

Case Report

Rare case report on Acitrom induced coagulopathy with seizure disorder

C. D. Shakthivel*, Janane Murugesan

Sri Ramakrishna Institute of Paramedical Sciences, College of Pharmacy, Sri Ramakrishna Hospital Campus, Coimbatore, India

Received: 06 June 2025

Accepted: 08 July 2025

*Correspondence:

Dr. C. D. Shakthivel,

E-mail: shakthineuropharm87@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Acitrom (nicoumalone), a vitamin K antagonist, is widely used for the prevention of thromboembolic disorders. However, its narrow therapeutic index mandates vigilant monitoring to avoid complications like coagulopathy. This case report presents a 59-year-old female with a history of cerebral venous thrombosis, coronary artery disease, and seizures who developed Acitrom-induced coagulopathy. She was admitted with symptoms of headache, vomiting, burning sensation in the lower limbs, and later with bleeding from the gums and oral cavity, melena, and a generalized tonic-clonic seizure. Her past medication included Acitrom, Thyroxine, Atorvastatin, Aspirin, and several other supportive drugs. Investigations revealed deranged coagulation parameters, with INR elevated beyond the therapeutic range. MRI and MRV indicated partial recanalization of cerebral venous sinuses, with no evidence of infarction or hemorrhage. She was managed with intravenous vitamin K, fresh frozen plasma, and antiepileptics including phenytoin and levetiracetam. The offending agent, Acitrom, was discontinued. The patient responded well to treatment and was discharged on antiepileptic and supportive therapy. This case emphasizes the importance of close INR monitoring and patient education to identify early signs of bleeding. Seizure in the context of anticoagulant-induced coagulopathy is rare and requires immediate attention. Interdisciplinary collaboration among neurology, internal medicine, and hematology is critical for optimizing patient outcomes. Early recognition, timely reversal of anticoagulation, and individualized care can significantly reduce morbidity in such complex clinical presentations.

Keywords: Coagulopathy, Seizures, Thrombotic risk

INTRODUCTION

Acitrom (nicoumalone), a derivative of coumarin, is an oral vitamin K antagonist (VKA) commonly used in the long-term management of thromboembolic disorders, including cerebral venous thrombosis, prosthetic heart valves, and atrial fibrillation. Acenocoumarol exerts its anticoagulant effect by inhibiting the enzyme vitamin K epoxide reductase complex 1 (VKORC1), which is essential for the cyclic conversion of inactive vitamin K epoxide to its active form.^{1,2} This inhibition leads to a reduction in the hepatic synthesis of active vitamin K-dependent clotting factors II, VII, IX, and X, as well as the anticoagulant proteins C and S.³ Due to its narrow therapeutic index and considerable inter-individual

variability in pharmacokinetics and pharmacodynamics, Acitrom therapy mandates frequent monitoring of coagulation parameters, especially the international normalized ratio (INR).⁴⁻⁶ Therapeutic INR targets vary based on the indication but generally range between 2.0 and 3.5. INR values below 2.0 are associated with a high risk of thromboembolic events, while values exceeding 4.0 substantially increase the risk of spontaneous bleeding, including mucosal, gastrointestinal, or intracranial hemorrhage.⁷ Therefore, strict compliance with dosing schedules, periodic INR checks, and dietary consistency with respect to vitamin K intake are essential to safe and effective anticoagulation management.^{8,9} While the common complications of Acitrom therapy include bleeding tendencies and bruising, neurological

manifestations such as seizures are rare and underrecognized. Seizures may occur in the context of anticoagulant-induced coagulopathy in several ways via direct intracerebral hemorrhage, through subtle metabolic derangements secondary to blood loss, or as an exacerbation of underlying neurological pathology in predisposed individuals.¹⁰ Importantly, patients with a history of stroke, cerebral venous thrombosis, or structural brain lesions are inherently at a higher risk of developing seizure disorders, which can be exacerbated by changes in systemic hemostasis.¹¹

