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SPONTANEOUS SUBLINGUAL HEMATOMA SECONDARY TO CONTINUOUS USE OF VARFARINE: A CLINICAL EMERGENCY

HEMATOMA SUBLINGUAL ESPONTÂNEO SECUNDÁRIO AO USO CONTÍNUO DE VARFARINA: UMA EMERGÊNCIA CLÍNICA

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ABSTRACT

Sublingual hematoma is characterized by elevation of the bruising/bleeding lingual floor, suggestion below the tongue bleeding after coagulation disorders and/or trauma in the region. The study aims to describe a case of sublingual hematoma spontaneous secondary to the use continuous of an anticoagulant, witch prognosed favorable after therapeutic approach conservative. Patient, MGC, 68 years old, admitted to the urgency/emergency service of the Hospital da Restauração Governador Paulo Guerra – SES/PE, witch history spontaneous swelling about 12 hours, with extensive bruise sublingual and below the jaw, difficulty talking, respiratory and pain complaint; well as bruises at the extremities, melena and intense arthralgia. Referred to use of the Marevan® 10 mg (Warfarin), acetyl salicylic acid (AAS)100 mg and Digoxin 0,25 mg after accident brain vascular ischemic. Due to the clinical condition, medication suspended, there was the request routine coagulogram, endoscopy, and ventilate support until the remission of the symptoms; for later adjustment of the appropriate dosage. Conservative treatment proved effective for such a case. Sublingual hematoma is fatal complication rare and potentially, being normaly due use of oral anticoagulants, essentially clinical diagnoses and therapeutic approach conservative is successful, since casual factors are controlled.
Keywords: Anticoagulants. Blood Coagulation Disorders. Mouth Abnormalities.

RESUMO

O hematoma sublingual é caracterizado pela elevação de assoalho lingual equimótico/hemorrágico, sugerindo sangramento submucoso, após distúrbios de coagulação e/ou trauma em região. O estudo visa descrever um caso de hematoma sublingual espontâneo secundário ao uso contínuo de um anticoagulante, com prognóstico favorável após abordagem terapêutica conservadora. Paciente, MGC, sexo feminino, 68 anos, deu entrada no serviço de urgência/emergência do Hospital da Restauração Governador Paulo Guerra - SES/UPE, com história de aumento de volume espontâneo dentro de 12 horas, apresentando extenso hematoma de região sublingual e submentual, queixa fonética, respiratória e álgica; bem como equimoses nas extremidades, melena e intensa artralgia. Referiu usar Marevan® 10mg (Varfarina), Ácido Acetilsalicílico (AAS) 100mg e Digoxina 0,25mg após acidente vascular isquêmico (AVCI). Devido ao quadro clínico, a medicação foi suspensa, houve a solicitação de coagulograma de rotina, endoscopia, e suporte ventilatório até a remissão dos sintomas; para posterior adequação da dosagem adequada. O tratamento conservador mostrou-se eficaz para tal caso. O hematoma sublingual é uma complicação rara e potencialmente fatal, sendo normalmente decorrente do uso de anticoagulantes orais, apresenta diagnóstico essencialmente clínico e a abordagem terapêutica conservadora é bem-sucedida, uma vez que os fatores causais forem controlados.
Palavras-chave: Anticoagulantes. Anormalidades da Boca. Transtornos da Coagulação Sanguínea.

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INTRODUCTION

Hematoma or sublingual hemorrhage, also described as a 'Pseudo-Ludwig' phenomenon, was distinguished in 1978 by Lepore as an elevation of the lingual floor, with a higher prevalence in patients with coagulation disorders (RANJAN *et al.*, 2015; SATPATHY *et al*., 2015). Such an entity is considered a rare and potentially fatal complication (KARMACHARYA *et al.*, 2015; GHOSH *et al.*, 2016; MOREIRA *et al.*, 2016; SPLINDER *et al.*, 2017; TAT *et al.*, 2018).

