ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuroanesthesia and Critical Care

Editor
Ramsis Ghaly, MD
Ghaly Neurosurgical Associates, Aurora, Illinois, USA

SNI
Open Access

Case Report

Adenomyosis-associated recurrent acute cerebral infarction mimicking Trousseau's syndrome: A case study and review of literature

Nobuhiko Arai, Kazunari Yachi, Ryutaro Ishihara, Takao Fukushima

Department of Neurosurgery, Takashimadaira Central General Hospital, Itabashiku, Tokyo, Japan.

E-mail: *Nobuhiko Arai - nopi0612@yahoo.co.jp; Kazunari Yachi - qqek25f9k@bronze.ocn.ne.jp; Ryutaro Ishihara - ryutaro.ishihara912@gmail.com; Takao Fukushima - fukushima27takao@gmail.com

***Corresponding author:**
Nobuhiko Arai,
Department of Neurosurgery,
Takashimadaira Central
General Hospital, Itabashiku,
Tokyo, Japan.

nopi0612@yahoo.co.jp

Received : 14 March 2022
Accepted : 12 April 2022
Published : 29 April 2022

DOI
10.25259/SNI_252_2022

Quick Response Code:

ABSTRACT

Background: Adenomyosis is a common and benign uterine disease. Acute cerebral infarction (CI) associated with adenomyosis is rarely reported and difficult to treat. We experienced successful treatment for this disease.

Case Description: A 50-year-old woman presented with a 2-day history of visual disturbance. Magnetic resonance imaging showed multiple tiny diffusion-weighted high-density spots on several lobes. No common risk factors for stroke were detected. Cancer antigen 125 level was 999 U/mL, along with massively expanded uterus and adnexa. Based on the diagnosis of benign adenomyosis, Xa inhibitor and GnRH agonists were administered for CI and adenomyosis, respectively. Acute CI recurred 7 days after admission. We suspected a relationship between infarction and adenomyosis and concluded hysterectomy as a proper treatment strategy based on the literature. Eighteen months after hysterectomy, no recurrence of CI without anti-thrombus medications has been detected.

Conclusion: Hysterectomy is a radical therapy that is effective in preventing acute CI due to adenomyosis associated with ischemic symptoms.

Keywords: Acute cerebral infarction, Adenomyosis, CA125, Hysterectomy, Trousseau's syndrome

INTRODUCTION

Adenomyosis is a common and benign uterine disease. The formation of uterine glands and stroma in the endometrial membrane is the pathological trait of this disease. This disease presents with abnormal uterine bleeding, pelvic pain, and uterine growth in volume with a prevalence of 20–35% in women.[9] Recently, acute cerebral infarction (CI) primarily associated with adenomyosis has been reported.[1,2,3,6,8,10,13-16] This extremely rare entity is possibly misdiagnosed as Trousseau's syndrome (TS) characterized by the cancer-related embolic events such as deep vein thrombosis/pulmonary embolism and a CI[11] because of the existence of pelvic unknown large mass and elevated tumor markers such as CA125 and CA 19-9. To date, only 16 cases of CI associated with adenomyosis resembling the TS have ever been reported.[1,2,3,6,8,10,13-16] The question is why only a small number of patients have ever been reported despite of the high frequency of adenomyosis. In addition, the proper treatment policy remains unknown even after thorough review of the past 16-case reports. We experienced successful treatment for acute CI associated with adenomyosis, which notably recurs only 7 days after the initial ischemic event.