Seizure-related coagulopathy refers to the presence of abnormal coagulation parameters either as a cause or consequence of seizure activity. Although seizures are a well-known complication following ischemic or hemorrhagic stroke, limited data exist on seizures induced directly by deranged coagulation profiles in the absence of identifiable neuroimaging abnormalities. In patients with multiple comorbidities-such as hypothyroidism, renal impairment, and cardiovascular disease-who are also on polypharmacy, the likelihood of adverse drug reactions including excessive anticoagulation increases markedly.^{12,13} Drug interactions, particularly with enzyme-inducing antiepileptics like phenytoin or carbamazepine, may unpredictably potentiate or reduce Acitrom's anticoagulant effects, further complicating clinical management.¹⁴

Prompt recognition and treatment of Acitrom-induced coagulopathy is essential to prevent serious complications. Management involves immediate discontinuation of the anticoagulant, administration of vitamin K to reverse its effects, and, in severe cases with active bleeding or very high INR values, the use of blood products such as fresh

frozen plasma (FFP) or prothrombin complex concentrate (PCC). Antiepileptic drugs (AEDs) such as levetiracetam or phenytoin may be indicated to control seizure episodes, especially in patients with co-existing neurological disorders.¹⁵ This case serves to highlight the rare but potentially life-threatening neurological presentation of Acitrom toxicity. It highlights the importance of individualized anticoagulation regimens, rigorous INR monitoring, and interdisciplinary collaboration between internal medicine, neurology, and hematology teams.

Moreover, it emphasizes the need for heightened clinical vigilance for atypical presentations such as seizures in anticoagulated patients, even in the absence of radiological evidence of intracranial hemorrhage. With increasing use of oral anticoagulants, especially in aging populations with complex multimorbidity, understanding the nuanced balance between thrombosis prevention and bleeding risk becomes essential.¹⁶ This case not only adds to the limited literature on seizure-related presentations of VKA toxicity but also provides insights into practical clinical strategies for timely intervention and holistic patient care.

CASE REPORT

A 63-year-old female presented to the general medicine department on August 15, 2024, with a constellation of symptoms including persistent headache, two episodes of non-bilious vomiting, burning sensations in both lower limbs, and retrosternal discomfort suggestive of heartburn. Notably, the patient had experienced a generalized tonic-clonic (GTC) seizure one day prior to admission, lasting approximately 15 minutes and associated with a transient loss of consciousness. The seizure episode was the first in nearly five years since her last documented event.

Table 1: Laboratory investigations during first and second admissions.

Parameter	1st admission	2nd admission	Reference range
Complete blood count			
Total leukocyte count (cells/cu.mm)	13,500	11,200	4,500–11,000
Haemoglobin (g/dl)	14.2	11.4	11–15
Packed cell volume (PCV) (%)	51.5	51.1	39–49
Red blood cell count (million/cu.mm)	6.6	5.6	4.6–5.9
Platelet count (lakhs/cu.mm)	4.3	4.0	1.5–4.5
Differential count (%)			
Neutrophils	80	75	40–70
Lymphocytes	16	18	20–40
Monocytes	4	7	2–6
Biochemistry			
Random blood sugar (mg/dl)	83	88	80–120
Liver function tests			
Total bilirubin (mg/dl)	0.8	0.7	0.1–1.2
Direct bilirubin (mg/dl)	0.4	0.3	0.0–0.3
Indirect bilirubin (mg/dl)	0.4	0.4	0.2–0.8
SGOT (AST) (IU/l)	30	26	5–40
SGPT (ALT) (IU/l)	36	25	7–96
Alkaline phosphatase (U/l)	92	95	44 – 147

Continued.

Parameter	1st admission	2nd admission	Reference range
Total protein (g/dl)	5.3	6.0	6.0 – 8.0
Renal function tests			
Blood urea (mg/dl)	56	36	8 – 40
Serum creatinine (mg/dl)	1.1	1.0	0.6 – 1.2
Electrolytes			
Sodium (mEq/l)	124	133	135 – 145
Potassium (mEq/l)	6.6	4.1	3.5 – 5.0
Chloride (mEq/l)	97	105	96 – 106
Coagulation profile			
Prothrombin time (seconds)	22.0	22.6	10 – 13
INR	1.8	1.9	<1.1 (normal); 2.0–3.5 (target in VKA)

Table 2: Medications administered during first admission.