The etiology of the sublingual hematoma may be the result of anticoagulant-induced coagulopathy, uncontrolled hypertension, aneurysms in the facial or lingual arteries, rupture of the atherosclerotic vessels that supply the tongue musculature and trauma to the face (KARMACHARYA *et al.*, 2015; SATPATHY *et al.*, 2015; MOREIRA *et al.*, 2016).

The lingual floor anatomy is composed of soft tissue covered only by a thin layer of mucosa and with multiple fascial spaces. When vessel rupture occurs in this region, it quickly progresses to blood accumulation in these spaces, thus initiating the process of expansion and formation of sublingual hematoma (ALAMOUDI *et al.*, 2017; SPLINDER *et al.*, 2017; TAT *et al.*, 2018).

The clinical characteristics can vary from simple symptoms, such as pain in the oropharynx region and dysphonia, or they can be severe, life-threatening, especially when the patient has dyspnea (GHOSH *et al.*, 2015; SERRALVO; ZAMBOTI; BREGANO, 2015).

The diagnosis is essentially clinical, with anamnesis including details of the use of anticoagulants or trauma and the physical examination confirming a tissue hematoma, thus differentiating from infectious processes (BUYUKLU *et al.*, 2014; SERRALVO; ZAMBOTI; BREGANO, 2015; MOREIRA *et al.*, 2016; ALAMOUDI *et al.*, 2017).

There is no consensus in the management of these patients in the current literature. The reversal of anticoagulation is necessary with careful observation. Therefore, without consensus, the diagnosis and management of this condition remains a challenge, thus requiring profound and further studies (SILVA, 2010; KARMACHARYA *et al.*, 2015; MOREIRA *et al.*, 2016; ALAMOUDI *et al.*, 2017; SPLINDER *et al.*, 2017).

Nevertheless, it is suggested as an initial conduct for these cases, as the lack of oxygen produces permanent brain damage or the death of the patient, and reversal of anticoagulation to observe the patient's airways. In severe cases, anticoagulation should be reversed with vitamin K, Prothrombin Complex Concentrate (PCC) and / or Fresh Frozen Plasma (FFP) (BUYUKLU *et al.*, 2014; SERRALVO; ZAMBOTI; BREGANO, 2015; TAT *et al.*, 2018; MAHTO *et al.*, 2019).

Therefore, the purpose of this present study is to describe a clinical case of spontaneous sublingual hematoma secondary to the continuous use of an anticoagulant, as well as to analyze and discuss the topic, emphasizing the clinical characteristics and therapeutic approaches, aiming at improving the knowledge and conduct employed.

CASE REPORT

A female patient, 68 years old, faioderm, was admitted to the Hospital da Restauração Governador Paulo Guerra, Recife/PE, went to the Service of Bucco Maxillofacial Surgery and Traumatology (CTBMF), undergoing hematoma in the sublingual region, dysphagia, dyslalia and complaint of nausea and epigastric and joint pain. The patient reported a history of ischemic stroke (stroke) approximately 01 month ago, using an oral anticoagulant, Marevan® 10 mg (Warfarin), since then; without medical supervision and control of the International Normalized Ratio (INR). In addition, she reported arterial hypertension without clinical follow-up or drug control.

During anamnesis, she also informed that she was using Therapeutic Acetylsalicylic Acid (ASA) 100mg and Digoxin 0.25mg, in addition to Marevan® 10mg (Warfarin).

On physical examination, she had ecchymosis in the cervical region and in the upper and lower left limbs. Examination of the oral cavity showed limited mouth opening, hematoma in the

sublingual region (Figure 1), analyzed by computed tomography, the occlusion was nonfunctional and without clinical signs that could suggest fracture of the facial bones.

Figure 1 - Edema and ecchymosis in the submandibular region

Source: the authors.

In the picture above, the diagnostic hypothesis raised was that of hematoma secondary to the use of anticoagulant, Marevan® 10mg (Warfarin), and to confirm the condition, complementary hematological (blood count and coagulogram) and biochemical tests (fasting blood glucose, urea) were requested, creatinine, ionogram, liver transaminases, urine summary).