CASE REPORT

A 50-year-old woman presented with a 2-day history of visual disturbance that was later identified as left-sided hemianopsia. Magnetic resonance imaging (MRI) revealed multiple acute CIs in almost all lobes [Figure 1]. The patient had a medical history of mild hypertension and adenomyosis with relatively severe symptoms that had not yet been officially diagnosed. An electrocardiogram showed no abnormal findings, such as arrhythmia or ST-wave changes. The results of common laboratory tests were as follows: Hb 9.2 g/dL and D-dimer 6.4 μg/mL. The patient's recent menstruation was initiated 2 days before the onset of visual disturbance and appeared heavier than ever before. Considering the distribution of acute CIs, elevated D-dimer levels, and gynecological medical history, TS was initially suspected. As a primary treatment, the patient was administered a 10,000 U/day dose of heparin to prevent recurrence of ischemia. In addition to routine screening tests, such as carotid sonography and echocardiography which turned out to be within normal later, malignancy confirmation checks, such as abdominal computed tomography (CT) or tumor markers, were performed; the analyses suggested cancer antigen (CA) 125 level to be 999 U/mL (normal value <35 U/mL) and CA 19-9 level to be 112 U/mL (normal value <37 U/mL). The values of protein C/S, anti-thrombin III, and homocysteine were within the normal range. Pelvic CT [Figure 2] showed massively expanded uterus and adnexa that were considered as malignant lesions, such as ovarian cancer. However, detailed radiological interpretation revealed no expanded lymph nodes, and thus, adenomyosis was the first differential diagnosis. We mistakenly excluded the relationship between adenomyosis and stroke. First, conservative therapy (GnRH agonist therapy) was administered for adenomyosis and direct oral anticoagulant (Xa inhibitor; apixaban 5.0 mg 2T2×) was prescribed for preventing ischemia. One day after discharge (on the 7th day after the first admission), the patient experienced recurrent acute CIs presenting with moderate dysarthria without any limb weakness. MRI showed several tiny acute CIs in the bilateral cerebellum [Figure 3]. A review of the literature on the relationship between acute CI and adenomyosis indicated simple hysterectomy to be a possible radical treatment for recurrent acute CI. The surgery was performed on the 14th day after the initial symptoms that revealed no histopathological malignancy in the uterine specimens. One month after the operation and after discontinuing Xa inhibitor, D-dimer, the CA 125 and CA

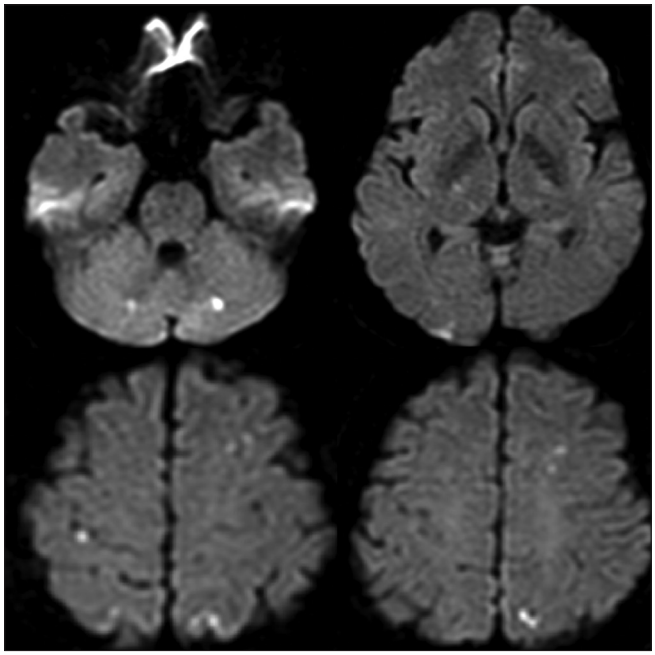

Figure 1: MRI showing spotty multiple cerebral infarctions in the frontal, parietal, occipital lobes, and cerebellum.

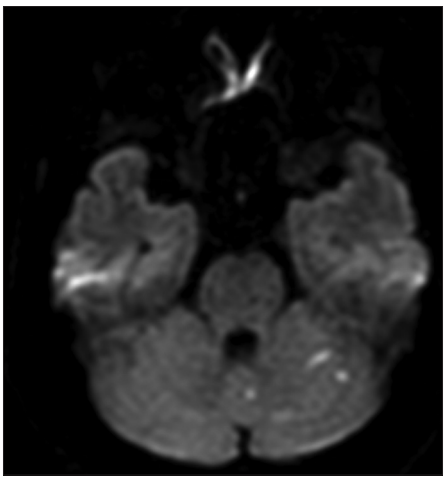

Figure 2: MRI showing tiny multiple cerebral infarctions in the cerebellum.