Medication	Dose	Route	Frequency	Duration (Days 1–6 unless otherwise noted)
Thyroxine	100 mcg	Oral	Once daily	Continued
Atorvastatin	10 mg	Oral	At bedtime	Continued
Vitamin B complex	30.5 mg	Oral	Once daily	Continued
Metoprolol	25 mg	Oral	Half tablet in morning only	Continued
Levetiracetam	10 mg	Oral	Twice daily	Continued
Nicoumalone (Acitrom)	2 mg	Oral	Once at night	Day 1–6
Calcium lactate	300 mg	Oral	Thrice daily	Continued
Phenytoin	100 mg	IV	Thrice daily	Continued
Ondansetron	2 mg/ml	IV	Twice daily	Day 1 only
Ranitidine	50 mg/ml	IV	Twice daily	Day 1 only
Aspirin	150 mg	Oral	Half tablet in afternoon	Day 2–6
Amitriptyline	25 mg	Oral	Once daily	Day 2–6
Sodium bicarbonate	325 mg	Oral	Thrice daily	Day 2–6
Ferrous sulphate	333.5 mg	Oral	Once daily	Day 2–6
Calcium gluconate	10%	IV (slow)	Once	As required
Omeprazole capsule	20 mg	Oral	Twice daily	Day 3–6

Table 3. Medications administered during second admission.

Medication	Dose	Route	Frequency	Duration
Vitamin K	10 mg	IM	Once daily	4 days
Streptochrome	1.2 g	IV	Once daily	4 days
Tranexamic acid	500 mg	IV	Once daily	4 days
Ranitidine	50 mg/2 ml	IV	Twice daily	4 days
Clopidogrel	75 mg	Oral	Once daily	4 days
Atorvastatin	10 mg	Oral	At bedtime	4 days
Metoprolol	25 mg	Oral	Half tab twice daily	4 days
Levetiracetam	100 mg	Oral	Twice daily	4 days
Phenytoin	100 mg	Oral	Twice daily	4 days
Amitriptyline	25 mg	Oral	Once daily	4 days
Sodium bicarbonate	325 mg	Oral	Thrice daily	4 days
Calcium carbonate	300 mg	Oral	Thrice daily	4 days
Paracetamol	500 mg	Oral	Thrice daily	2 days (Day 3–4)

On clinical evaluation, she was found to be conscious, well-oriented to time, place, and person, afebrile, with a regular pulse rate of 88 beats per minute, blood pressure

within the normal range, and an oxygen saturation of 99% on room air. Her past medical history was significant for cerebral venous thrombosis (CVT) and coronary artery

disease (CAD), both diagnosed seven years ago, alongside comorbid hypothyroidism and Grade II bilateral mild renal dysfunction, for which she was receiving routine medical management. Her long-standing pharmacotherapy included nicoumalone (Acitrom) 2 mg once daily for anticoagulation, thyroxine 100 mcg once daily for hypothyroidism, atorvastatin 10 mg at bedtime and aspirin 150 mg daily for secondary cardiovascular prevention, spironolactone 25 mg and enalapril 2.5 mg for cardiac support, ranitidine 150 mg twice daily for gastrointestinal protection, and calcium lactate 300 mg once daily for supplementation.

Three months later, on December 24, 2024, the patient was readmitted to the same department with alarming symptoms indicative of bleeding diathesis. She reported persistent gum and oral cavity bleeding occurring 5 to 6 times over two days, as well as the passage of black tarry stools (melena) for one day, which was preceded by three similar episodes the day before admission. She denied any history of trauma or use of over-the-counter medications that could independently precipitate bleeding. Given the patient's anticoagulant regimen with Acitrom and clinical presentation, Acitrom-induced coagulopathy was suspected.

