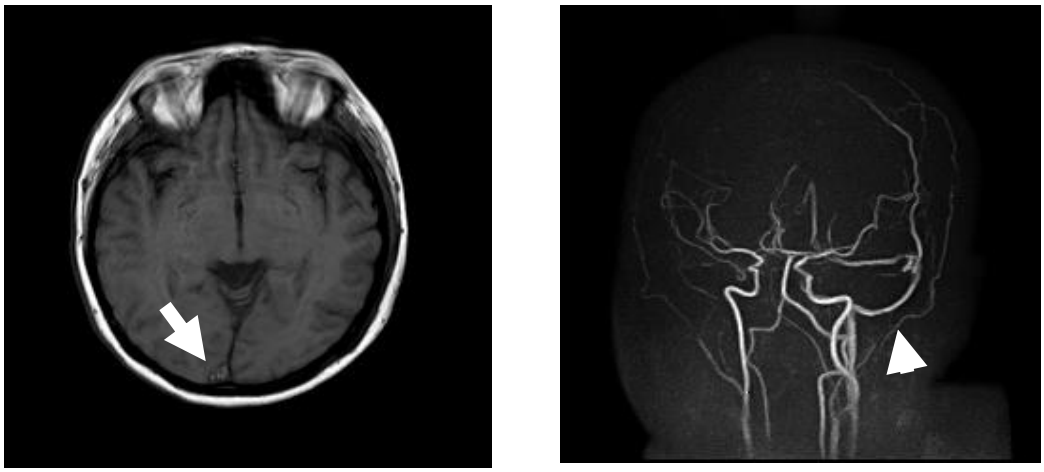


Figure 2. Non-Contrast Head MRI and MRA

A. Occipital Hemorrhage B. Spared Left Sigmoid Sinus

Based on this result, we assessed the patient with cerebral venous thrombosis with intracerebral hemorrhage. We stopped the tranexamic acid and planned anticoagulation with low dose unfractionated heparin, initial bolus dose of 60 U/kgBW continued with 12

U/kg/BW/hour. We targeted APTT 1,5-2 x control with fast bridging with warfarin 1 x 2 mg oral.

Six hours after anticoagulation, there was no seizure, and the neurological deficit improved with NIHSS score 5. After 4 days of anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3, and no bleeding complication. After 5 days of anticoagulation, we stopped the anticoagulant and then the patient was discharged with 2 mg oral warfarin for anticoagulation. The remaining neurological deficit when the patient discharged was left hemiparesis (muscle strength 4 in left upper and left-lower extremities) with NIHSS score 3.

Table 1. Follow-up during anticoagulation

	Before anticoagulation	Day 1 (during Anticoagulation)	Day 4 (during Anticoagulation)	Day 5 (during anticoagulation)
Subjective	Seizure recurrence, left-side weakness	No Seizure, improvement of left-sided weakness	No Seizure, improvement of left-sided weakness	No seizure
Objective	Left Hemiparesis on Upper and Lower Extremities (Muscle Strength: 1) NIHSS score: 9	Left Hemiparesis (Muscle Strength 4 on upper extremities, 3 on lower extremities) NIHSS score: 5	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities) NIHSS Score 3	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities) NIHSS Score 3
Therapy	Phenytoin 100 mg/8 hours IV	intravenous UFH	intravenous UFH	Intravenous UFH Stopped
Plan	Anticoagulation with UFH		Oral warfarin 2 mg	Oral warfarin 2 mg/day, discharged

DISCUSSION

We presented a case of CVT in post-partum period with postpartum cardiomyopathy. The postpartum period is a risk factor for CVT because transient prothrombotic condition. Pregnancy induces prothrombotic changes in the coagulation system dan persists during early puerperium. Volume depletion and trauma after pregnancy worsen the hypercoagulable state (Ferro et al., 2017). In this patient, cardiomyopathy also worsens the prothrombotic state and hypercoagulable state and increases the risk of venous thromboembolism in CVT (Fanola et al., 2020).

Computed Tomography (CT) is used as initial imaging in patients suspected of CVT. Anatomic variability of venous sinuses makes CT diagnosis of CVT insensitive. Hyperdensity of a cortical sign is a primary sign of acute CVT on non-contrast CT. Acutely thrombosed cortical veins and dural sinuses appear as a homogeneous hyperdensity that may be mimicking subdural hemorrhage as resulted in the initial CT of this patient (Pongmoragot & Saposnik, 2012).

The main target of CVT therapy is initiating anticoagulant therapy, treating underlying causes such as sepsis, dehydration, prothrombotic drugs, and risk factors that trigger CVT, while ensuring patient stability by stopping seizures and managing elevated intracranial pressure if necessary (Al-Sulaiman, 2019; Ulivi et al., 2020). Hemorrhage is one of the clinical

features that occur in CVT patients, either naturally or associated with anticoagulation drugs (Ferro et al., 2017). In this case, the bleeding was present at the time of admission, which created a dilemma in anticoagulation administration. Anticoagulant therapy is still recommended despite hemorrhage features in CVT (Gordon, 2004; Pongmoragot & Saposnik, 2012).

Evidence for choosing anticoagulation in treating cases of CVT remains weak because of the rarity of CVT. Therapy for CVT is guided by consensus and not from high-quality trials. Treatment with Unfractionated Heparin (UFH) or Low-Molecular-Weight Heparin (LMWH) is recommended in the acute phase of CVT (Field & Hill, 2019). In the previous report, it was found that cases of death were found to be higher following the administration of UFH compared to LMWH but in general, the clinician must balance the risks and benefits of anticoagulation depending on the clinical situation (Gordon, 2004; Misra et al., 2012).

The choice of therapy recommendations in cases of pregnancy and puerperium is not different from cases of acute CVT in adults in general, the choice of therapy in pregnant women remains with LMWH because it has lower side effects such as osteoporosis, although both are safe because they do not cross the placenta. In breastfeeding mothers and in the puerperium, LMWH and UFH and warfarin may be used (Ferro et al., 2017). The guideline also suggest giving anticoagulant in pregnant and puerperal women with acute CVT. Some anticoagulants that often used may be transferred to breast milk but no adverse effects reported and well-tolerated (Ferro et al., 2017). In this case report, we use UFH because of the readiness of protamine sulfate as antidote and short-acting feature so that we may control the bleeding complication during anticoagulation.

The duration of oral anticoagulant therapy for CVT will depend on the patient's condition. The evidence of whether long-term (>6 months) anticoagulation improves outcome in CVT remains weak. Long-term therapy is required for life in recurrent CVT, CVT followed by VTE, CVT with thrombophilia with INR target 2-3 (Idiculla et al., 2020b). It is suggested that using oral anticoagulant therapy with Vitamin K Antagonist (VKA) for 3-12 months to prevent recurrent CVT and other thromboembolic events (Ferro et al., 2017). Data regarded the recurrence of CVT are very limited. Although very rare, some studies found that history of venous thromboembolism and the presence of one or more anti-phospholipid antibodies (Shu et al., 2022). Pregnant women and women in the puerperium period can be given oral anticoagulant therapy for up to 6 weeks postpartum. It is also recommended to replace all hormonal contraceptives to become non-hormonal (Idiculla et al., 2020).