At the same time, a therapeutic approach was initiated for the patient's symptomatic treatment, with the following schedule: suspension of Marevan® 10mg (Warfarin) and Acetylsalicylic Acid (ASA) 100mg until coagulation stabilization and verification of the need to resume; start of volume replacement with 1000mL of 0.9% intravenous saline; start of Ranitidine - 50 mg diluted in distilled water every 12 hours intravenously to protect and relieve epigastric pain; start of Plasil® - 1 vial every 8 hours intravenously to relieve nausea; start of Sodium Dipyrone - 1g diluted in distilled water every 6 hours in case of pain complaint; start Captoten® 25mg orally if systolic blood pressure = 160 mmHg and diastolic blood pressure = 110 mmHg; Glucose 50% - 3 ampoules if Hgt <80%; maintenance of Digoxin - 0.25mg orally in the morning.

In addition to the medication regimen, a rigorous blood pressure (BP) check was established every six hours, and this proved to be controlled for most of the hospital stay (130x80mmHg), with the highest peak being 160 x 80 mmHg on the third day after hospitalization, and lower 70x40mmHg on the second day after hospitalization.

After the results of the tests requested in the initial care, the following changes were verified: Hemoglobin = 7.4 [g / dL]; Hematocrit = 23.1 [%]; Red blood cells = 2.41 [103 / uL]; INR = inconclusive. Reference values for females: Hemoglobin = 12 - 16.5 [g / dL], Hematocrit = 35 - 47 [%], Red blood cells = 4 - 5.6 [103 / uL]; INR, the reference value for a healthy person should vary between 0.8 and 1. In the case of the use of oral anticoagulants the value must be between 2 and 3 (ROSENFELD *et al*., 2019).

Having verified the hematological alterations that corroborated for the confirmation of the diagnosis of anemia and coagulopathy secondary to drug therapy, the evaluation of the medical clinic for the due multidisciplinary treatment was requested.

Once the diagnosis was maintained, it was established that laboratory tests should be ordered every 24 hours (Table 1) in order to observe the hematological patterns after the warfarin suspension. In

addition to the measurement of vital signs and Hgt every six hours, and the request for an electrocardiogram to analyze cardiac function.

Table 1 - Evolution of Hematological Tests

Exams	24 hours	48 hours	96 hours	On discharge day
Hemoglobin	7,23 [g/dL]	7,5 [g/dL]	9,6 [g/dL]	9,6 [g/dL]
Hematocrit	21,69 [%]	22,5 [%]	28,8 [%]	28,8 [%]
Hematocrit	2.41 [10^6/uL]	2,5 [10^6/uL]	3,2 [10^6/uL]	3,2 [10^6/uL]
INR	3.1	2.98	1.90	1.23

Note: INR – Prothrombin Time.
Source: the authors.

In order to optimize the treatment initiated in the first hour of hospitalization, an intramuscular vitamin K ampoule was applied at 12 in 12 hours associated with the administration of 300 mL of Fresh Frozen Plasma (PFC) in 8 in 8 hours, intravenously, for 03 days.

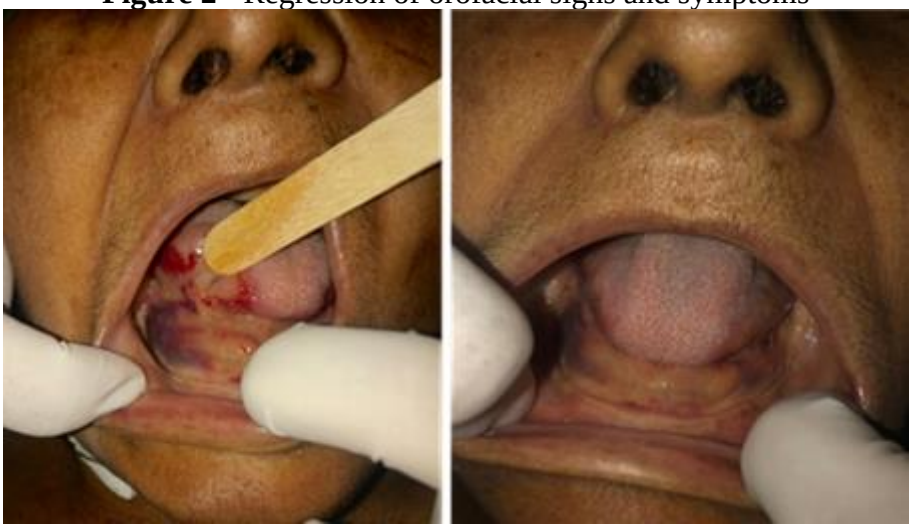
After 48 hours of hospitalization, he progressed to dyspnea, where it was necessary to use oxygen therapy through a nasal catheter for 72 hours, while there was breathing difficulty, and even when necessary at specific times after removal.

