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Akutni angioedem i urtikarija vezana za infekciju virusom herpes simplex

Acute Angioedema and Urticaria Associated with Herpes Simplex Infection

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Sažetak

U radu je predstavljen akutni angioedem s urtikarijom koji je možda potaknula infekcija virusom herpes simplex. Japanac u dobi od 58 godina imao je na liječničkom pregledu urtikariju i eritematozni osip na udovima i torzu. Žalio se i na angioedem s oticanjem usana, jezika, lica te periorbitalnoga tkiva, pa je imao poteškoće u disanju i govoru, a osjećao je i ispunjenost ždrijela. Nakon šest dana na donjoj su se usni pojavili ulkusi s krastama. Od pretraga su liječnici tražili kompletnu krvnu sliku, biokemijski screening za titrove antitijela kod viralnih infekcija te test za preosjetljivost na lijekove. Zanimljiva je bila serumska fiksacija titra antitijela na HSV - iznositelja je 1:32. Osim oralne ulceracije, pacijentu je bila postavljena i dijagnoza herpes labialis. Bio je primljen u bolnicu te intravenski liječen antihistaminom, penicilinom i kortikosteroidom, te su se nakon tri dana simptomi znatno popravili. Tijekom trogodišnjeg praćenja kod njega se nisu razvili ni angioedem ni urtikarija. U ovom radu opisani su klinička slika, liječenje i moguća povezanost angioedema i urtikarije s infekcijom virusom herpes simplex. Ipak, treba uzeti u obzir mogućnost slučajnog istodobnog pojavljivanja i virusa herpes simplex.

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Ključne riječi

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Uvod

Urtikarija je dosta česta, a opisuje se kao ovjenčan, uzdignut, eritematozan, često i svrbljiv osip, bilo izoliran bilo konfluentan. Edem kod urtikarije zahvaća površinske dijelove kože (dermisa), a eritematozni proces angioedema proteže se duboko u kožu ili u subkutane i submukozne slojeve (1-2). Mjesta zahvaćena angioedemom uključuju lice, osobito periorbitalno tkivo i usne, jezik, ždrijelo i grkljan te šake i stopala, a urtikarija se najčešće javlja na srednjem dijelu tijela i udovima (3-4). Kod urtikarije lezije uobičajno traju manje od 24

Introduction

Urticaria is a fairly common condition characterized by circumscribed, raised, erythematous, usually pruritic rashes and may be isolated from each other or confluent. Edema of urticaria involves the superficial portions of the dermis, whereas edematous process of angioedema extends into the deep dermis or subcutaneous and submucosal layers (1-2). The involved sites of angioedema include the face, especially periorbital tissue and lips, tongue, pharynx, larynx, hands and feet but urticaria mostly occur at trunk and extremities (3-4). Lesions of ur-

sata, a one kod angioedema mogu perzistirati i do 72 sata (1, 3).

Angioedem i urtikarija mogu se pojaviti kao kliničke manifestacije različitih imunskih i upalnih mehanizama, a mogu biti i idiopatske (2, 5). Specifični su antigeni hrana, lijekovi i inhalanti (2-11). Napad se može dogoditi zbog stresa, mehaničkih trauma, prehlade i nekih sustavnih bolesti (2, 9-17). Virusne infekcije poput hepatitisa, citomegalovirusa (CMV-a), Epstein-Barrova virusa (EBV-a), infektivne mononukleoze, adenovirusa i parvovirusa B19, mogu prouzročiti urtikarije i angioedem (13,15,18-23). Svrha je ovoga rada predstaviti ponovno javljanje infekcije HSV-om možda povezane s akutnom urtikarijom i angioedemom.

Prikaz slučaja

Japanac u dobi od 58 godina došao je godine 2000. u Kliniku za oralnu kirurgiju Stomatološkog fakulteta Tokijskoga sveučilišta (na Department of Oral Surgery, Oral Reconstitution, Oral Health Sciences, Graduate School of Tokyo Medical and Dental University) i žalio se na bezbolno oticanje donje usne i jezika. Rekao je da je tijekom trinaest dana doživio tri epizode, ali mu se stanje svaki puta popravilo pet sati nakon što su počeli simptomi. U njegovoj povijesti bolesti bili su navedeni astma, nefritis, ulkus dvanaestnika, ishemična srčana bolest i kamenac u mokraćnom sustavu. Ipak, opovrgnuo je infekciju HSV-om i alergiju na bilo kakve antigene. Uzimao je tada acetilsalicilni antikoagulant (Aspirin), natrijev pravastatin (Mevalotin) i nefidipine (Adalat), kao preventivnu terapiju kod ishemičnog napada. U povijesti bolesti nije bilo podataka o angioedemu među članovima njegove obitelji.