CONCLUSION

Cerebral venous thrombosis is one type of uncommon stroke type. The manifestation of cerebral venous thrombosis may mimic other neurological diseases. The most common manifestations of cerebral venous thrombosis are headache and seizure. Cerebral venous thrombosis may be a diagnostic challenge, the recognition of risk factors and the clinical manifestation are important for the suspicion of cerebral venous thrombosis. Brain imaging combined with blood D-dimer levels may lead clinicians to confirm cerebral venous thrombosis diagnosis.

Imaging of cerebral venous thrombosis may accompanied with hemorrhage. Anticoagulation remains the first-line treatment for cerebral venous thrombosis. The evidence regarding the anticoagulant type, dose, and optimal timing for hemorrhagic CVT remains unclear. Despite this limited evidence, we suggest clinicians to treat hemorrhagic CVT with anticoagulant while considering the benefits and risks of anticoagulant.

REFERENCES

Al-Sulaiman, A. (2019). Clinical aspects, diagnosis and management of cerebral vein and dural sinus thrombosis: A literature review. *Saudi Journal of Medicine and Medical Sciences*, *7*(3), 137. https://doi.org/10.4103/sjmms.sjmms_22_19

Bose, G., Graveline, J., Yogendrakumar, V., Fergusson, D., & Dowlatshahi, D. (2019). Direct oral anticoagulants in treatment of cerebral venous thrombosis: A systematic review protocol. In *Systematic Reviews* (Vol. 8, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13643-019-1022-8

Fanola, C. L., Norby, F. L., Shah, A. M., Chang, P. P., Lutsey, P. L., Rosamond, W. D., Cushman, M., & Folsom, A. R. (2020). Incident Heart Failure and Long-Term Risk for Venous Thromboembolism. *Journal of the American College of Cardiology*, *75*(2), 148–158. https://doi.org/10.1016/j.jacc.2019.10.058

Ferro, J. M., Bousser, M. G., Canhão, P., Coutinho, J. M., Crassard, I., Dentali, F., di Minno, M., Maino, A., Martinelli, I., Masuhr, F., de Sousa, D. A., & Stam, J. (2017). European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – Endorsed by the European Academy of Neurology. *European Stroke Journal*, *2*(3), 195–221. https://doi.org/10.1177/2396987317719364

Ferro, J. M., Bousser, M.-G., Canh~ Ao, P., Coutinho, J. M., Crassard, I., Dentali, F., Di Minno, M., Maino, A., Martinelli, I., Masuhr, F., Aguiar De Sousa, D., & Stam, J. (2017). European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis-endorsed by the European Academy of Neurology. *European Journal of Neurology*, *24*, 1203–1213. https://doi.org/10.1111/ene.13381

Field, T. S., & Hill, M. D. (2019). Cerebral Venous Thrombosis: We Should Ask the Right Questions to Get Better Answers. In *Stroke* (Vol. 50, Issue 6, pp. 1598–1604). Lippincott Williams and Wilkins. https://doi.org/10.1161/STROKEAHA.119.025334

Ghandehari, K., Riasi, H. R., Noureddine, A., Masoudinezhad, S., Yazdani, S., Mirzae, M. M., Razavi, A. S., & Ghandehari, K. (2013). Safety assessment of anticoagulation therapy in patients with hemorrhagic cerebral venous thrombosis. In *Ir J neurol* (Vol. 12, Issue 3). http://ijnl.tums.ac.ir

Gordon, D. L. (2004). The diagnosis and management of cerebral venous thrombosis. In *Handbook of Cerebrovascular Diseases, Second Edition, Revised and Expanded* (pp. 605–635). CRC Press. https://doi.org/10.1161/str.0b013e31820a8364

Hegazi, M. O., Ahmed, S., Sakr, M. G., & Hassanien, O. A. (2009). Anticoagulation for cerebral venous thrombosis with subarachnoid hemorrhage: A case report. *Medical Principles and Practice*, *19*(1), 73–75. https://doi.org/10.1159/000252839

Idiculla, P. S., Gurala, D., Palanisamy, M., Vijayakumar, R., Dhandapani, S., & Nagarajan, E. (2020). Cerebral Venous Thrombosis: A Comprehensive Review. In *European Neurology* (Vol. 83, Issue 4, pp. 369–379). S. Karger AG. https://doi.org/10.1159/000509802

Misra, U. K., Kalita, J., Chandra, S., Kumar, B., & Bansal, V. (2012). Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: A randomized controlled trial. *European Journal of Neurology*, *19*(7), 1030–1036. https://doi.org/10.1111/j.1468-1331.2012.03690.x

Pongmoragot, J., & Saposnik, G. (2012). Intracerebral hemorrhage from cerebral venous thrombosis. *Current Atherosclerosis Reports*, *14*(4), 382–389. https://doi.org/10.1007/s11883-012-0260-1

Shrestha, G. S., Poudyal, B. S., Sedain, G., Mahmud, K. I., & Acharya, N. (2016). Cerebral venous thrombosis presenting with intracerebral hemorrhage in a patient with paroxysmal nocturnal hemoglobinuria. *Indian Journal of Critical Care Medicine*, *20*(2), 117–119. https://doi.org/10.4103/0972-5229.175948

Shu, L., Bakradze, E., Omran, S. S., Giles, J., Amar, J., Henninger, N., Elnazeir, M., Liberman, A., Moncrieffe, K., Rotblat, J., Sharma, R., Cheng, Y., Zubair, A. S., Simpkins, A., Li, G., Kung, J., Perez, D., Heldner, M. R., Scutelnic, A., … Yaghi, S. (2022). Predictors of Recurrent Venous Thrombosis after Cerebral Venous Thrombosis: Analysis of the ACTION-CVT Study. *Neurology*, *99*(21), E2368–E2377. https://doi.org/10.1212/WNL.0000000000201122

Ulivi, L., Squitieri, M., Cohen, H., Cowley, P., & Werring, D. J. (2020). Cerebral venous thrombosis: A practical guide. In *Practical Neurology* (Vol. 20, Issue 5, pp. 356–367). BMJ Publishing Group. https://doi.org/10.1136/practneurol-2019-002415

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Summary | Review | Editing

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- Update citation using Mendeley Reference Manager with APA 7th Style (red highlight)
- Please make conclusion part more concise

Subject: Anticoagulation in Hemorrhagic Cerebral Venous Thrombosis

Comments *

Anticoagulation in haemorrhagic cerebral venous thrombosis with post-partum cardiomyopathy: Case Report

Lothar Matheus Manson Vanende Silalahi[1,2*], Justinus Agung Putranto[1]

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ABSTRACT

Introduction: Cerebral venous thrombosis (CVT) is one type of uncommon stroke. The postpartum period is a risk factor for CVT. Cardiomyopathy increases the risk of CVT because of prothrombotic state. CVT may be accompanied with haemorrhage. Anticoagulant remains the first-line treatment for CVT despite the presence of haemorrhage. We reported a haemorrhage CVT with favourably responded with anticoagulant.

