Fırat Tıp Dergisi 2012; 17(4, ek sayı 1): 30-33

Case Report

www.firattipdergisi.com

Sublingual Hematoma Linked to Uncontrolled Warfarin Use: A Case Report

Hasan KARA[a], Aysegul BAYIR, Ahmet AK, Selim DEGIRMENCI, Demet ACAR, Rabia ISTANBULLUOGLU

Selcuk University, Faculty of Medicine, Emergency Medicine, Konya, Turkey

ABSTRACT

Anticoagulant treatment is a vital treatment method used in prophylaxis and treatment of tromboembolic diseases. In anticoagulant treatment, the most significant complication that can sometimes threaten patient's life is hemorrhage. Therefore, planning anticoagulant treatment in a way not to cause thrombosis or bleeding and meticulous clinical and laboratory follow-up is vital. Hemorrhage in sublingual area is very rare. However, warfarin related bleeding in this area is life threatening and it might require securing patient's airway. In its treatment, it is recommended that anticoagulation with vitamin K, pro-thrombin complex concentrate (PCC) and fresh frozen plasma (FFP) be reversed immediately. In this article, a case who developed sublingual hemorrhage caused by prophylactic warfarin intake due to Coronary Artery Bypass Graft (CABG) has been presented.

Key words: *Warfarin, Overdose, Sublingual haemorrhage*

ÖZET

Kontrolsüz Warfarin Kullanımına Bağlı Gelişen Sublingual Kanama: Olgu Sunumu

Antikoagülan tedavi, tromboembolik hastalıkların profilaksi ve tedavisinde yaşamsal önem taşıyan bir tedavi yöntemidir. Antikoagülan tedavinin hasta hayatını tehdit edebilen en önemli komplikasyonu kanamadır. Bu nedenle antikoagülan tedavinin tromboz veya kanamaya yol açmayacak şekilde planlanması, klinik ve laboratuvar takibinin titizlikle yapılması yaşamsal önem taşımaktadır. Sublingual bölgeye kanama çok nadir görülmektedir. Ancak warfarine bağlı bu bölgedeki kanamalar hayatı tehdit edici bir durumdur ve hastanın havayolunun güvence altına alınması gerekebilir. Tedavide K vitamini, protrombin kompleks konsantresi ve taze donmuş plazma ile antikoagülasyonun biran önce tersine çevrilmesi önerilmektedir. Bu makalede Coronary Artery Bypass Graft nedeniyle profilaktik olarak warfarin alımına bağlı sublingual hematom gelişen bir olgu sunulmuştur.

Anahtar Sözcükler: *Warfarin, Doz Aşımı, Sublingual Kanama*

Warfarin is an oral anticoagulant which is widely used to prevent arterial and venous thromboembolic incidences. It takes its anticoagulant effect by decreasing vitamin K amount needed for the activation of coagulation factors II, VII, IX and X. Anticoagulant respond is very variable and is influenced by the genetic polymorphism of the enzyme required for medicine metabolism, vitamin K intake with diet, various medicines, food and herbal treatment. The most important side effect of warfarin use is bleeding. Bleeding is more frequently seen in intra-cerebral, skin, gastrointestinal system, genitourinary system, adrenal glands, epidural space, peritoneal cavity and subconjuntival area. Laryngeal or retropharyngeal hemorrhage secondary to the use of oral anticoagulants can cause upper airway obstruction. Sublingual hemorrhage are extremely rare (1, 2). Ideal oral anticoagulation can be achieved by laboratory monitoring individually. While paracetamol, amiodarone, erythromycin, flukonazol, fluoxetine, metronidazole, salicylate, sulfamethoxazole, tamoxifen and triode hormone increase warfarin's anticoagulant effect, antitroide medicines, barbiturates and carbamazepine decreases its effect (3, 4). If it is not diagnosed and treated early, it shows fast progression and threatens life. In this article, a case who developed sublingual hemorrhage caused by oral warfarin use as an anticoagulant treatment and recovered with conservative treatment has been presented.

CASE REPORT

A 72-year-old female patient applied to emergency service with sore throat, expectoration, sublingual panicula and cyanosis complaints that had been going on for the previous 48 hours. In the physical examination of the patient, blood pressure was 140/86