Kliničkim je pregledom otkriveno bezbolno oticanje donje usne, jezika i obraza obostrano, s povišenom temperaturom do 38°C. Četvrtoga dana javili su se svrbež i gigantski crveni osip na udovima i torzu kod temperature od 37,7°C (Slika 1.). Petog se dana javio liječniku zbog poteškoća u disanju i govoru, te s osjećajem ispunjenosti grla, ali mu se sljedeće jutro stanje postupno smirilo. Šestog su se dana razvili ulkusi prekriveni krastama s eritematозnim rubom na desnoj strani donje usne te edemi gornje usne i jezika (Slika 2A i 2B). Sedmog dana vidljiv je bio periorbitalni edem (Slika 3.) te je pacijent upućen dermatologu i primljen u bolnicu.

urticaria usually persist for less than 24 hours, whereas those of angioedema can persist for as long as 72 hours (1,3).

Angioedema and urticaria may occur as clinical manifestations of various immunologic and inflammatory mechanisms or may be idiopathic (2,5). Specific antigens are foods, various drugs and inhalants (2-11). Attacks may also be precipitated by emotional stress, mechanical trauma, cold, and some systemic diseases (2,9-17). Viral infections, such as hepatitis, cytomegalovirus (CMV), Epstein-Barr virus (EBV), infectious mononucleosis, adenovirus and parvovirus B19 may precipitate urticaria and angioedema (13,15,18-23). However, a few studies have shown the association between angioedema and urticaria with herpes simplex virus (HSV) infection (5,13,15,24). The purpose of this communication is to present that the recurrence of HSV infection may be related to acute urticaria and angioedema.

Case Report

A 58-year-old Japanese male patient presented at Department of Oral Surgery, Oral Reconstitution, Oral Health Sciences, Graduate School of Tokyo Medical and Dental University in 2000 with a chief complaint of painless swelling of lower lip and tongue. He claimed to have had three episodes during 13 days before the first visit but his condition resolved after 5 hours of onset. He had a history of asthma, nephritis, duodenal ulcer, ischemic heart disease and urinary calculus. However, he denied history of HSV infection and allergy due to any agents. He had been taking Acetylsalicylic acid-anticoagulant (Aspirin), Pravastatin sodium (Mevalotin) and Nifedipine (Adalat) at the time for the prevention of ischemic attack. There was no history of angioedema among other family members.

A clinical examination revealed marked painless swelling of lower lip, tongue and both sides of cheek with fever at 38°C. On day 4, he presented signs of itching erythematous giant rashes at extremities and trunk with fever at 37.7°C (Fig. 1). On day 5, he claimed that he had difficulty in breathing, speaking and fullness in his throat, but this condition was gradually subsided on the next morning. On day 6, he developed crust ulcers with erythematous margin at the right side of lower lip accompanied by edema of upper lip and tongue (Figs. 2A and 2B). On day 7, he had right periorbital edema (Fig. 3), thus he was referred to dermatologist and was admitted.

Routine biological and biochemical screening tests included complete blood studies, serologi-



Slika 1. Urtikarija sa svojstvenim uzdignutim pruritičnim eritematoznim osipom na trupu - četvrti dan
Figure 1 Urticaria characterized by raised pruritic erythematous rashes on the trunk on day 4

cal studies for thyroid function, liver function, antibody titer for HSV, coxsackie virus, hepatitis B virus (HBV), hepatitis C virus (HCV) and urinalysis. Complete blood count was normal except for elevated levels of white blood cell (WBC) and neutrophils and decreased levels of lymphocytes. Thyroid function tests including thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4) were within normal range. Electrolytes and liver enzymes were normal, except for increased levels of γ -glutamyl transpeptidase (γ -GTP), alkaline phosphatase (ALP), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Urinalysis was normal with no blood, glucose, or protein detected. Levels of serum complement fixation anti-



Slika 2. Cijeljenje ulkusa s krastama na desnoj strani donje usnice (strelica) (A) i angioedem kojem je svojstvena edematozna gornja usnica (A) i difuzno edematozan jezik (B) - šesti dan
Figure 2 Coalescence of crusted ulcers at the right side of lower lip (arrow) (A) and angioedema which are characterized by edematous upper lip (A) and diffuse edematous tongue (B) on day 6