Case Presentation : We reported a 29-year-old Female, with acute onset headache, tingling, and left-sided weakness. She had a history of preeclampsia, postpartum cardiomyopathy, and mitral regurgitation. On non-contrast head CT scan revealed right occipital subdural haemorrhage. During hospitalization, the neurological deficit worsened with new-onset seizures. Non-contrast head MRI MRA revealed occipital subacute hematoma and loss of right cerebral vein topography. The patient was treated with low-dose unfractionated heparin. After 5 days of anticoagulation, the neurological deficit improved with no bleeding complication.

Discussion :

Conclusion : CVT may accompanied with haemorrhage. Anticoagulation remains the first-line treatment in CVT. We suggest clinicians to treat CVT with anticoagulant despite the presence of haemorrhage while considering the benefits and risks of the anticoagulant.

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and the reported annual incidence is about 5 per million (Al-Sulaiman, 2019). CVT may be present with multiple signs and symptoms, mimicking other neurological disorders. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish (Idiculla et al.,

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On Imaging, CVT may be accompanied with haemorrhage (Pongmoragot & Saposnik, 2012). One-third of CVT patients develop intracerebral haemorrhage or haemorrhagic venous infarct (Ghandehari et al., 2013). Presentation of haemorrhage in CVT makes a diagnostic and therapeutic challenge (Pongmoragot & Saposnik, 2012a; Shrestha et al., 2016). There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factor in haemorrhagic CVT (Pongmoragot & Saposnik, 2012).

Anticoagulation remains the first-line treatment for CVT. Anticoagulation may prevent thrombus growth, facilitate recanalization, and prevent deep vein thrombus (Ghandehari et al., 2013). When managing CVT with haemorrhagic, physicians must consider the benefits and risks of anticoagulation. Many literatures report no adverse outcome when managing haemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of haemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established (Hegazi et al., 2009). We reported a haemorrhagic CVT with favorably responded with anticoagulation. This case report has passed the research ethics review from the Health Research Ethics Comission of Siloam Hospitals Yogyakarta.

CASE PRESENTATION

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On examination, she was fully alert, mild headache (VAS Score: 3), and had normal vital signs. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). The total NIHSS score was 3. Laboratory results were normal. A non-contrast Head CT scan revealed a subdural haemorrhage on the right occipital.

A.

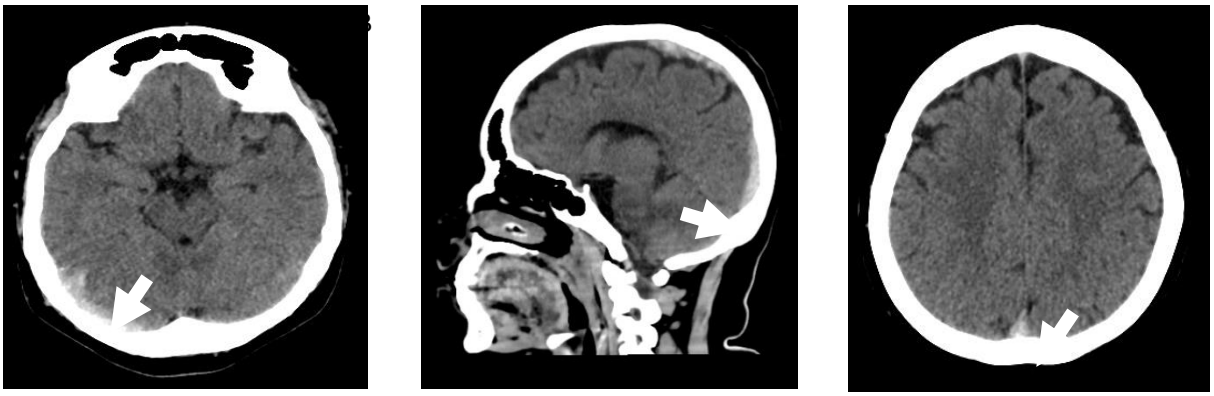

Figure 1. Non-contrast Head CT scan

A and C: Axial view of subdural haemorrhage especially on right occipital

B: Subdural Haemorrhage on sagittal view

We assessed the patient as acute subdural haemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and mecobalamin. Oral candesartan, furosemide, spironolactone, and bisoprolol were given after consultation with cardiologist for her cardiomyopathy and mitral regurgitation condition.

Six hours after admission, a focal-aware seizure occurred on the left side of body lasted for 2 minutes, and spontaneously resolved. After the seizure, the left body weakness worsened especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. While waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, lasting for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

Head MRI showed a subacute haemorrhagic lesion in the occipital and revealed no subdural haemorrhage. On Head MRA revealed loss of normal cerebral vein topography on the right side. The blood D-dimer level was 4300 ng/mL.

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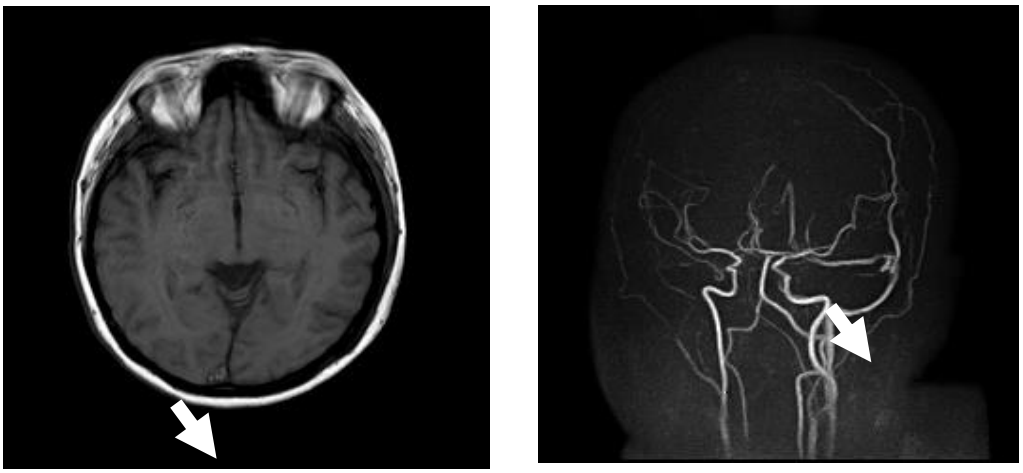

Figure 2. Non-Contrast Head MRI and MRA

A: Occipital Haemorrhage B: Spared Left Sigmoid Sinus

Based on this result, we assessed the patient with cerebral venous thrombosis with intracerebral haemorrhage. We stopped the tranexamic acid and planned anticoagulation with low dose unfractionated heparin, initial bolus dose of 60 U/kgBW continued with 12 U/kg/BW/hour. We targeted APTT 1,5-2 x control with fast bridging with warfarin 1 x 2 mg oral.

