

## Tongue Hematoma Induced by Warfarin Overdose

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**Abstract:** Warfarin is one of the common oral anticoagulants. Anticoagulant response is affected by the amount of dietary Vitamin K, various drugs, foods and herbal treatments. Although, hemorrhage is one of the side effects of warfarin, tongue hematoma is a rare complication. In this research, 50 years old male patient developed tongue hematoma during the prophylactic warfarin treatment due to the atrial fibrillation is presented.

**Key words:** Warfarin, overdose, hematoma, tongue, complication, dietary

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### INTRODUCTION

Warfarin is a common oral anticoagulant used in the prevention of arterial and venous thromboembolic events. Warfarin is exerted anticoagulant effect by reducing the amount of Vitamin K which is required for the activation of clotting factors II, VII, IX and X. Anticoagulant response is very variable and is affected by genetic polymorphism in the enzyme of drug metabolism, the amount of dietary Vitamin K, a variety of pharmaceutical, food and herbal treatments. As with the other anticoagulants, warfarin use increases bleeding risk. Tongue hematoma is extremely rare complication of warfarin use. Unless early diagnosis and treatment, it becomes life-threatening with rapid progression. In this research, clinical and laboratory findings of a patient developed tongue hematoma due to the warfarin drug interactions.

### CASE

The 50 years old male patient was admitted to the emergency room with complaints of tongue swelling and bruising. In his physical examination, blood pressure was 120/80 mmHg, pulse was 96/min and rhythmic, respiratory rate was 23/min, body temperature was 36.8°C. He had CABG 2 years ago and he was on prophylactic oral anticoagulant therapy with Coumadin® 5 mg/day.

He had started to use Propycil 100 mg 1 month ago due to the diagnosis of hyperthyroidism. ECG revealed atrial fibrillation. Results of laboratory tests performed in emergency department as follows: hemoglobin: 13.3 mg dL<sup>-1</sup>; hematocrit: 40.7%, platelets:

226000/mm<sup>3</sup> and WBC: 7700/mm<sup>3</sup>. Results of the other biochemical examination were normal. International Normalized Ratio (INR) levels were found 10.50. After diagnosed as tongue hematoma induced by warfarin overdose, one unit of fresh frozen plasma was administered. During this period prophylaxis was switched to (Low-Molecular-Weight Heparin (LMWH). INR was found 5.74 after the treatment. Laboratory test after 12 h, INR was found 1.90. Patient was discharged with improvement.

### DISCUSSION

Generally, anticoagulant agents are used in acute ischemic stroke, deep vein thrombosis, pulmonary embolism, heart valve disease, acute myocardial infarction and atrial fibrillation. The mechanism of action of warfarin is to block gamma carboxylation of glutamate residues in Vitamin K dependent coagulation factors (factors II, VII, IX and X), prothrombin, protein C and S (Hambleton, 2004; Visser *et al.*, 2004). Bleeding is the most important complication in patients receiving anticoagulant therapy with the frequency of 2-10%. Bleeding sites are soft tissue (21%), gastrointestinal system (15%), urinary system (15%), nose and pharynx (35%), intracranial (4%), thorax (3%), intraocular (2%), retroperitoneum (1%) and joints (0.5%) (Landefeld and Beyth, 1993). During the warfarin (Coumadin®) use, 1 year major bleeding risk is 0.5-7.0% and it is dose proportional. While paracetamol, amiodarone, erythromycin, fluconazole, fluoxetine, metronidazole, salicylates, sulfamethoxazole, tamoxifen and thyroid hormone increases the anticoagulant effect of warfarin, antithyroid drugs, barbiturates and carbamazepine reduce anticoagulant effect of warfarin



Fig. 1: Tongue hematoma by Warfarin



Fig. 2: Sublingual hematoma view

(Schulman, 2003; Feldstein *et al.*, 2006). Despite the literature, tongue hematoma occurred on concomitant use of antithyroid drug and warfarin.

Warfarin acts by antagonizing the effect of Vitamin K. Onset of effect takes at least 48-72 h. The bioavailability of warfarin is approximately 100%. Bile is needed for absorption from the gastrointestinal tract. Because warfarin bound albumin in plasma by 99%, renal elimination is slow. Plasma half-life is 36 h (Hirsh *et al.*, 2001). During warfarin therapy, in addition to the varying degree of bleeding other side effects such as urticaria, rash, dermatitis, alopecia, diarrhea, skin necrosis, pancreatitis, jaundice and toe bruising may occur. Warfarin has teratogenic effect during pregnancy particularly in the first trimester. It may cause hemorrhage passing through the placenta. In addition, it may cause venous thrombosis and hemorrhagic infarction reducing the levels of protein C. Antidote of warfarin is Vitamin K1. In overdose fresh frozen plasma (10-20 mL) is used (Ginsberg *et al.*, 2001). Kucher *et al.* (2004) reported that incidence of bleeding increase over time. The vast majority of patients who developed bleeding have used

nonsteroidal anti-inflammatory drugs, antiplatelets, etc. concomitantly with warfarin (Kucher *et al.*, 2004) (Fig. 1 and 2).

## CONCLUSION

As a result, during the warfarin therapy, tongue hematoma should be considered in differential diagnosis in patients with bruising and swelling of the tongue. Physicians in emergency department should take into consideration the rare complications of warfarin treatment. Uncontrolled use of warfarin has great risk as seen in the case. Oral anticoagulants are commonly used. The regular use of the drug and dose has critical importance. Thus, patients and caregivers should be fully informed about the side effects of the drug.

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