ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Angioedema Of Lower Lip And Gingiva Due To Oral Hormonal Therapy: A Case Report.

Gabric D[1], Loncar Brzak B[2]*, Vucicevic Boras V [2,3], Sumilin L[4], Skrinjar I[3].

[1]Department of Oral Surgery, School of Dental Medicine, University of Zagreb, Croatia.
[2]Department of Oral Medicine, School of Dental Medicine, University of Zagreb, Croatia .
[3]Department of Oral Medicine, University Clinical Hospital Center Zagreb, Croatia.
[4]Polyclinic Aviva, Zagreb, Croatia.

ABSTRACT

We present a case of a 25-year-old female who developed angioedema of lower lip and gingiva which lasted for two weeks, due to oral hormonal therapy. Her medical history revealed polycystic ovarian syndrome for which she was taking ethinylestradiol and cyproterone for the previous several months. Oral examination revealed angioedema of lower lip together with erythematous and edematous gingiva. The gingival biopsy was taken and histopathological finding showed chronic inflammatory infiltrate. The serum findings of C2, C3, C4 and C1 inhibitor were normal. The patient was treated with local corticosteroid (betamethasone (Beloderm, Belupo, Croatia) in orabase) which was applied three times a day and antifungal gel (miconazole (Rojazol, Belupo, Croatia) therapy. Patient's gynecologist has withdrawn the drug and regression of oral lesions was noticed after one week.

Keywords: angioedema; swelling; oral hormonal therapy

https://doi.org/10.33887/rjpbcs/2019.10.3.25

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Angioedema describes localized swelling of the peripheral body parts such as face, oral cavity, larynx, respiratory and gastrointestinal systems due to the release of vasoactive mediators such as bradykinin which affects around 15% of the population. It can be divided into several forms such as: idiopathic, allergic, hereditary or acquired, associated with thyroid disease, physically (trauma, pressure) or drug-induced angioedema (angiotensine-converting enzyme or estrogens) or triggered by stress [1].

Angioedema attacks develop in the hereditary or acquired C1 esterase inhibitor deficiency with uncontrolled activation of the factor XII, prekallikrein and high-molecular weigth kininogen [2].

Hereditary angioedema (HEA) with normal C1 inhibitor was first reported in 1986 by Warin et al. [3] in two sisters after combined oral contraceptive pill intake and also during the latter half of pregnancy.

Three forms of HEA are known: mutation in the gene that encodes the C1 inhibitor of the complement factor (INHC1), inducing a decrease in its synthesis (Type 1 HEA); formation of the dysfunctional protein (type Ii HEA); and type 3 which occurrs dominantly in women where INHC1 is normal and it can not be distinguished from other two types [4].

Study by Visy et al. [5] confirmed that the number of attacks were significantly higher in females with high progesterone and sex hormone binding globulin levels. Two afore mentioned might be useful in the prediction of attacks in HEA.

Hereditary angioedema (HAE), a rare but life-threatening condition, manifests as acute attacks of facial, laryngeal, genital, or peripheral swelling or abdominal pain secondary to intra-abdominal edema. Resulting from mutations affecting C1 esterase inhibitor (C1-INH), inhibitor of the first complement system component, attacks are not histamine-mediated and do not respond to antihistamines or corticosteroids. Low awareness and resemblance to other disorders often delay diagnosis; despite availability of C1-INH replacement in some countries, no approved, safe acute attack therapy exists in the United States.

Hormone therapy such as intake of oral contraceptives or hormone replacement therapy can precipitate attacks of hereditary angioedema or induce acquired forms. The exact ethiopathology of these reactions is still unknown [6].