A comprehensive physical examination revealed no focal neurological deficits, signs of active seizure, or hemodynamic instability. Initial laboratory investigations, including complete blood count, renal and liver function tests, and coagulation profile, were performed. Notably, the prothrombin time (PT) and international normalized ratio (INR) were found to be significantly elevated, confirming a supratherapeutic anticoagulation state.

To further explore the etiology of the seizure and assess for any intracranial bleeding, the patient underwent magnetic resonance imaging (MRI) of the brain, which revealed prominent bilateral perioptic cerebrospinal fluid (CSF) spaces, and chronic small vessel ischemic changes classified as Fazeka Grade I. T1, T2, and FLAIR hyperintensities were noted in the right transverse sinus. MRI findings also indicated bilateral maxillary and ethmoidal sinusitis. Magnetic resonance angiography (MRA) of the cerebral vessels was normal, while magnetic resonance venography (MRV) demonstrated irregularities and partial recanalization in the bilateral transverse, sigmoid, and superior sagittal sinuses, suggestive of prior thrombosis. Importantly, no evidence of intracerebral hemorrhage or infarction was noted, ruling out acute structural causes of the seizure.

Cardiac work-up included a transthoracic echocardiogram, which showed a left ventricular internal diameter of 5.0 cm in diastole and 3.5 cm in systole, indicative of mild left ventricular diastolic dysfunction with preserved systolic function. The left ventricular ejection fraction (LVEF) was calculated at 60%. Mild (Grade I) mitral regurgitation was observed, with no intracardiac thrombi or clots. Serial electrocardiograms (ECGs) revealed a normal sinus

rhythm during the first admission; however, during the second admission, the ECG showed first-degree atrioventricular (AV) block with findings suggestive of a possible inferior myocardial infarction. Upon confirmation of Acitrom-induced coagulopathy, immediate cessation of Acitrom was initiated. The patient received intravenous vitamin K and fresh frozen plasma (FFP) over the first four days of hospitalization, with doses adjusted based on serial INR values. Her bleeding symptoms gradually subsided. Concurrently, the seizure episode was managed with intravenous and oral phenytoin and levetiracetam. Supportive care including electrolyte correction, gastric protection, cardiovascular stabilization, and analgesics was provided as per symptomatology.

During her first hospitalization in March, Acitrom was continued until day 6, as the bleeding risk had not yet manifested. However, by the second admission, given the bleeding complications and INR derangement, Acitrom was permanently discontinued.

At the time of discharge, her clinical condition had significantly improved, with stabilization of coagulation parameters and resolution of mucosal and gastrointestinal bleeding. Her revised medication regimen included atorvastatin 2 mg once daily, metoprolol 25 mg (half tablet twice daily) for blood pressure and cardiac rhythm control, levetiracetam 5 mg twice daily, phenytoin 100 mg twice daily for seizure prophylaxis, thyroxine 150 mcg once daily, paracetamol 500 mg thrice daily for symptomatic relief, amitriptyline 25 mg once daily for neuropathic pain, sodium valproate 20 mg once daily as adjunctive antiepileptic therapy, and acetazolamide 25 mg once daily for intracranial pressure control. She was scheduled for follow-up evaluation after 30 days and was thoroughly counselled regarding adherence to medication, the importance of INR monitoring (should future anticoagulation be necessary), recognition of bleeding symptoms, and seizure precautions.

DISCUSSION

This case emphasizes the complex interplay between anticoagulant therapy and neurological manifestations, specifically the rare but clinically significant occurrence of seizures in the context of Acitrom (nicoumalone)-induced coagulopathy. Nicoumalone is a vitamin K antagonist (VKA) used widely for the prevention and treatment of thromboembolic conditions such as cerebral venous thrombosis (CVT), atrial fibrillation, and coronary artery disease. Although effective, VKAs carry a high risk of complications due to their narrow therapeutic index and variability in individual patient response. In this patient, long-term administration of Acitrom resulted in supratherapeutic anticoagulation, with laboratory investigations revealing elevated prothrombin time (PT) and international normalized ratio (INR), consistent with excessive anticoagulant activity.

