IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES
ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 12, Iss 1, 2023

CASE REPORT: NICOUMALONE INDUCED SUBDURAL HEMATOMA

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ABSTRACT
Subdural hematoma is a critical medical condition where blood accumulates between the layers surrounding the brain, posing severe risks due to pressure on brain tissues. Factors such as age, head trauma, use of anticoagulant medications like Nicoumalone (Acenocoumarol), and alcohol consumption elevate the likelihood of developing subdural hematoma. Clinical symptoms include intense headaches, difficulty swallowing, hoarseness, confusion, or excessive drowsiness. This case study involves a 60-year-old female patient admitted to a tertiary care hospital presenting with complaints of headache and vomiting. The patient had a medical history of rheumatic heart disease status post mitral valve replacement in 1996, atrial fibrillation with cardiovascular risk, hypertension, and dyslipidemia, all managed under ongoing treatment. Due to inadequate monitoring and prolonged administration of T.NICOUMALONE 3mg, the patient developed a subdural hematoma over time.

KEYWORDS: Subdural hematoma, Hypertension, Dyslipidemia, Craniotomy, RHD (Rheumatoid Heart Disease), S/P MVR (Status Post Mitral Valve Repair), AF (Atrial Fibrillation), CVR (Cardiovascular Reactivity).

INTRODUCTION
Subdural hematoma refers to an abnormal accumulation of blood beneath the dura mater, the tough outer membrane situated directly beneath the skull and spinal column. This condition arises from the rupture of blood vessels, leading to active bleeding into the space between the dura mater and the arachnoid mater, termed as subdural hemorrhage [1].

The primary causes of subdural hematoma include head injuries, trauma, and prolonged use of specific medications such as Warfarin, Aspirin, and Nicoumalone. This condition disrupts normal cerebral vasculature, resulting in bleeding within the subdural space. The subsequent mass effect and neurological impairments stem from increased intracranial pressure [2].

Nicoumalone, also known as Acenocoumarol, belongs to the class of anticoagulants known as Vitamin K antagonists. It is utilized to prevent and manage clot formation, thereby

reducing the risk of stroke or heart attack. These medications inhibit the enzyme Vitamin K epoxide reductase (VKOR), which is crucial for the production of active hydroquinone form of Vitamin K. This hydroquinone form acts as a co-factor for gamma glutamyl carboxylase, essential for the gamma carboxylation of glutamate residues in prothrombin and clotting factors VI, IX, and X. This carboxylation process is vital for the clotting factors to bind with calcium ions and phospholipid surfaces, necessary for the progression of the coagulation cascade [3].

Here, we present a case of Nicoumalone-induced subdural hematoma, where T. NICOUMALONE 3mg was administered for over 27 years without adequate monitoring of International Normalized Ratio (INR) levels and follow-up care[4].

CASE REPORT

A 60-year-old female patient presented to the neurology department with a history of headache and vomiting persisting for the past week. Initially treated at a general hospital, she sought further management at our facility. Her medical history included systemic hypertension and dyslipidemia spanning over 20 years. Additionally, she had undergone mitral valve repair in 1996 for rheumatic heart disease and was diagnosed with atrial fibrillation with cerebrovascular reactivity. Her current medications included T. NICOUMALONE 3mg P/O OD, T. ATORVASTATIN 10mg P/O 0-0-1, T. SPIRONOLACTONE 25mg P/O 1-0-0, T. METOPROLOL SUCCINATE 25mg P/O 1-0-0, and T. ASPIRIN 75mg P/O 0-1-0[5].

On examination, the patient was conscious, oriented, and able to move all limbs without difficulty. Heart sounds revealed a murmur, chest examination was clear, and gastrointestinal examination indicated a non-tender abdomen. Initial vital signs included a pulse rate of 132 beats/min, respiratory rate of 20 breaths/min, blood pressure of 150/90 mmHg, and oxygen saturation of 99%. Laboratory investigations revealed elevated Troponin I (6.7 ng/L), BNP (415 pg/ml), and INR levels (ranging from 1.130 to 3.840) during her hospital stay [6].

A CT scan demonstrated an acute on chronic subdural hematoma in the right frontotemporo-parietal region measuring 15 mm, with midline shift to 8 mm causing compression of the right lateral ventricle and minimal distension of the left ventricle. No bleeding was observed in the basal cisterns, cerebellum, or brain stem. Plain CT brain further revealed acute on chronic subdural hematoma with mass effect characterized by right hemicranial cerebral edema and midline shift, in addition to age-related atrophic changes.

Treatment commenced with INJ. VITAMIN K 1ml IV to activate clotting factors. T. NICOUMALONE dosage was adjusted from 3mg to 2mg P/O 0-0-1 based on INR levels. Initially, INJ. CEFOPERAZONE + SULBACTUM 1.5g IV BD was administered for infection prevention, later switched to oral tablets. INJ. ESOMEPRAZOLE 40mg IV BD was provided for gastric irritation prophylaxis for the first 5 days, then converted to tablets.

INJ. LEVETIRACETAM 500mg IV 1-1-1 was given for seizure prophylaxis initially, transitioning to tablets (1-1-2 dosing). INJ. PARACETAMOL 500mg IV 1-1-1 was administered for the first 6 days, subsequently switched to T. PARACETAMOL 650mg P/O 1-1-1 for pain relief. T. BISOPROLOL 2.5mg P/O 1-0-0 and T. SPIRONOLACTONE 25mg P/O 1-0-0 were prescribed for blood pressure management. INJ. ONDANSETRON 4mg IV 1-1-1 was used for vomiting prophylaxis for the first 6 days, then converted to tablets. T. NAPROXEN SODIUM + DOMPERIDONE 500mg P/O was administered as needed for inflammation. SYP. ALUMINA + MAGNESIA + SIMETHICONE 10ml P/O 1-0-0 was given for stomach upset. T. AMITRYPTYLINE HYDROCHLORIDE 10mg P/O 0-0-1/2 was prescribed for chronic headache, and T. FEXOFENADINE HYDROCHLORIDE 120mg P/O 1-0-1 for managing allergic symptoms. T. CEFEROXIME AXETIL 500mg P/O 1-0-1 was provided for infection prevention, and T. BILASTINE 20mg P/O 0-0-1 for rhinorrhea. OXYMETAZOLINE HYDROCHLORIDE NASAL DROPS P/N 2°-2°-2° were used for nasal congestion.