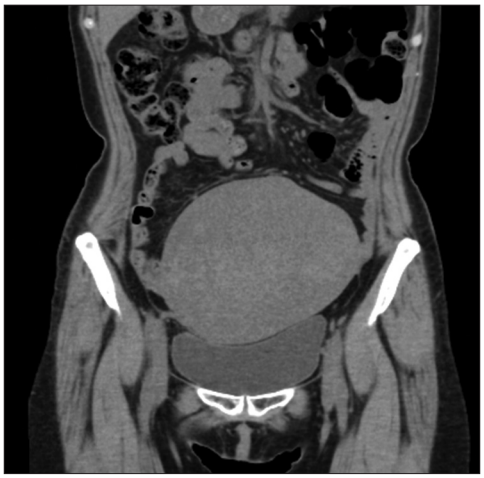

Figure 3: Plain CT showing expanded organ in the pelvis without any enlarged lymph nodes.

Table 1: Review of the literatures of acute cerebral infarctions associated with adenomyosis.

Case	Age	Symptom	Recurrence	Onset during menstruation	CA125	CA19-9	D-dimer	Hb	Major artery occusion	Treatment for CI	Treatment for recurrent CI	Treatment for adenomyosis
1	45	Impaired consciousness and weakness	No	No	159	N.D.	N.D.	8.4	No	Heparin and antiplatelet		GnRH ago
2	44	Plegia	No	No	N.D.	N.D.	N.D.	7	No	Heparin and warfarin		GnRH ago
3	50	Weakness	No	Yes	42.6	N.D.	0.57	6.9	No	Aspirin		GnRH ago
4	42	Aphasia	Yes	Yes	1750	N.D.	6	8.6	No	Antiplatelet therapy	Heparin, warfarin	GnRH ago
5	59	Aphasia	No	No	334.8	N.D.	N.D.	N.D.	No	Antithrombotic therapy		N.D.
6	48	Plegia and aphasia	No	No	901	1791	1.9	8.5	MCA	Heparin and warfarin		Hysterectomy
7	49	Dysarthria and weakness	No	No	379	69.2	3.99	9.9	No	Anticoagulant		Hysterectomy
8	44	Weakness	Yes	Yes	2115	1824	17	10.3	MCA distal	Heparin and rivaroxaban		GnRH ago
9	42	Weakness and aphasia	No	No	395	N.D.	N.D.	N.D.	MCA distal	Warfarin		N.D.
10	50	Weakness and aphasia	No	No	143	N.D.	N.D.	N.D.	MCA	rivaroxaban		N.D.
11	34	Vertigo	No	Yes	937.1	462.5	1.05	13.4	No	N.D.		N.D.
12	37	Weakness	No	Yes	735.7	43.2	12.04	10.8	No	N.D.		N.D.
13	46	Plegia	No	Yes	546.5	1076.6	2.34	12.1	No	N.D.		Hysterectomy
14	34	Fever and weakness	No	Yes	937.7	N.D.	27.4	11.2	No	Heparin and antiplatelet		N.D.
15	48	Dysarthria and weakness	No	Yes	3536.2	892.1	79.3	8.2	MCA	Heparin, edoxaban, and Endovascular therapy		Hysterectomy
16	47	Weakness and aphasia	Yes	Yes	90.3	52.3	3.8	11.3	No	Heparin and edoxaban	Heparin	Hysterectomy
17	50	Visual disturbance	Yes	Yes	999	112	6.4	9.7	No	Heparin and apixaban	Heparin	Hysterectomy

19-9 levels were within normal ranges. The patient had not experienced any CI relapse for 18 months.