The sublingual hematoma regressed after nine days of hospitalization. Due to the history of Ischemic Stroke (CVA), it was decided to request a new assessment from the neurology team to assess possible neurological impairments. After 3D computed tomography scan of the skull without contrast, such changes were discarded.

This being the most stable moment of the patient's hospitalization, values of the International Ratio System (INR) within the normal range for anticoagulated patients, the medical clinic team opted to restart the prescription of Marevan® (Warfarin), with the dosage four times less than the previous one (2.5mg of Warfarin).

With the regression of orofacial signs and symptoms, the patient was discharged from the buccomaxillofacial surgery and traumatology service. She remained hospitalized to adjust the warfarin dose to the ideal value of the International Ratio System (INR), for subsequent discharge from hospital, on the 14th day (Figure 2).

Figure 2 - Regression of orofacial signs and symptoms



Source: the authors.

DISCUSSION

Sublingual hematoma is a hemorrhagic complication resulting from spontaneous bleeding that affects the sublingual and submaxillary spaces (RANJAN *et al.*, 2015; SATPATHY *et al.*, 2015). Despite a rare condition, it can be considered a clinical emergency with fatal potential (SPLINDER *et al.*, 2017; TAT *et al.*, 2018).

Satpathy (2015) describes the main etiological factor of sublingual hematoma as anticoagulant-induced coagulopathy associated with uncontrolled hypertension. Such etiological factors corroborate those presented in the case report described, where the patient used oral anticoagulant Marevan® 10 mg (Warfarin), associated with Acetylsalicylic Acid (ASA) 100mg and Digoxin 0.25mg, after a history of Ischemic Stroke (CVA) and uncontrolled hypertension.

The prevalence of sublingual hematoma is described in the studies by Moreira *et al.* (2016) and Tat *et al*. (2018) with a greater predilection for elderly patients with coagulation disorders, due to the fact that they are the ones who most benefit from anticoagulant treatment, thus becoming more susceptible to hemorrhagic complications and consequently bruising. Tat et al. (2018) exposes that the hemorrhagic risk becomes greater in the first year of administration of the oral anticoagulant, especially when associated with other medications, as in the case described here.

Elderly patients with coagulation disorders are more susceptible to the risk of hemorrhagic complications and consequently bruising, due to the fact that they are the ones that most benefit from anticoagulant treatment (ALAMOUDI *et al*., 2017).

The area of involvement of a hematoma must be considered when assessing the patient's risk of life. Satpathy *et al.* (2015) describes that the sublingual space is a place of low risk of bleeding, however when it occurs, the lingual artery is often related, and due to the expansion of this region, such an entity can be considered as an emergency.

Because it is potentially fatal, it needs a quick diagnosis to get immediate treatment. Moreira *et al.* (2016) describes that the diagnosis must be clinical, performing a detailed anamnesis, differentiating through signs and symptoms, from some acute infectious process, such as Ludwig's angina, followed by the correct analysis of laboratory tests, such as INR and blood count, and at the end of imaging tests, preferably using computed tomography (BUYUKLU *et al.*, 2014; MOREIRA *et al.*, 2016; TAT *et al.*, 2018).

The World Health Organization (WHO) in 1982 introduced the INR system in an attempt to minimize the variability in the results of Prothrombin Time (PT), due to differences in the sensitivity of the reagents (SILVA, 2010; KATZUNG; TREVOR, 2017). In the study in question, the patient had no history of monitoring and control of laboratory tests after starting anticoagulant therapy. Tests carried out after hospitalization indicate the value of the extended INR during the first 72 hours of hospitalization.