Table 1. Follow-up during anticoagulation

	Before anticoagulation	**Day 1 (during Anticoagulation)**	**Day 4 (during Anticoagulation)**	**Day 5 (during anticoagulation)**
Subjective	Seizure recurrence, left-side weakness	No Seizure, improvement of left-sided weakness	No Seizure, improvement of left-sided weakness	No seizure
Objective	Left Hemiparesis on Upper and Lower Extremities (Muscle Strength: 1)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 3 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)
	NIHSS score: 9	NIHSS score: 5	NIHSS Score 3	NIHSS Score 3
Therapy	Phenytoin 100 mg/8 hours IV	intravenous UFH	intravenous UFH	Intravenous UFH Stopped
Plan	Anticoagulation with UFH		Oral warfarin 2 mg	Oral warfarin 2 mg/day, discharged

Six hours after anticoagulation, there was no seizure, and the neurological deficit improved with NIHSS score 5. After 4 days of anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3, and no bleeding complication. After 5 days of anticoagulation, we stopped the anticoagulant and then the patient was discharged with 2 mg oral warfarin for anticoagulation. The remaining neurological deficit when the patient discharged was left hemiparesis (muscle strength 4 in left upper and left-lower extremities) with NIHSS score 3.

DISCUSSION

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Evidence for choosing anticoagulation in treating cases of CVT remains weak because of the rarity of CVT. Therapy for CVT is guided by consensus and not from high-quality trials. Treatment with Unfractionated Heparin (UFH) or Low-Molecular-Weight Heparin (LMWH) is recommended in the acute phase of CVT (Field & Hill, 2019). In the previous report, it was found that cases of death were found to be higher following the administration of UFH compared to LMWH but in general, the clinician must balance the risks and benefits of anticoagulation depending on the clinical situation (Gordon, 2004; Misra et al., 2012).

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CONCLUSION

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Imaging of cerebral venous thrombosis may accompany with haemorrhage. Anticoagulation remains the first-line treatment for cerebral venous thrombosis. The evidence regarding the anticoagulant

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REFERENCES

Al-Sulaiman, A. (2019a). Clinical aspects, diagnosis and management of cerebral vein and dural sinus thrombosis: A literature review. *Saudi Journal of Medicine and Medical Sciences*, *7*(3), 137. https://doi.org/10.4103/sjmms.sjmms_22_19

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Gordon, D. L. (2004). The diagnosis and management of cerebral venous thrombosis. In *Handbook of Cerebrovascular Diseases, Second Edition, Revised and Expanded* (pp. 605–635). CRC Press. https://doi.org/10.1161/str.0b013e31820a8364

Hegazi, M. O., Ahmed, S., Sakr, M. G., & Hassanien, O. A. (2009). Anticoagulation for cerebral venous thrombosis with subarachnoid hemorrhage: A case report. *Medical Principles and Practice*, *19*(1), 73–75. https://doi.org/10.1159/000252839

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Misra, U. K., Kalita, J., Chandra, S., Kumar, B., & Bansal, V. (2012). Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: A randomized controlled trial. *European Journal of Neurology*, *19*(7), 1030–1036. https://doi.org/10.1111/j.1468-1331.2012.03690.x

Pongmoragot, J., & Saposnik, G. (2012a). Intracerebral hemorrhage from cerebral venous thrombosis. *Current Atherosclerosis Reports*, *14*(4), 382–389. https://doi.org/10.1007/s11883-012-0260-1

Pongmoragot, J., & Saposnik, G. (2012b). Intracerebral hemorrhage from cerebral venous thrombosis. *Current Atherosclerosis Reports*, *14*(4), 382–389. https://doi.org/10.1007/s11883-012-0260-1

Shrestha, G. S., Poudyal, B. S., Sedain, G., Mahmud, K. I., & Acharya, N. (2016). Cerebral venous thrombosis presenting with intracerebral hemorrhage in a patient with paroxysmal nocturnal hemoglobinuria. *Indian Journal of Critical Care Medicine*, *20*(2), 117–119. https://doi.org/10.4103/0972-5229.175948

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Ulivi, L., Squitieri, M., Cohen, H., Cowley, P., & Werring, D. J. (2020). Cerebral venous thrombosis: A practical guide. In *Practical Neurology* (Vol. 20, Issue 5, pp. 356–367). BMJ Publishing Group. https://doi.org/10.1136/practneurol-2019-002415

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Anticoagulation in haemorrhagic cerebral venous thrombosis with post-partum cardiomyopathy: Case Report

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ABSTRACT

Introduction: Cerebral venous thrombosis (CVT) is one type of uncommon stroke. The postpartum period is a risk factor for CVT. Cardiomyopathy increases the risk of CVT because of prothrombotic state. CVT may be accompanied with haemorrhage. We reported a haemorrhage CVT with favourably responded with anticoagulant.

Case Presentation : We reported a 29-year-old Female, with acute onset headache, tingling, and left-sided weakness. She had a history of preeclampsia, postpartum cardiomyopathy, and mitral regurgitation. On non-contrast head CT scan revealed right occipital subdural haemorrhage. During hospitalization, the neurological deficit worsened with new-onset seizures. Non-contrast head MRI MRA revealed occipital subacute hematoma and loss of right cerebral vein topography. The patient was treated with low-dose unfractionated heparin (UFH). After 5 days of anticoagulation, the neurological deficit improved with no bleeding complication.

Discussion : Anticoagulant therapy is still recommended despite haemorrhage features in CVT. The choice of CVT therapy recommendations in cases of pregnancy and puerperium is not different. We use UFH because of the readiness of protamine sulfate as antidote and short-acting feature so that we may control the bleeding complication.

Conclusion : CVT may accompanied with haemorrhage. Anticoagulation remains the first-line treatment in CVT. We suggest clinicians to treat CVT with anticoagulant despite the presence of haemorrhage while considering the benefits and risks of the anticoagulant.

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and the reported annual incidence is about 5 per million (Al-Sulaiman, 2019). CVT may be present with multiple signs and symptoms, mimicking other neurological disorders. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish (Idiculla et al., 2020). Patients with CVT have a high mortality and morbidity, early recognition of symptoms and treatment will improve the outcome of these patients (Bose et al., 2019; Idiculla et al., 2020).