DISCUSSION

In this case, we experienced acute CI associated with adenomyosis which recurs as early as 7 days after the initial attack under the Xa inhibitor. From this case, we found that Xa inhibitor is not potent enough to prevent recurrence of CI and hysterectomy which assumed to be radical treatment for CI and adenomyosis should be performed within 7 days after the first symptom.

Adenomyosis is relatively common female disease, from which around 20–30% of all woman have suffered in the world.[9] Although adenomyosis is common condition, this disease inducing the acute CI has rarely been reported in the literature. [Table 1] shows the all reported adenomyosis related with CI including the current case. Apart from misdiagnosis of adenomyosis inducing CI due its unfamiliarity, we presume only a handful of adenomyosis excrete multitude of CA 125. In addition, CA125 is reported to be slightly elevated; 91.2U/ml in the adenomyosis patients (n = 80). On the contrary, the average level of CA 125 of ovarian cancer, whose pathology was adenocarcinoma (n = 11) which is likely to cause the TS, was significantly elevated to 415.2U/ml.[7] Recent article reported that CA-125 could be a potential biomarker for TS.[4] Reviewing the past 16 cases, the median value of CA 125 in adenomyosis with acute CIs is much higher (645.1IU/ml) than reported CA 125 level in adenomyosis (91.2) and even higher than highest level of CA 125 in ovarian cancer. CA 125 is a member of the mucin family glycoproteins which commonly elevated in women with ovarian tumors, pelvic inflammatory disease, and endometriosis.[12] This molecule activates the coagulation system by stimulating factor X. Thus, Xa inhibitor can in theory prevent the coagulation and recurrence of CI. However, the present case suffered from recurrence of CI even under the Xa inhibitor. Probably, this is because the anticoagulant strength was not enough or another mechanism may be involved. Actually, apart from CA 125, some papers remarked that the infection or anemia plays a crucial role to development of infarctions in adenomyosis.[2,16] In addition, menstruation can be a potent induction factor for CI. The serum CA 125 levels vary depending on the cycle of menstrual reaching the highest value during the menstruation.[5] Among the reported cases, ten out of all reported 17 cases (59%) experienced the CI during the menstruation, which also support the harmful influence of CA 125 for coagulation. CA 125 can be a potential biomarker to detect the malignant adenomyosis which can lead to acute CI.

The radical treatment for adenomyosis associated with acute CIs must be hysterectomy. The present case showed recurrent CI under the anti-coagulant agents which is Xa inhibitor which would be ideal theoretically. In the past two cases presented recurrent CI under the anti-thrombus medication with GnRH agonists for adenomyosis.[2,14] We have newly found that the median levels of CA125 of CI recurrent group and 1374.5IU/ml were a lot higher than that of groups without recurrent CI (395IU/ml). In this calculation, one case for which hysterectomy was ideally just 6 days after the onset was deleted from no-recurrent groups.[10] Actually, anti-thrombus medication exacerbates the menorrhagia and should be eschewed for the patients with massive uterine bleeding being distinctive of adenomyosis. Therefore, we firmly propose that at least for the patients with high CA 125 and do not plan having babies, early radical hysterectomy within 7 days after the first attack must be an appropriate treatment currently. The most controversial issue is the choice of therapy for the women with the hope of having babies, especially showing high CA 125 values though the average age (45.3 years old) of the reported patients[1,2,3,6,8,10,13-16] does not lay in the period of most fecund for women. More accumulation of the patients can elucidate the best treatment for those cases. In the near future, by collecting data of CA 125 in benign status of adenomyosis, threshold of CA 125 for presuming the potentiality of acute CIs can be obtained and will be promising biomarker.