Tat *et al*. (2018), clinically describes the sublingual hematoma with hoarseness alteration, painless edema in the oral cavity or in the cervical region and hematoma in the sublingual and / or submaxillary spaces. In the present study, it was clinically possible to observe dysphagia, difficulties in articulating words, limited mouth opening, edema and ecchymosis in the sublingual region, evolving to dyspnea and abdominal pain.

Serralvo, Zamboti and Bregano (2015) and Alamoudi *et al*. (2017) complement the clinical characteristics with the possibility of patients presenting with hepatic impairment, being also observed in the case described here, by means of ultrasound of the upper abdomen with images suggestive of mild hepatic steatosis.

A large sublingual hematoma can mimic the characteristics of Ludwig's angina. Bahathiq (2018) refers to the descriptor "Angina de Pseudo-Ludwig" as the sublingual edema due to non-infectious causes, in confrontation with the true condition, Ludwig's angina, which is a manifestation of regional suppuration in the neck (SILVA, 2010; WANNMACHER; FUCHS, 2014).

According to Ghosh *et al.* (2016) warfarin is the most used drug for the prevention of embolic events, and is often the drug of choice for cases of ischemic stroke. Multiple reports of sublingual

hematoma secondary to hemorrhage in anticoagulated patients with warfarin are described in the literature. Due to the great individual variability in the dose-response relationship, the effects of anticoagulants should be monitored (BUYUKLU *et al.*, 2014; SERRALVO; ZAMBOTI; BREGANO, 2015; MOREIRA *et al.*, 2016; ALAMOUDI *et al.*, 2017).

The treatment lines are chosen according to the severity of the patient's clinical condition. As discussed in this study, Karmacharya *et al*. (2015) describes that the initial management should be conservative with a prescription of vitamin K, PFC or Prothrombin Complex Concentrate (CCP).

Most cases reported in the literature demonstrate spontaneous resolution within a few days after discontinuation of anticoagulant therapy, with normalization of coagulation parameters (MOREIRA *et al.*, 2016; MAHTO *et al.*, 2019).

According to Buyuklu *et al.* (2014) the use of warfarin can be restarted with regular monitoring of laboratory tests. In the reported case, warfarin restart was performed after normalization of the INR, with the patient under clinical observation for about 72 hours to monitor it. Outpatient follow-up will also be necessary to prevent recurrence.

However, some more severe cases have airway involvement, and for that reason some urgent procedures are necessary, such as nasotracheal intubation, endotracheal intubation, tracheostomy, and monitoring in an intensive care unit (ALAMOUDI *et al*., 2017; MASSEY *et al.*, 2019).

Satpathy *et al.* (2015) describes that the surgical evacuation of the sublingual hematoma is not considered the therapeutic approach of choice, since it increases the risk of edema and consequently the compromise of the airways, being chosen only in cases in which the other conducts were not successful (RIVOSECCHI; GARAVAGLIA; KANE-GILL, 2015).

According to Buyuklu *et al.* (2014) and MOREIRA *et al.* (2016) the sublingual hematoma has a favorable prognosis, however it can present a significant morbidity rate, normally, when concomitant respiratory impairment has occurred. The exposed case presented a good prognosis, the sublingual hematoma completely regressed in nine days after the suspension of the oral anticoagulant and therapeutic measures with intravenous Vitamin K and Fresh Plasma (PF).

CONCLUSION

Sublingual hematoma and a spontaneous bleeding condition affects the sublingual and submaxillary spaces. It presents a clinical diagnosis, being described as edema and ecchymosis in the sublingual region, symptom of dysphagia, hoarseness and dyspnea.

Early diagnosis is essential for a good prognosis, and it is important to differentiate this condition from infectious processes, such as Ludwig's angina, since they have different treatments.

The conservative therapeutic approach proved to be effective in such a case. By suspending the oral anticoagulant, prescribing vitamin K and fresh frozen plasma, associated with continuous monitoring of the airways, regression of the orofacial signs and symptoms was achieved in nine days.