On Imaging, CVT may be accompanied with haemorrhage (Pongmoragot & Saposnik, 2012). One-third of CVT patients develop intracerebral haemorrhage or haemorrhagic venous infarct (Ghandehari et al., 2013). Presentation of haemorrhage in CVT makes a diagnostic and therapeutic challenge (Pongmoragot & Saposnik, 2012a; Shrestha et al., 2016). There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factor in haemorrhagic CVT (Pongmoragot & Saposnik, 2012).

Anticoagulation remains the first-line treatment for CVT. Anticoagulation may prevent thrombus growth, facilitate recanalization, and prevent deep vein thrombus (Ghandehari et al., 2013). When managing CVT with haemorrhagic, physicians must consider the benefits and risks of anticoagulation. Many literatures report no adverse outcome when managing haemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of haemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established (Hegazi et al., 2009). We reported a haemorrhagic CVT with favorably responded with anticoagulation. This case report has passed the research ethics review from the Health Research Ethics Comission of Siloam Hospitals Yogyakarta.

CASE PRESENTATION

A 29-year-old Indonesian female, presented to the emergency department with 8 hours onset of weakness and tingling sensation in her left side of body accompanied with progressive headache one day before admission. She denied any head trauma, fever, nausea, and vomiting. She had a history of postpartum cardiomyopathy with mitral regurgitation and severe preeclampsia 1 month before.

On examination, she was fully alert, mild headache (VAS Score: 3), and had normal vital signs. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). The total NIHSS score was 3. Laboratory results were normal. A non-contrast Head CT scan revealed a subdural haemorrhage on the right occipital.

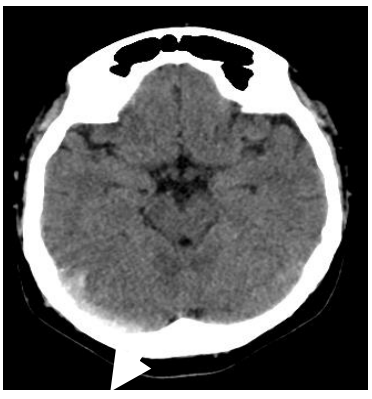
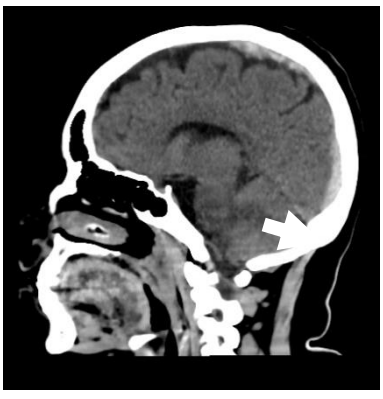
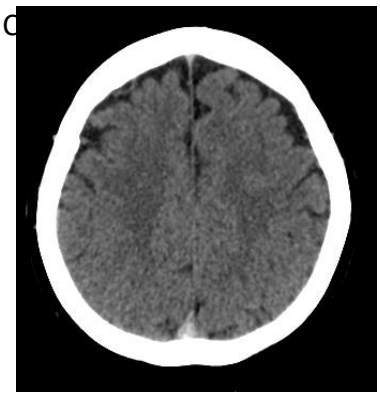
A.  B  C 

Figure 1. Non-contrast Head CT scan

A and C: Axial view of subdural haemorrhage especially on right occipital

B: Subdural Haemorrhage on sagittal view

We assessed the patient as acute subdural haemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and mecobalamin. Oral candesartan, furosemide, spironolactone, and bisoprolol were given after consultation with cardiologist for her cardiomyopathy and mitral regurgitation condition.

Six hours after admission, a focal-aware seizure occurred on the left side of body lasted for 2 minutes, and spontaneously resolved. After the seizure, the left body weakness worsened especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. While waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, lasting for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

Head MRI showed a subacute haemorrhagic lesion in the occipital and revealed no subdural haemorrhage. On Head MRA revealed loss of normal cerebral vein topography on the right side. The blood D-dimer level was 4300 ng/mL.

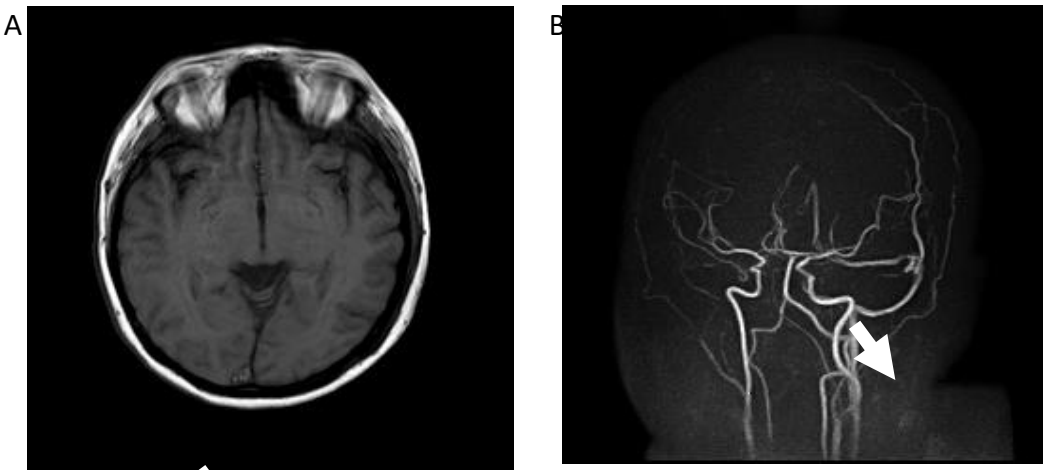


Figure 2. Non-Contrast Head MRI and MRA

A: Occipital Haemorrhage B: Spared Left Sigmoid Sinus

Based on this result, we assessed the patient with cerebral venous thrombosis with intracerebral haemorrhage. We stopped the tranexamic acid and planned anticoagulation with low dose unfractionated heparin, initial bolus dose of 60 U/kgBW continued with 12 U/kg/BW/hour. We targeted APTT 1,5-2 x control with fast bridging with warfarin 1 x 2 mg oral.

Table 1. Follow-up during anticoagulation

	Before anticoagulation	Day 1 (during Anticoagulation)	Day 4 (during Anticoagulation)	Day 5 (during anticoagulation)
Subjective	Seizure recurrence, left-side weakness	No Seizure, improvement of left-sided weakness	No Seizure, improvement of left-sided weakness	No seizure
Objective	Left Hemiparesis on Upper and Lower Extremities (Muscle Strength: 1)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 3 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)
Therapy	NIHSS score: 9 Phenytoin 100 mg/8 hours IV	NIHSS score: 5 intravenous UFH	NIHSS Score 3 intravenous UFH	NIHSS Score 3 Intravenous UFH Stopped
Plan	Anticoagulation with UFH		Oral warfarin 2 mg	Oral warfarin 2 mg/day, discharged

Six hours after anticoagulation, there was no seizure, and the neurological deficit improved with NIHSS score 5. After 4 days of anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3, and no bleeding complication. After 5 days of anticoagulation, we stopped the anticoagulant and then the patient was discharged with 2 mg oral warfarin for anticoagulation. The remaining neurological deficit when the patient discharged was left hemiparesis (muscle strength 4 in left upper and left-lower extremities) with NIHSS score 3.