CONCLUSION

Adenomyosis can lead to the recurrent acute CIs. Hysterectomy could be a radical and appropriate treatment for those condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Aiura R, Nakayama S, Yamaga H, Kato Y, Fujishima H. Systemic thromboembolism including multiple cerebral infarctions with middle cerebral artery occlusion caused by the progression of adenomyosis with benign gynecological tumor: A case report. BMC Neurol 2021;21:14.
2. Aso Y, Chikazawa R, Kimura Y, Kimura N, Matsubara E. Recurrent multiple cerebral infarctions related to the progression of adenomyosis: A case report. BMC Neurol 2018;18:119.
3. Hijikata N, Sakamoto Y, Nito C, Matsumoto N, Abe A, Nogami A, *et al*. Multiple cerebral infarctions in a patient with

adenomyosis on hormone replacement therapy: A case report. J Stroke Cerebrovasc Dis 2016;25:e183-4.
4. Ishikawa M, Nakayama K, Ishibashi T, Sato E, Nakamura K, Katagiri H, *et al*. Case series of cerebral infarction with Trousseau's syndrome associated with malignant gynecological tumors. Mol Clin Oncol 2016;5:138-42.
5. Kan YY, Yeh SH, Ng HT, Lou CM. Effect of menstruation on serum CA125 levels. Asia Oceania J Obstet Gynaecol 1992;18:339-43.
6. Kim B, Kim SH, Kim T. Cerebral infarcts by nonbacterial thrombotic endocarditis associated with adenomyosis: A case report. J Stroke Cerebrovasc Dis 2018;27:e50-3.
7. Kim B, Park Y, Kim B, Ahn HJ, Lee KA, Chung JE, Han SW. Diagnostic performance of CA 125, HE4, and risk of ovarian malignancy algorithm for ovarian cance. J Clin Lab Anal 2019;33:e22624.
8. Okazaki K, Oka F, Ishihara H, Suzuki M. Cerebral infarction associated with benign mucin-producing adenomyosis: report of two cases. BMC Neurol 2018;18:166.
9. Raffone A, Seracchioli R, Raimondo D, Maletta M, Travaglino A, Raimondo I, *et al*. Prevalence of adenomyosis in endometrial cancer patients: A systematic review and meta-analysis. Arch Gynecol Obstet 2021;303:47-53.
10. Uchino K, Shimizu T, Mizukami H, Isahaya K, Ogura H, Shinohara K, *et al*. Nonbacterial thrombotic endocarditis complicated by cerebral infarction in a patient with adenomyosis with high serum CA125 level: A case report. J Stroke Cerebrovasc Dis 2018;27:e42-5.
11. Varki A. Trousseau's syndrome: Multiple definitions and multiple mechanisms. Blood 2007;110:1723-9.
12. Yamanaka A, Kimura F, Yoshida T, Kita N, Takahashi K, Kushima R, *et al*. Dysfunctional coagulation and fibrinolysis systems due to adenomyosis is a possible cause of thrombosis and menorrhagia. J Obstet Gynecol Reprod Biol 2016;15:811-24.
13. Yamashiro K, Tanaka R, Nishioka K, Ueno Y, Shimura H, Okuma Y, *et al*. Cerebral infarcts associated with adenomyosis among middle-aged women. J Stroke Cerebrovasc Dis 2012;21:910.e1-5.
14. Yasuda M, Yamanaka Y, Kano H, Araki N, Ishikawa H, Ikeda JI, *et al*. Recurrent cerebral infarcts associated with uterine adenomyosis: Successful prevention by surgical removal. Intern Med 2022 1;61:735-8.
15. Yin X, Wu J, Song S, Zhang B, Chen Y. Cerebral infarcts associated with adenomyosis: A rare risk factor for stroke in middle-aged women: A case series. BMC Neurol 2018;18:213.
16. Zhao Y, Zhang Y, Yang Y. Acute cerebral infarction with adenomyosis in a patient with fever: A case report. BMC Neurol 2020;20:210.

How to cite this article: Arai N, Yachi K, Ishihara R, Fukushima T. Adenomyosis-associated recurrent acute cerebral infarction mimicking Trousseau's syndrome: A case study and review of literature. Surg Neurol Int 2022;13:179.