CASE REPORT

We present a case of a young woman who developed angioedema of lower lip and gingiva due to oral hormonal therapy. A 25-year-old woman was referred to the Department of Oral Medicine, University Clinical Hospital Zagreb, Croatia due to angioedema of the lower lip and gingiva which lasted for two weeks. Her medical history revealed policystic ovarian syndrome. She was taking a drug which included ethinylestradiol and cyproterone for several months. Oral examinations revealed angioedema of lower lip (Figure 1.) and erythematous and edematous gingiva. The biopsy of gingival changes was taken and histopathological finding showed chronic inflammatory infiltrate. The findings of C2, C3, C4 and C1 inhibitor were normal. The patient was treated by local corticosteroid (betamethasone (Beloderm, Belupo, Croatia) in orabase) and antifungal (miconazole (Rojazol, Belupo, Croatia) therapy. The suspected drug was abolished by the patient's gynecologist and regression of oral lesions was noticed after one week (Figure 2.).

ISSN: 0975-8585

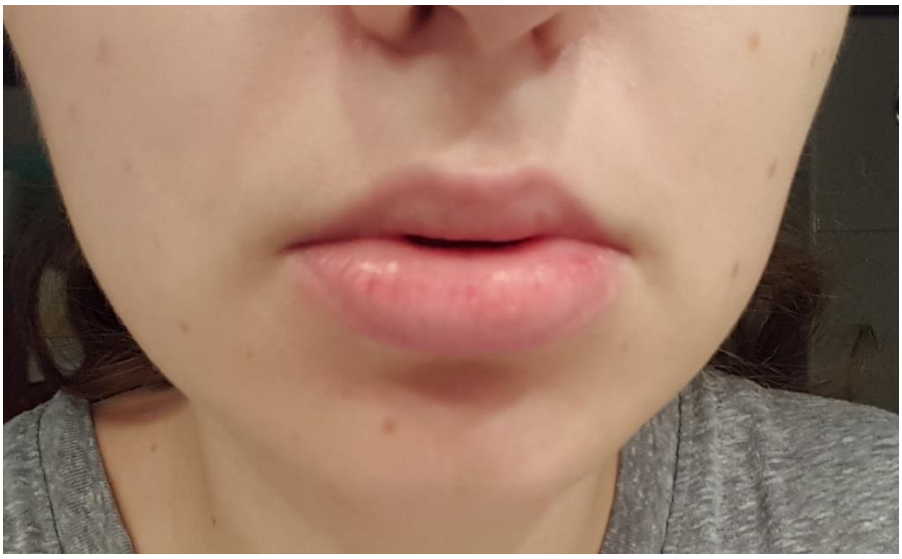

Figure 1. Angioedema of the lower lip due to the hormonal therapy.

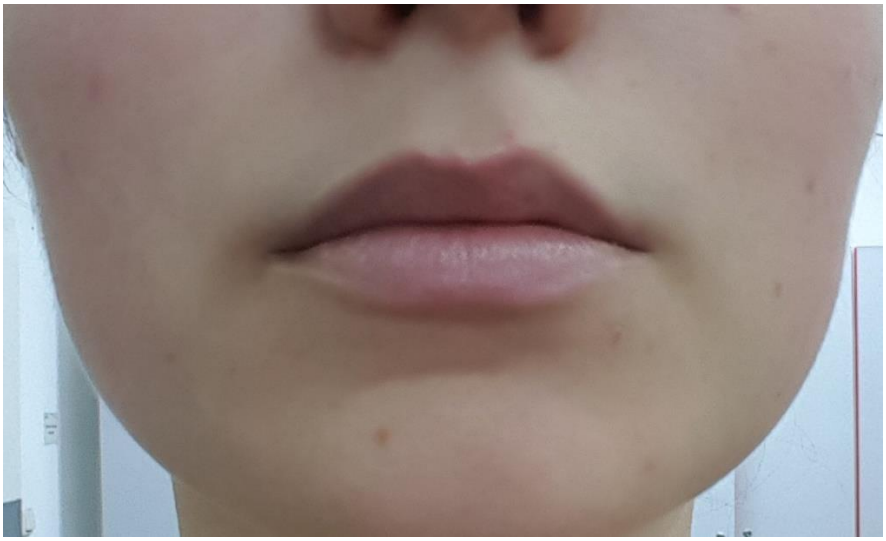

Figure 2. Regression of angioedema one week after the cessation of the suspected drug intake.