DISCUSSION

We presented a case of CVT in post-partum period with postpartum cardiomyopathy. The postpartum period is a risk factor for CVT because transient prothrombotic condition. Pregnancy induces prothrombotic changes in the coagulation system dan persists during early puerperium. Volume depletion and trauma after pregnancy worsen the hypercoagulable state (Ferro et al., 2017). In this patient, cardiomyopathy also worsens the prothrombotic state and hypercoagulable state and increases the risk of venous thromboembolism in CVT (Fanola et al., 2020).

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REFERENCES

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Anticoagulation in haemorrhagic cerebral venous thrombosis with post-partum cardiomyopathy: Case Report

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ABSTRACT

Introduction: Cerebral venous thrombosis (CVT) is one type of uncommon stroke. The postpartum period is a risk factor for CVT. Cardiomyopathy increases the risk of CVT because of prothrombotic state. CVT may be accompanied with haemorrhage. We reported a haemorrhage CVT with favourably responded with anticoagulant.
Case Presentation: We reported a 29-year-old Female, with acute onset headache, tingling, and left-sided weakness. She had a history of preeclampsia, postpartum cardiomyopathy, and mitral regurgitation. On non-contrast head CT scan revealed right occipital subdural haemorrhage. During hospitalization, the neurological deficit worsened with new-onset seizures. Non-contrast head MRI MRA revealed occipital subacute hematoma and loss of right cerebral vein topography. The patient was treated with low-dose unfractionated heparin (UFH). After 5 days of anticoagulation, the neurological deficit improved with no bleeding complication.
Discussion: Anticoagulant therapy is still recommended despite haemorrhage features in CVT. The choice of CVT therapy recommendations in cases of pregnancy and puerperium is not different. We use UFH because of the readiness of protamine sulphate as antidote and short-acting feature so that we may control the bleeding complication.
Conclusion: CVT may accompanied with haemorrhage. Anticoagulation remains the first-line treatment in CVT. We suggest clinicians to treat CVT with anticoagulant despite the presence of haemorrhage while considering the benefits and risks of the anticoagulant.

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is one type of stroke commonly affecting younger age and female. CVT is uncommon and the reported annual incidence is about 5 per million (Al-Sulaiman, 2019). CVT may be present with multiple signs and symptoms, mimicking other neurological disorders. Its uncommon case and various signs and symptoms, make CVT difficult to distinguish (Idiculla et al., 2020). Patients with CVT have a high mortality and morbidity, early recognition of symptoms and treatment will improve the outcome of these patients (Bose et al., 2019; Idiculla et al., 2020).

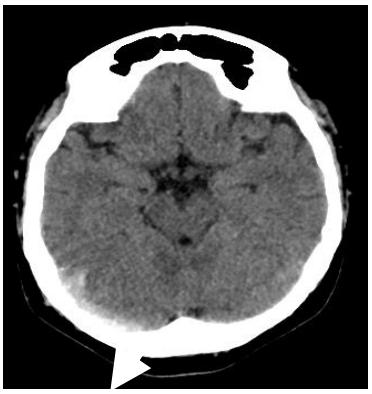
On Imaging, CVT may be accompanied with haemorrhage (Pongmoragot & Saposnik, 2012). One-third of CVT patients develop intracerebral haemorrhage or haemorrhagic venous infarct (Ghandehari et al., 2013). Presentation of haemorrhage in CVT makes a diagnostic and therapeutic challenge (Pongmoragot & Saposnik, 2012a; Shrestha et al., 2016). There are several established risk factors for CVT. Pregnancy and puerperium were reported to be an independent risk factor in haemorrhagic CVT (Pongmoragot & Saposnik, 2012).

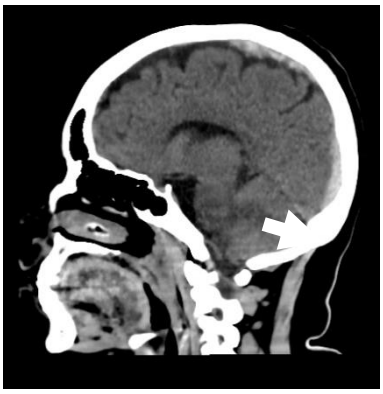
Anticoagulation remains the first-line treatment for CVT. Anticoagulation may prevent thrombus growth, facilitate recanalization, and prevent deep vein thrombus (Ghandehari et al., 2013). When managing CVT with haemorrhagic, physicians must consider the benefits and risks of anticoagulation. Many literatures report no adverse outcome when managing haemorrhagic CVT with anticoagulant. Although anticoagulant for CVT is beneficial despite the presence of haemorrhage, the evidence regarding anticoagulant type, dose, and optimum time to start anticoagulation is not yet established (Hegazi et al., 2009). We reported a haemorrhagic CVT with favorably responded with anticoagulation. This case report has passed the research ethics review from the Health Research Ethics Comission of Siloam Hospitals Yogyakarta.

CASE PRESENTATION

A 29-year-old Indonesian female, presented to the emergency department with 8 hours onset of weakness and tingling sensation in her left side of body accompanied with progressive headache one day before admission. She denied any head trauma, fever, nausea, and vomiting. She had a history of postpartum cardiomyopathy with mitral regurgitation and severe preeclampsia 1 month before.

On examination, she was fully alert, mild headache (VAS Score: 3), and had normal vital signs. Neurological examination results were normal cranial nerve, left-sided hypoesthesia, and left hemiparesis (muscle strength 4 on upper and lower extremities). The total NIHSS score was 3. Laboratory results were normal. A non-contrast Head CT scan revealed a subdural haemorrhage on the right occipital.

A. 

B 

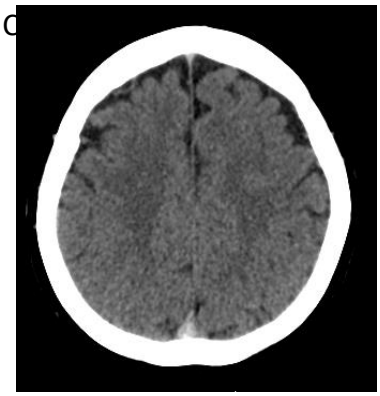
C 

Figure 1. Non-contrast Head CT scan

A and C: Axial view of subdural haemorrhage especially on right occipital

B: Subdural Haemorrhage on sagittal view

We assessed the patient as acute subdural haemorrhage with postpartum cardiomyopathy and mitral regurgitation. We treated the patient with intravenous tranexamic acid and mecobalamin. Oral candesartan, furosemide, spironolactone, and bisoprolol were given after consultation with cardiologist for her cardiomyopathy and mitral regurgitation condition.