The patient's initial presentation with a generalized tonic-clonic seizure followed by episodes of mucosal bleeding and melena was unusual and prompted an extensive diagnostic workup. Seizures in patients on VKAs may be the result of overt intracranial hemorrhage, ischemic stroke, metabolic disturbances, or, less commonly, a consequence of bleeding-induced hypoxia or hypotension. In this case, imaging studies including MRI and MRV ruled out acute hemorrhage or infarction, suggesting that the seizure may have been precipitated by either subtle microvascular bleeding not detectable on standard imaging or systemic coagulopathy with associated neurochemical alterations. The link between excessive anticoagulation and neurological symptoms is underrecognized in routine clinical practice. While intracranial hemorrhage is the most feared complication of VKA therapy, it is important to consider non-hemorrhagic neurological events such as seizures, particularly in patients with underlying cerebrovascular pathology. Our patient had a history of CVT and chronic small vessel ischemic changes, which could have predisposed her to seizure activity in the presence of systemic derangements. Furthermore, electrolyte imbalances and renal dysfunction, both of which were noted in this case, are well-established contributors to neuronal excitability and seizure thresholds.

Acitrom-induced coagulopathy can occur due to multiple reasons, including dose miscalculation, drug interactions (especially with antibiotics, antiepileptics, or NSAIDs), hepatic or renal dysfunction, and erratic dietary intake of vitamin K. In this patient, while no clear external trigger such as medication changes or infection was identified, her renal function and age could have contributed to drug accumulation and enhanced anticoagulant effect. Additionally, her use of multiple medications increases the potential for pharmacokinetic and pharmacodynamic interactions that may alter the anticoagulant response.

Management of such cases requires a rapid, multidisciplinary approach. The cornerstone of treatment includes the immediate cessation of the offending anticoagulant, reversal of its effects with vitamin K, and administration of blood products such as fresh frozen plasma (FFP) or prothrombin complex concentrates (PCC) in cases of life-threatening bleeding. In our case, the patient was treated effectively with intravenous vitamin K and FFP over several days, resulting in gradual normalization of INR and resolution of bleeding. For seizure control, a combination of phenytoin and levetiracetam was employed, both of which have well-established efficacy in the management of acute symptomatic seizures. Importantly, phenytoin, being a cytochrome P450 inducer, can potentially alter the metabolism of VKAs; however, since Acitrom was already discontinued, this interaction was not clinically significant during the acute phase of management.

Electrocardiographic changes observed during the second admission, including first-degree AV block and signs of

possible inferior infarction, raise the possibility of transient myocardial ischemia contributing to systemic instability, although this remained subclinical. The presence of mild mitral regurgitation and preserved ejection fraction on echocardiography suggested no structural abnormalities that could independently predispose to thromboembolic events or seizures.

This case also highlights the importance of regular and individualized INR monitoring in patients on long-term VKA therapy, especially those with comorbid conditions like renal dysfunction, cardiovascular disease, or prior cerebrovascular incidents. Patient education plays a vital role in minimizing the risk of complications. Patients should be counselled on recognizing early signs of bleeding (e.g., gum bleeding, melena, petechiae), the importance of compliance with medication and dietary restrictions, and the necessity for timely follow-up. This case thus adds valuable insight into the potential for non-hemorrhagic neurological manifestations in the setting of coagulopathy. It emphasizes that seizure in an anticoagulated patient should prompt a thorough evaluation for both structural and metabolic etiologies, including subclinical coagulopathies.