The patient declined surgical intervention and was discharged on T. ESOMEPRAZOLE 40mg P/O 1-0-1, T. PARACETAMOL 650mg P/O SOS, T. ONDANSETRONE 4mg P/O SOS for 10 days, T. LEVETIRACETAM 500mg P/O 1-0-1, T. AMITRYPTYLINE HYDROCHLORIDE 10mg P/O 0-0-1/2 for 1 month, T. BISOPROLOL 2.5mg P/O 1-0-0, T. SPIRONOLACTONE 25mg P/O 1-1-0, T. ATORVASTATIN 10mg P/O 0-0-1 for 10 days, T. NICOUMALONE 2mg P/O 0-0-1 from Monday to Friday, 3mg P/O 0-0-1 on Saturday and Sunday, and SYP. ALUMINA + MAGNESIA + SIMETHICONE 10ml P/O 1-0-0 for 7 days. At the time of discharge, the patient was stable.

DISCUSSION

Nicoumalone, a Vitamin K antagonist utilized to prevent clot formation, is available in doses of 0.5mg, 1mg, 2mg, and 3mg. Prolonged use and inadequate monitoring of Nicoumalone can lead to excessive anticoagulation, heightening the risk of bleeding, including subdural hematoma, characterized by blood accumulation between the dura mater and arachnoid mater of the brain. Monitoring Nicoumalone therapy involves assessing the International Normalized Ratio (INR), which gauges blood clotting ability. The target INR varies based on therapeutic indications but generally falls between 2 and 3 for most conditions. Additionally, vigilance for signs of bleeding or bruising is crucial.

Effective management of subdural hematoma typically involves two surgical techniques: Craniotomy and Burr holes. Craniotomy serves as the primary treatment for acute subdural hematoma, involving temporary removal of a section of the skull to access and evacuate the hematoma. During the procedure, the hematoma is suctioned and irrigated, flushing it out with fluid. Subsequently, the skull section is replaced and secured using metal plates or screws.

A case study by Ismail Aissa et al. reported an instance of an unusual bleeding complication under Acenocoumarol: spinal subdural hematoma. An 82-year-old patient with a history of ischemic heart disease and atrial fibrillation, under Acenocoumarol therapy, presented with

sudden paraplegia, severe back pain, urinary incontinence, and anal sphincter dysfunction. Examination revealed complete loss of lower limb power (MRC grade 0) and an elevated INR of 10. MRI confirmed a spinal hematoma at the T12 level, measuring 36mm, causing compression of the spinal cord. Treatment involved T11-L1 laminectomy with evacuation of the subdural hematoma.

In this reported case, the patient presented with headaches, and CT brain imaging confirmed a subdural hematoma attributed to chronic use of T. NICOUMALONE over 27 years without adequate monitoring. The Naranjo adverse drug reaction probability scale scored 6, indicating a probable adverse drug reaction. According to the WHO classification of adverse drug reactions, this falls under Type C (Continuous), typically dose-related and associated with long-term drug use. The severity assessed by the Hartwig severity assessment scale was categorized as Severe level 5, indicating that the adverse reaction caused permanent damage to the patient.

CONCLUSION

Subdural hematoma refers to an abnormal accumulation of blood within the dura mater. In this case, it resulted from prolonged use of T. NICOUMALONE, prescribed to prevent clot formation. The diagnosis was supported by both subjective symptoms and objective findings. However, confirmation through methods such as serum drug concentration or therapeutic drug monitoring was not pursued.

The patient declined surgical intervention and opted for discharge, receiving anticonvulsants and other supportive medications. The incident underscores the importance of patient education and effective management in preventing adverse drug reactions. Based on its severity, this case represents a severe adverse drug reaction, characterized by potential life-threatening risks, permanent damage, and the need for intensive medical care.

REFERENCE

1. Pharmacotherapy 5th edition by Joseph T Dipiro, et al. 2002; 356-57.
2. Ellie Edlmann, Susan Giorgi-Coll, Peter C Whitfield, Keri L H Carpenter and Peter J Hutchinson. Pathophysiology of chronic Subdural Hematoma: inflammation angiogenisis and implications for pharmacotherapy. Journal of neuroinflammation. 2017; 108.
3. A J Brafield. Nicoumalone: A new anticoagulant. British Medical Journal 1959; 1: 1211
4. Essentials of Medical Pharmacology 8th edition by KD Tripathi. 2019; 660-68.
5. Amit Kumar Thotakura and Nageswara Rao Marabathina. The role of Medical Treatment in Chronic Subdural ematoma. Asian Journal of eurosurgery. 2018; 13(4): 976-83.
6. Ismail Aissa, bdelghafour Elkoundi, Rabi Andalousi, Azis Benakrout, Abdelatif Chlouchi Mohimed Moutaoukil, Jawad Laaguili, Mustapha Bensghir, Hicham Balkhi, Salim Jafar Lalaoui. Unusual localization of bleeding under Acenocoumarol; Spinal Subdural Hematoma. International Journal of surgery case reports. 2019; 59: 15-18