Six hours after admission, a focal-aware seizure occurred on the left side of body lasted for 2 minutes, and spontaneously resolved. After the seizure, the left body weakness worsened especially on the left hand. NIHSS Score after the seizure was 5. We treated the seizure with intravenous phenytoin 300 mg/day. We plan the patient for non-contrast head MRI MRA examination and blood D-dimer level. While waiting for the non-contrast head MRI MRA examination, the seizure occurred, with the same type of seizure, lasting for 3 minutes. The left side weakness worsened and the NIHSS score after the second seizure was 9.

Head MRI showed a subacute haemorrhagic lesion in the occipital and revealed no subdural haemorrhage. On Head MRA revealed loss of normal cerebral vein topography on the right side. The blood D-dimer level was 4300 ng/mL.

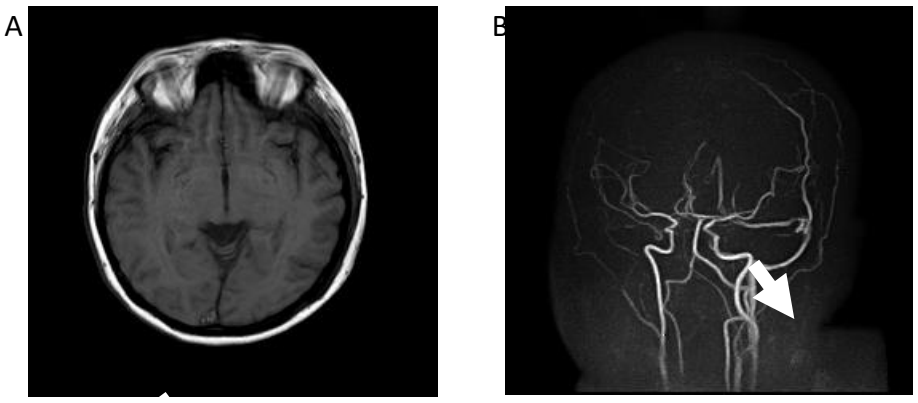


Figure 2. Non-Contrast Head MRI and MRA

A: Occipital Haemorrhage B: Spared Left Sigmoid Sinus

Based on this result, we assessed the patient with cerebral venous thrombosis with intracerebral haemorrhage. We stopped the tranexamic acid and planned anticoagulation with low dose unfractionated heparin, initial bolus dose of 60 U/kgBW continued with 12 U/kg/BW/hour. We targeted APTT 1,5-2 x control with fast bridging with warfarin 1 x 2 mg oral.

Table 1. Follow-up during anticoagulation

	Before anticoagulation	**Day 1 (during Anticoagulation)**	**Day 4 (during Anticoagulation)**	**Day 5 (during anticoagulation)**
Subjective	Seizure recurrence, left-side weakness	No Seizure, improvement of left-sided weakness	No Seizure, improvement of left-sided weakness	No seizure
Objective	Left Hemiparesis on Upper and Lower Extremities (Muscle Strength: 1)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 3 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)	Left Hemiparesis (Muscle Strength 4 on upper extremities, 4 on lower extremities)
Therapy	NIHSS score: 9 Phenytoin 100 mg/8 hours IV	NIHSS score: 5 intravenous UFH	NIHSS Score 3 intravenous UFH	NIHSS Score 3 Intravenous UFH Stopped
Plan	Anticoagulation with UFH		Oral warfarin 2 mg	Oral warfarin 2 mg/day, discharged

Six hours after anticoagulation, there was no seizure, and the neurological deficit improved with NIHSS score 5. After 4 days of anticoagulation, no seizure occurred, the neurological deficit improved with NIHSS score 3, and no bleeding complication. After 5 days of anticoagulation, we stopped the anticoagulant and then the patient was discharged with 2 mg oral warfarin for anticoagulation. The remaining neurological deficit when the patient discharged was left hemiparesis (muscle strength 4 in left upper and left-lower extremities) with NIHSS score 3.

DISCUSSION

We presented a case of CVT in post-partum period with postpartum cardiomyopathy. The postpartum period is a risk factor for CVT because transient prothrombotic condition. Pregnancy induces prothrombotic changes in the coagulation system dan persists during early puerperium. Volume depletion and trauma after pregnancy worsen the hypercoagulable state (Ferro et al., 2017). In this patient, cardiomyopathy also worsens the prothrombotic state and hypercoagulable state and increases the risk of venous thromboembolism in CVT (Fanola et al., 2020).

Computed Tomography (CT) is used as initial imaging in patients suspected of CVT. Anatomic variability of venous sinuses makes CT diagnosis of CVT insensitive. Hyperdensity of a cortical sign is a primary sign of acute CVT on non-contrast CT. Acutely thrombosed cortical veins and dural sinuses appear as a homogeneous hyperdensity that may be mimicking subdural haemorrhage as resulted in the initial CT of this patient (Pongmoragot & Saposnik, 2012).

The main target of CVT therapy is initiating anticoagulant therapy, treating underlying causes such as sepsis, dehydration, prothrombotic drugs, and risk factors that trigger CVT, while ensuring patient stability by stopping seizures and managing elevated intracranial pressure if necessary (Al-Sulaiman, 2019; Ulivi et al., 2020). Haemorrhage is one of the clinical features that occur in CVT patients, either naturally or associated with anticoagulation drugs (Ferro et al., 2017). In this case, the bleeding was

present at the time of admission, which created a dilemma in anticoagulation administration. Anticoagulant therapy is still recommended despite haemorrhage features in CVT (Gordon, 2004; Pongmoragot & Saposnik, 2012).

Evidence for choosing anticoagulation in treating cases of CVT remains weak because of the rarity of CVT. Therapy for CVT is guided by consensus and not from high-quality trials. Treatment with Unfractionated Heparin (UFH) or Low-Molecular-Weight Heparin (LMWH) is recommended in the acute phase of CVT (Field & Hill, 2019). In the previous report, it was found that cases of death were found to be higher following the administration of UFH compared to LMWH but in general, the clinician must balance the risks and benefits of anticoagulation depending on the clinical situation (Gordon, 2004; Misra et al., 2012).

The choice of therapy recommendations in cases of pregnancy and puerperium is not different from cases of acute CVT in adults in general, the choice of therapy in pregnant women remains with LMWH because it has lower side effects such as osteoporosis, although both are safe because they do not cross the placenta. In breastfeeding mothers and in the puerperium, LMWH and UFH and warfarin may be used. The guideline also suggests giving anticoagulant in pregnant and puerperal women with acute CVT. Some anticoagulants that often used may be transferred to breast milk but no adverse effects reported and well-tolerated (Ferro et al., 2017). In this case report, we use UFH because of the readiness of protamine sulfate as antidote and short-acting feature so that we may control the bleeding complication during anticoagulation.