The knowledge of adverse reactions, which affect the oral cavity, of oral anticoagulants, favors the diagnosis and multidisciplinary management of the case, increasing survival and reducing tissue damage.

REFERENCES

ALAMOUDI, U. *et al.* Spontaneous submental hematoma, a pseudo-Ludwig's phenomenon in 101-year-old patient: case report and literature review. **International Journal of Surgery Case Reports**, v. 36, p. 98-102, 2017.

BUYUKLU, M. *et al*. Spontaneous lingual and sublingual haematoma: a rare complication of warfarin use. **Case Reports**, v. 2014, p. bcr2014204168, 2014.

BAHATHIQ, A. O. A case report on sublingual hematoma. **Global Journal of Medical and Clinical Case Reports**, v. 5, n. 4, p. 23-24, 2018.

GHOSH, S. K. *et al*. Spontaneous sublingual hematoma due to warfarin: An emergency presenting to the dermatologist. **Indian Journal of Dermatology, Venereology and Leprology**, v. 82, n. 4, p. 432-433, 2016.

KARMACHARYA, P. *et al.* Upper airway hematoma secondary to warfarin therapy: A systematic review of reported cases. **North American Journal of Medical Sciences**, v. 7, n. 11, p. 494-502, 2015.

KATZUNG, B.; TREVOR, A. **Farmacologia básica e clínica**. 13. ed. Porto Alegre: AMGH, 2017, p. 304-311.

MAHTO, S. K. *et al*. A Rare and Lethal Complication of Oral Warfarin Therapy. **Indian Journal of Critical Care Medicine**, v. 23, n. 4, p. 197-198, 2019.

MASSEY, B. *et al.* Case report: Traumatic lingual hematoma. **Trauma Case Reports**, v. 20, p. 100177, 2019.

MOREIRA, E.; FERREIRA, J.; BURGHI, G. Hematoma sublingual espontâneo secundário à terapia anticoagulante com varfarina. **Revista Médica do Uruguai**, v. 32, n. 2, p. 118-122, 2016.

RAJAN, P. *et al.* Warfarin induced sublingual hematoma: a Ludwig angina mimic. **American Journal of Otolaryngology**, v. 36, n. 1, p. 84-86, 2015.

RIVOSECCHI, R.; GARAVAGLIA, J.; KANE-GILL, S. An evaluation of intravenous vitamin k for warfarin reversal: are guideline recommendations being followed? **Hospital Pharmacy**, v. 50, n. 1, p. 18-24, 2015.

ROSENFELD, L. G. *et al*. Valores de referência para exames laboratoriais de hemograma da população adulta brasileira: Pesquisa Nacional de Saúde. **Revista Brasileira de Epidemiologia**, v. 22, n. suppl. 2, e190003, 2019.

SATPATHY, S. *et al*. Spontaneous sublingual space hematoma secondary to hypertension: A case report and review of literature. **National Journal of Maxillofacial Surgery**, v. 6, n. 1, p. 96-98, 2015.

SERRALVO, F. D.; ZAMBOTI, J. L.; BREGANO, J. W. Variabilidade nos resultados de INR (International Normalized Ratio): comparação de seis marcas comerciais de tromboplastina. **Semina: Ciências Biológicas e da Saúde**, v. 36, n. 1 Suppl., p. 225-232, 2015.

SILVA, P. **Farmacologia**. 8. ed. Rio de Janeiro: Guanabara Koogan, 2010, p. 588-602.

SPINDLER, T. *et al.* Spontaneous sublingual haematoma in acquired haemophilia: case report. **British Journal of Oral and Maxillofacial Surgery**, v. 55, n. 4, p. e17-e18, 2017.

TAT, Y. B.; MUNIANDY, R. K.; HANG, L. N. M. Denture Induced Submandibular Hematoma in a Patient on Warfarin. **Case Reports in Anesthesiology**, n. 11, p. 1-3, 2018.

WANNMACHER, L.; FUCS, F. D. **Farmacologia Clínica**. 4. ed. Rio de Janeiro: Guanabara Koogan, 2014, p. 891-907.