[a]Corresponding Adress: Dr. Hasan KARA, Selcuk University, Faculty of Medicine, Emergency Medicine, Konya, Turkey
e-mail: hasankara42@gmail.com

mm/Hg, pulse was 96/min rhythmic, respiration was 23/min, and temperature was 36.8 Cº. At the bottom of the patient's mouth was a reddish panicula reported that had been spreading rapidly for the last one day. The voice of the patient thickened after the panicula was seen but there was no defined respiratory difficulty. The examination of the patient's oral cavity revealed that there was soft, red and submucosal located swelling which involved the bottom of the mouth and bilateral ventral surface of the tongue (Figure 1-3). There was no finding of airway failure in the flexible endoscopic examination of pharynx and larynx and laryngeal mobility was natural. The story of the patient revealed that CABG had been applied two years ago and Warfarin (Coumadin®) 5mg/day was started as an oral anticoagulant treatment. In the electro-cardiograph (ECG) there was normal sinus rhythm. In the laboratory examination at submission, it was determined that hemoglobin was 13.0 gr/dl, thrombocyte value was 292000/mm^3, International Normalized Ratio (INR) level was 12. Besides clinical findings, the patient, who was diagnosed with clinical findings that she had sublingual hemorrhage caused by excessive dose of warfarin, was given 2 units of FFP. INR level after the treatment was established as 5.74. Twelve hours later, INR value was measured as 1.90. The patient who was observed to have recovered clinically was discharged on the 4^{th} day.

Figure 1. *Wiev of the hematoma under the oral mucosa in the sublingual space*

Figure 2. *Sublingual hematoma in the floor of mouth*

Figure 3. *The presence of sublingual hematoma with swelling sublingual mucosa*

DISCUSSION

Anticoagulant agents are mostly used in acute ischemic strokes, deep venous thrombosis, pulmonary emboli, heart valve diseases, acute myocardium infarction and atrial fibrillation. The oral anticoagulant agents currently used are warfarin, acenocoumarol and fenindione. The effect mechanism of warfarin is to block gama-carboxilation of various glutamate residues of vitamin K dependent coagulation factors (factor 2, 7, 9, 10) in prothrombin, C and S proteins in combination with the expoid reductase activity of vitamin K found in microcosms of the liver (3). Bleeding is the most important complication in patients who receive anticoagulant treatment and has a prevalence rate of 2 to 10%.

Bleeding is seen in intracranial area, skin, gastrointestinal system, genitourinary system, adrenal glands, epidural space, soft tissues, nose, pharynx, peritoneal cavity, subconjuctival area, thorax, intraocular, retroperitoneum and joints (1, 4). During warfarin (Coumadin®) application major bleeding risk within one year ranges between 0.5 to 7.0 % and this risk is directly proportional to anticoagulation level.

Particularly, in the case of life-threatening bleedings, the decision whether to stop or continue the treatment is vital. It should be taken into consideration that if treatment continues patient may bleed again and if it is stopped, there is a risk of thromboemboli. Thromboemboli is very low compared to re-bleeding risk. It is stated that vitamin K or factor replacement is only induced in patients with major bleeding caused by warfarin. It is known that hemorrhage risk increase in patients who use anticoagulant and who have INR level 6 or more (5). Kucher et al. (6) have reported that incidence of bleeding caused by warfarin use has increased considerably recently. It has been reported most of the patients who develop bleeding use other non-steroid anti-inflammatory, anti-agregante medicines together with warfarin.

In the story of our patient, it was observed that she used other non-steroid anti-inflammatory, anti-agregante medicines together with warfarin. Our patient also had mandibular totally removable denture which can lead to traumatic damage in the sublingual area. While upper airway obstruction generally developed as a result of sublingual, retropharyngeal or epiglottic bleeding in the patient who received anticoagulant treatment, it can be difficult to diagnose bleedings in submaxillary or retro-pharyngeal areas. Symptoms related to sublingual bleeding are frequently seen in cervical mass, sublingual or retro-pharyngeal panicula and tachypnea and stridor, respectively. Bleedings or hematomas in the sublingual area can be diagnosed with inspection. While bleeding are seen locally only in sublingual area at the beginning, upper airway entrance can be invisible as hematoma spreads to submaxillary area. Therefore, patients to be followed medically should be in intensive care units or in places where they can be monitored closely. Urgent airway control unit which includes tracheostomy application should be ready on the bedside (7, 8). In our case, there were sore throat, hemoptysis, sublingual panicula and cyanosis complaints. However, no airway obstruction was determined in the inspection. Every patient who comes with sore throat complaint and who has received anticoagulant treatment should be taken seriously because this state is often observed just before acute airway obstructions (9). Surgical drainage of sublingual hematoma is defined but its effectiveness is controversial (10). Surgical intervention was also applied on our patient.