The duration of oral anticoagulant therapy for CVT will depend on the patient's condition. The evidence of whether long-term (>6 months) anticoagulation improves outcome in CVT remains weak. Long-term therapy is required for life in recurrent CVT, CVT followed by VTE, CVT with thrombophilia with INR target 2-3 (Idiculla et al., 2020b). It is suggested that using oral anticoagulant therapy with Vitamin K Antagonist (VKA) for 3-12 months to prevent recurrent CVT and other thromboembolic events (Ferro et al., 2017). Data regarded the recurrence of CVT are very limited. Although very rare, some studies found that history of venous thromboembolism and the presence of one or more anti-phospholipid antibodies (Shu et al., 2022). Pregnant women and women in the puerperium period can be given oral anticoagulant therapy for up to 6 weeks postpartum. It is also recommended to replace all hormonal contraceptives to become non-hormonal (Idiculla et al., 2020).

CONCLUSION

Cerebral venous thrombosis is one type of uncommon stroke type. The manifestation of cerebral venous thrombosis may mimic other neurological diseases. The most common manifestations of cerebral venous thrombosis are headache and seizure. Cerebral venous thrombosis may be a diagnostic challenge, the recognition of risk factors and the clinical manifestation are important for the suspicion of cerebral venous thrombosis. Brain imaging combined with blood D-dimer levels may lead clinicians to confirm cerebral venous thrombosis diagnosis.

Imaging of cerebral venous thrombosis may accompany with haemorrhage. Anticoagulation remains the first-line treatment for cerebral venous thrombosis. The evidence regarding the anticoagulant type, dose, and optimal timing for haemorrhagic CVT remains unclear. Despite this

limited evidence, we suggest clinicians to treat haemorrhagic CVT with anticoagulant while considering the benefits and risks of anticoagulant.

REFERENCES

Al-Sulaiman, A. (2019). Clinical aspects, diagnosis and management of cerebral vein and dural sinus thrombosis: A literature review. *Saudi Journal of Medicine and Medical Sciences*, *7*(3), 137. https://doi.org/10.4103/sjmms.sjmms_22_19

Bose, G., Graveline, J., Yogendrakumar, V., Fergusson, D., & Dowlatshahi, D. (2019). Direct oral anticoagulants in treatment of cerebral venous thrombosis: A systematic review protocol. In *Systematic Reviews* (Vol. 8, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13643-019-1022-8

Fanola, C. L., Norby, F. L., Shah, A. M., Chang, P. P., Lutsey, P. L., Rosamond, W. D., Cushman, M., & Folsom, A. R. (2020). Incident Heart Failure and Long-Term Risk for Venous Thromboembolism. *Journal of the American College of Cardiology*, *75*(2), 148–158. https://doi.org/10.1016/j.jacc.2019.10.058

Ferro, J. M., Bousser, M.-G., Canh~ Ao, P., Coutinho, J. M., Crassard, I., Dentali, F., Di Minno, M., Maino, A., Martinelli, I., Masuhr, F., Aguiar De Sousa, D., & Stam, J. (2017). European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis-endorsed by the European Academy of Neurology. *European Journal of Neurology*, *24*, 1203–1213. https://doi.org/10.1111/ene.13381

Field, T. S., & Hill, M. D. (2019). Cerebral Venous Thrombosis: We Should Ask the Right Questions to Get Better Answers. In *Stroke* (Vol. 50, Issue 6, pp. 1598–1604). Lippincott Williams and Wilkins. https://doi.org/10.1161/STROKEAHA.119.025334

Ghandehari, K., Riasi, H. R., Noureddine, A., Masoudinezhad, S., Yazdani, S., Mirzae, M. M., Razavi, A. S., & Ghandehari, K. (2013). Safety assessment of anticoagulation therapy in patients with hemorrhagic cerebral venous thrombosis. In *Ir J neurol* (Vol. 12, Issue 3). http://ijnl.tums.ac.ir

Gordon, D. L. (2004). The diagnosis and management of cerebral venous thrombosis. In *Handbook of Cerebrovascular Diseases, Second Edition, Revised and Expanded* (pp. 605–635). CRC Press. https://doi.org/10.1161/str.0b013e31820a8364

Hegazi, M. O., Ahmed, S., Sakr, M. G., & Hassanien, O. A. (2009). Anticoagulation for cerebral venous thrombosis with subarachnoid hemorrhage: A case report. *Medical Principles and Practice*, *19*(1), 73–75. https://doi.org/10.1159/000252839

Idiculla, P. S., Gurala, D., Palanisamy, M., Vijayakumar, R., Dhandapani, S., & Nagarajan, E. (2020a). Cerebral Venous Thrombosis: A Comprehensive Review. In *European Neurology* (Vol. 83, Issue 4, pp. 369–379). S. Karger AG. https://doi.org/10.1159/000509802

Misra, U. K., Kalita, J., Chandra, S., Kumar, B., & Bansal, V. (2012). Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: A randomized controlled trial. *European Journal of Neurology*, *19*(7), 1030–1036. https://doi.org/10.1111/j.1468-1331.2012.03690.x

Pongmoragot, J., & Saposnik, G. (2012). Intracerebral hemorrhage from cerebral venous thrombosis. *Current Atherosclerosis Reports*, *14*(4), 382–389. https://doi.org/10.1007/s11883-012-0260-1

Shrestha, G. S., Poudyal, B. S., Sedain, G., Mahmud, K. I., & Acharya, N. (2016). Cerebral venous thrombosis presenting with intracerebral hemorrhage in a patient with paroxysmal nocturnal hemoglobinuria. *Indian Journal of Critical Care Medicine*, *20*(2), 117–119. https://doi.org/10.4103/0972-5229.175948

Shu, L., Bakradze, E., Omran, S. S., Giles, J., Amar, J., Henninger, N., Elnazeir, M., Liberman, A., Moncrieffe, K., Rotblat, J., Sharma, R., Cheng, Y., Zubair, A. S., Simpkins, A., Li, G., Kung, J., Perez, D., Heldner, M. R., Scutelnic, A., … Yaghi, S. (2022). Predictors of Recurrent Venous Thrombosis after Cerebral Venous Thrombosis: Analysis of the ACTION-CVT Study. *Neurology*, *99*(21), E2368–E2377. https://doi.org/10.1212/WNL.0000000000201122

Ulivi, L., Squitieri, M., Cohen, H., Cowley, P., & Werring, D. J. (2020). Cerebral venous thrombosis: A practical guide. In *Practical Neurology* (Vol. 20, Issue 5, pp. 356–367). BMJ Publishing Group. https://doi.org/10.1136/practneurol-2019-002415