DISCUSSION

In many of the affected women, oral contraceptives, hormone replacement therapy containing estrogens, and pregnancies triggered the clinical symptoms [7].

Bouillet et al. [8] reported five patients who were taking oral contraceptives and developed angioedema. It is interesting to note that the symptoms developed during the first year or later after starting hormone therapy which has also been seen in our patient. Their patients reported relapsing swelling of the lips, hands, larynx and abdomen while our patient had lip and gingival swelling solely. All patients from the study of Bouillet et al. [8] had normal serum C1 and C4 antigen levels which was also seen in our patient.

Differential diagnosis in this case might be cellulitis due to the tooth infection, abscess due to the foreign body, orofacial granulomatosis (within sarcoidosis, tuberculosis, Crohn's disease), allergic lip swelling due to cosmetic products (lipstick, toothpaste etc) and drugs, insect bite.

The treatment lies in the avoidance of triggering factors and treatment of acute symptoms. It has been shown in many case reports that antihistamines, corticosteroids and adrenaline do not lead to the therapeutic response in patients. In the acute phase characterized with severe swelling, concentrated INCH1, fresh frozen plasma, ecallantide and icatibant might be helpful [4]. However, several other prophylactic treatments are available in patients who do not have remission even with the discontinuitation of the estrogens, such as attenuated androgens (danazol), antifibrinolytic agents (tranexamic acid) and progesterone [4]. However, after 7 months of cessation of an oral contraceptive, our patient does not have relapses, therefore she was not given prophylactic regimen. Sanhuenza [9] described an interesting case where patient with HEA due to the estrogens was given an transdermal contraceptive which did not lead to the HEA as the drug did not pass hepatic metabolism as it would if has been taken orally.

CONCLUSION

A detailed medical history is the first step necessary to set accurate diagnosis. Patients who develop adverse drug side effects should be advised to avoid drugs with the same active ingredients. Although the exact ethiopathology of these changes remains unknown and the evidence of treatment efficacy are mostly based on case reports and case series, recent years have enabled new prophylactic and therapeutic regimens for patients with angioedema.

REFERENCES

[1] Patel NN, Patel DN. Hereditary angioedema with normal C1 inhibitor. Am J Med. 2008; 121 (11): 949-951.
[2] Hentges F, Hilger C, Kohnen M, Gilson G. Angioedema and estrogen-dependent angioedema with activation of the contact system. J Allergy Clin Immunol. 2009; 123:262–4.
[3] Warin RP, Cunliffe WJ, Greaves MW, Wallington TB. Recurrent angioedema: familial and oestrogen-induced. Br J Dermatol. 1986;115(6):731-4.
[4] Miranda AR, Ue AP, Sabbag DV, Furlani Wde J, Souza PK, Rotta O. Hereditary angioedema type III (estrogen-dependent) report of three cases and literature review. An Bras Dermatol. 2013; 88(4):578-84.
[5] Visy B, Füst G, Varga L, Szendei G, Takács E, Karádi I, Fekete B, Harmat G, Farkas H. Sex hormones in hereditary angioneurotic oedema. Clin Endocrinol (Oxf). 2004; 60(4):508-15.
[6] Bork K. Hereditary angioedema with normal C1 inhibitor. Immunol Allergy Clin North Am. 2013 Nov;33(4):457-70.
[7] Bork K, Fischer B, Dewald G. Recurrent episodes of skin angioedema and severe attacks of abdominal pain induced by oral contraceptives or hormone replacement therapy. Am J Med. 2003;114(4):294-8.
[8] Bouillet L, Ponard D, Drouet C, Jullien D, Massot C. Angioedema and oral contraception. Dermatology. 2003;206(2):106-9.
[9] Sanhueza PI. Contraception in hereditary angioedema. Fertil Steril. 2008;90(5):2015.e21-2.