Superwarfarin Intoxication of Unknown Etiology

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Abstract

superwarfarins are popular and are readily accessible, they are associated with intoxication, leading to prolonged and sometimes life-threatening coagulopathies. We report our experience managing 2 patients who had clinical evidence of superwarfarin intoxication at Kyung Hee Medical Center in Seoul, Korea. Superwarfarin exposure or poisoning is an important public health concern in South Korea, affecting those of all ages. The diagnosis of superwarfarin poisoning is usually straightforward in cases of acute poisoning, but because many cases present with obscure history of exposure, clinical suspicion is the key to early diagnosis and timely intervention. Prolonged treatment with large doses of vitamin K is needed for superwarfarin intoxication.

(Key words: Superwarfarin, broadifacoum, coagulopathy, Vitamin K)

Introduction

Superwarfarins are 4-hydroxycoumarin anticoagulants that have been developed in the 1970’s as rodenticides. They are 100 times more potent than warfarin with a half-life of at least 16 to 69 days. Commercially available superwarfarins include brodifacoum, difenacoum, bromodialone, and chlorphacinone. Because superwarfarins
are popular and are readily accessible, they are associated with intoxication, leading to prolonged and sometimes life-threatening coagulopathies. Self-administration by adults with Munchausen syndrome or those attempting suicide, accidental ingestion by children, and even malicious poisoning have been reported. The main route of superwarfarin exposure is via oral ingestion. However, absorption through skin or inhalation can also occur, and in some cases the origin of exposure remains obscure. The Poison Control Centers Toxic Exposure Surveillance System in the United States have reported over 10,000 cases of superwarfarin intoxication annually since 2008, and superwarfarin intoxication is recognized as an important public health problem. Although several previous reports suggest an increase in the incidence of superwarfarin in Korea for past few years, there is yet to be a systemized and detailed report on the issue. We report our experience managing 2 patients who had clinical evidence of superwarfarin intoxication at Kyung Hee Medical Center in Seoul, Korea.

Case Report

Case 1

A 53-year-old male, who had been admitted to another hospital for gross hematuria and epistaxis, was transferred to our medical center for management of hemoperitoneum. His medical history was unremarkable except for fluconazole intake 1 week prior to his admission in another hospital for treatment of tinea pedis. Blood tests showed a prolonged prothrombin time (PT) of 50.7 seconds with international normalized ratio (INR) of 5.2, activated partial thromboplastin time (aPTT) of 87.8 seconds, which was fully corrected when mixed with normal plasma (50:50). Other laboratory test results, including thrombin time, complete blood count with differentials, fibrinogen, renal and liver function tests, and electrolytes were normal. Tests for fibrin degradation products (FDP) and D-dimer were negative. Coagulation factor levels were as follows: factor II 5% of normal; V 69%; VII 8%; IX 4%; and X 6%. Protein C activity was 16% (70–130%), protein S activity 19% (73.7–146.3%), protein C antigen level 25 μg/ml (72–160 μg/ml), and protein S antigen level 24 μg/ml (60–150 μg/ml). The patient denied ingestion of any illicit drugs, including rodenticides and anticoagulants, or suicidal attempts. Since his blood test results were confirmatory for vitamin K dependent coagulation factor deficiency, superwarfarin intoxication was suspected. Subsequently, his serum brodifacoum level was checked using high-performance liquid chromatography (HPLC)/ tandem mass spectrometry (LC–MS/MS), and came back positive. For hemoperitoneum, the patient was put through surgical drainage of hemoperitoneum. For coagulopathy, he received 4 pints of fresh frozen plasma (FFP) transfusion on day 1,