CONCLUSION

This case highlights a rare but clinically significant presentation of Acitrom-induced coagulopathy manifesting as seizure activity and mucosal bleeding in a patient with multiple comorbidities, including cerebral venous thrombosis, coronary artery disease, and renal dysfunction. Despite the absence of intracranial hemorrhage on neuroimaging, the presence of elevated INR and PT values pointed to an over-anticoagulated state that likely contributed to the neurological episode. The patient responded well to the withdrawal of Acitrom, reversal with vitamin K and fresh frozen plasma, and initiation of antiepileptic therapy. In patients with a history of cerebrovascular disorders or seizure predisposition, even subtle changes in coagulation status can result in serious clinical consequences. Moreover, the case emphasizes the need for a multidisciplinary approach involving internal medicine, neurology, cardiology, and hematology to ensure timely diagnosis and optimal management. Patient education regarding medication adherence, symptom recognition, and regular follow-up plays a pivotal role in preventing such complications. As newer anticoagulants gain popularity, understanding the potential adverse effects of traditional VKAs like Acitrom remains essential, particularly in resource-limited settings where these agents are still widely used. In future clinical practice, early recognition of non-hemorrhagic neurologic manifestations in anticoagulated patients should prompt immediate investigation and intervention. This will help mitigate risks, reduce morbidity, and improve patient outcomes in those requiring long-term anticoagulation therapy.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Carcas AJ, Borobia AM, Velasco M, Abad- Santos F, Díaz MQ, FernándezCapitán C, et al. Efficiency and effectiveness of the use of an acenocoumarol pharmacogenetic dosing algorithm versus usual care in patients with venous thromboembolic disease initiating oral anticoagulation: Study protocol for a randomized controlled trial. *Trials*. 2012;13(2):239.
2. Oden A, Fahlen M. Oral anticoagulation and risk of death: a medical record linkage study. *BMJ*. 2002;325:1073–5.
3. Dentali F, Ageno W. Treatment of coumarin-associated Coagulopathy: a systematic review and proposed treatment algorithms *Journal of Thrombosis and Haemostasis*, 2006;4:1853–63.
4. Fredenburgh JC, Weitz JI. Factor XI as a target for new anticoagulants. *Hämostaseologie*. 2021;41(02):104-10.
5. Lüscher TF, Davies A, Beer JH, Valgimigli M, Nienaber CA, Camm JA, et al. Towards personalized antithrombotic management with drugs and devices across the cardiovascular spectrum. *European Heart J*. 2022;43(10):940-58.
6. Rosand J, Eckman MH, Knudsen KA, et al. The effect of warfarin and intensity of anticoagulation on outcome of intracerebral hemorrhage. *Arch Intern Med*. 2004;7:76.
7. Kirshner H, Schrag M. Management of intracerebral hemorrhage: update and future therapies. *Current Neurol Neurosci Rep*. 2021;21:1-5.
8. Hankins GD, Koen S, Gei AF, Lopez SM, Van Hook JW, Anderson GD. Neonatal organ system injury in acute birth asphyxia sufficient to result in neonatal encephalopathy. *Obstet Gynecol*. 2002;99(1):688–91.
9. Cendes F, Theodore WH, Brinkmann BH, Sulc V, Cascino GD. Neuroimaging of epilepsy. *Handbook of clinical neurology*. 2016;136:985-1014.
10. Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. *Neurology*. 1991;41(7):965-8.
11. Roberts MA, Godfrey JW. Epileptic seizures in the elderly. I. Aetiology and type of seizure. *Age and Ageing*. 1982;11:24–8.
12. Myint PK, Staufenberg EFA, Sabanathan K. Post-stroke seizure and post-stroke epilepsy. *Postgraduate Medical Journal* 2006;82:568– 72.
13. Nakken KO, Refsland G, Lillestølen KM, Solaas MH. Seizure-precipitating factors in epilepsy-- what do patients report. *Tidsskrift for den Norske lægeforening: tidsskrift for praktisk medicin, ny raekke*. 2005;125(16):2172-4.
14. Sánchez S, Rincon F. Status epilepticus: epidemiology and public health needs. *J Clin Med*. 2016;5(8):71.
15. Alvarez V, Rossetti AO. Clinical Consequences of Generalized Convulsive Status Epilepticus. *Status Epilepticus: A Clinical Perspective*. 2018:111-21.
16. Neuenfeldt FS, Weigand MA, Fischer D. Coagulopathies in intensive care medicine: balancing act between thrombosis and bleeding. *J Clin Med*. 2021;10(22):5369.

Cite this article as: Shakthivel CD, Murugesan J. Rare case report on acitrom induced coagulopathy with seizure disorder. *Int J Res Med Sci* 2025;13:3516-21.