However, frequently spontaneous resolution was realized with the coagulation returning to normal within a few days. Airway obstruction due to sublingual hematoma should be considered as an emergency case and the prior target should be to guarantee the patients' airway. The treatment of the patients with bleeding complication includes discontinuing oral anticoagulant, vitamin K for non-urgent cases and coagulation factor concentrations like PCC and FFP for emergency cases. In the patients who apply with serious sublingual hematoma, anticoagulation should be reversed immediately with vitamin K, PCC or FFP. In minor bleedings, decreasing only oral anticoagulant can be enough to reverse anticoagulation. However, if vitamin K is to be given in minor bleedings, the half life of plasma antagonist and the action time should be taken into consideration. In intravenous applications, vitamin K lead to significant but not complete INR respond within 4-6 hours and if it is taken orally, this period is 24 hours. In major bleedings, functional coagulation factors should be applied fast to reverse the effect of oral anticoagulant and it is necessary to achieve recycle safety as fast as possible. The reversion of anticoagulation in PCC can be achieved realized more successfully than FFP. However, PCC and in particular the new generation PCCs are associated with a more rapid normalisation of the INR and a better clinical outcome than is FFP due to the balanced ratio of four vitamin K-dependent clotting factors plus the coagulation inhibitors proteins C and S. Other advantages of PCC compared to FFP is that it has smaller infusion volumes and does not require blood type tests and does not include blood products in which viruses are inactivated. FFP replaces functional vitamin K-related coagulation factors and can partially improve coagulation and this takes time. However, PCC can reverse oral anticoagulant effect within 10-15 minutes (7). Strict control of airway can lead to a process which can result with endotracheal intubation, tracheostomy or cricothyroidotomy (5). Surgical drainage of sublingual hematoma is defined but its effectiveness is controversial (10). Our patient underwent surgical intervention too. However, frequently spontaneous resolution was observed within a few days after coagulation returned to normal. The placement of an endotracheal tube due to the obstructive effects of endotracheal intubation of the sublingual hematoma causes the risk of bleeding (8).

In the patients who are considered to be applied endotracheal intubation or surgical airway intervention, invasive procedure should be performed after anticoagulation is immediately reversed preferably with PCC. In the treatment of our case, oral anticoagulant was discontinued and FFP was given. Besides, in the treatment of our case there was no a condition determined to require endotracheal intubation or surgical drainage of hematoma. It is stated that vitamin K or factor replacement is only induced in patients with major bleeding caused by warfarin. Discontinuation of warfarin is recommended in patients with high INR value but without bleeding. Discontinuation of warfarin and follow-up are recommended in patients with INR value lower than 5 and with bleeding (11).

Conclusion

As oral anticoagulant drugs have vital importance, patient and his/her relatives should be very well

informed about the side effects of the drug. Sublingual hematoma which is a rare complication should be considered as a differential diagnosis in the patients who receieve warfarin treatment and apply with the complaints of cyanosis, panicula and bleeding in the tongue. However, as life-threatening conditions develop very fast in such cases, early diagnosis and application of appropriate medical treatment prevent the need for artificial airway**.**

REFERENCES

1. Lee NJ, Peckitt NS. Treatment of a sublingual hematoma with medicinal leeches: report of case. J Oral Maxillofac Surg 1996; 54: 101-3.
2. Feldstein AC, Smith DH, Perrin N, et al. Reducing warfarin medication interactions: an interrupted time series evaluation. Arch Intern Med 2006; 166: 1009-15.
3. Visser LE, Bleumink GS, Trienekens PH, et al. The risk of overanticoagulation in patients with heart failure on coumarin anticoagulants. Br J Haematol 2004; 127: 85-9.
4. Landefeld CS, Beyth RJ. Anticoagulant-related bleeding: clinical epidemiology, prediction and prevention. Am J Med 1993; 95: 315-28.
5. Kucher N, Castellanos LR, Quiroz R, et al. Time trends in warfarin-associated hemorrhage. Am J Cardiol 2004; 94: 403-6.
6. Lee M, Berger HW, Granada MG. Akut upper airway obstruction. Sodium warfarin-induced hemorrhage into the base of the tongue and epiglottis. Chest 1980; 77: 454-5.
7. Cohen AF, Warman SP. Upper airway obstruction secondary to warfarin-induced sublingual hematoma. Arch Otolaryngol Head Neck Surg 1989; 115: 718-20.
8. Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 94: 57-64.
9. Wiedermann CJ, Stockner I. Warfarin-induced bleeding complications-clinical presentation and therapeutic options. Thromb Res 2008; 122: 13-8.
10. Gupta MK, McClymont LG, El-Hakim Hamdy. Case of sublingual hematoma threatening airway obstruction. Med Sci Monit 2003; 9: 95-7.
11. Weber JE, Charles MJ, Pollack V. Anticoagulants, antiplatelet agents and fibrinolytics. In: Tintinalli JE, Kelen GD, Stapczynski JS, editors. Emergency medicine a comprehensive study guide. 6th ed. New York: McGraw-Hill, 2004; 1354-63.

Gönderilme Tarihi: 04.06.2012