Rutinsko biološko i biokemijsko ispitivanje uključivalo je kompletnu krvnu sliku, serološka ispitivanja funkcije štitne žlijezde i jetre, titra antitijela za HSV, virus coxsackie, hepatitis B virus (HBV), hepatitis C virus (HCV) i analizu urina. Krvna slika bila je u redu, osim što je imao povišenu razinu bijelih krvnih stanica (WBC-a) i neutrofila, te sniženu razinu limfocita. Testovi funkcije štitne žlijezde - tiroidni stimularajući hormon (TSH), trijodtirozin (T3) i tirozin (T4) dali su rezultate u granicama normalnih vrijednosti. Elektroliti i jetreni enzimi bili su u redu, osim povišenih razina γ -glutamyl transpeptidaze (γ -GTP-a), alkalne fosfataze (ALP-a), C reaktivnog proteina (CRP-a) i stope sedimentacije eritrocita (ESR-a). U urinu nije bilo ni krvi, ni glukoze ili proteina. Razine antitijela fiksacije serumskih komplemenata coxsackie A9, B1-6 virus



Slika 3. Angioedem okarakteriziran desnim periorbitalnim edemom - sedmi dan
Figure 3 Angioedema characterized by right periorbital edema on day 7

bile su normalne kod 1:4, ali mu je antitijelo serum-ske fiksacije za HSV bilo povišeno na 1:32 (Tablica 1.). U pretragama nisu bili pronađeni anti-hepatitis B površinska protutijela (HBVs Ab), ni hepatitis B površinski antigen (HBVs Ag), te anti-hepatitis C antitijelo (HCV Ab). Scratch test na preosjetljivost na lijekove, uključujući aspirin, natrijev pravastatin i nefidipine, bio je negativan. Na temelju kliničkih i laboratorijskih nalaza pacijentu je bila postavljena dijagnoza akutnog angioedema i urtikarije, vjerojatno vezana s infekcijom HSV-a.

bodies for coxsackie A9, B1-6 virus were normal as 1:4 but his serum complement fixation antibody for HSV was elevated as 1:32 (Table 1). No anti-hepatitis B surface antibody (HBVs Ab), hepatitis B surface antigen (HBVs Ag) and anti-hepatitis C antibody (HCV Ab) were detected. Scratch test for drug hypersensitivity, including Aspirin, Pravastatin sodium and Nefidipine was negative. From clinical and laboratory findings, he was diagnosed as acute angioedema and urticaria probably associated with HSV infection.

Tablica 1. Abnormalne vrijednosti rezultata laboratorijskih ispitivanja kod pacijenta s akutnom urtikarijom i angioedemom
Table 1 Abnormal laboratory values in the patient with acute urticaria and angioedema

Laboratorijski test • Laboratory test	Normalan raspon • Normal range	Rezultati • Results
WBC	$4,5-9 \times 10^3/\text{mm}^3$	$11,6 \times 10^3/\text{mm}^3$
Neutrofil • Neutrophil	44-72 %	84 %
Limfocit • Lymphocyte	27-47 %	10 %
γ -GTP	6-51 mU/ml	54 mU/ml
ALP	78-208 mU/ml	264 mU/ml
CRP	0-0,5 mg/dl	10 mg/dl
ESR	0-15 mm/h	51 mm/h
titar Ab za HSV • Ab titer for HSV	1:4	1:32

Terapija je počela intravenskom primjenom 500 ml elektrolitne otopine za transfuziju (Solita-T3), prednisolonom u fiziološkoj otopini 40 mg/100 ml i d-klorfeniraminom (Polaramine) u glicirizinu (Neo-minophagen C) 100 mg/20 ml jedanput na dan, a ordiniran je i penicilin u 5-postotnoj glukozi 1 g/100 ml dva puta na dan tijekom dva dana. Nakon prvog dana liječenja kutani je eritematozni osip nestao, ali je pacijent još imao poteškoće u disanju i periorbitalni edem. Nakon tri dana oporavio se i pušten je kući, ali mu je određena jednotjedna terapija penicilinom od 500 mg tri puta na dan, zatim d-klorfeniramin 6 mg dva puta na dan tijekom deset dana i difenhidramin (Restanin) za primjenu na zahvaćenim dijelovima tijela. Tijekom kontrole nakon tjedan dana edem i osip bili su znatno manji te su se svi simptomi činili normalnima. Tijekom trogodišnjega praćenja pacijentu se nisu razvili ni angioedem ni urtikarije.

Rasprava

Klinički nalazi kod pacijenta bili su naglo bezbolno oticanje usnica, jezika, lica, periorbitalnoga tkiva te poteškoće u disanju i govoru, ali i osjećaj ispunjenosti grla. To je bio angioedem, a eritematozni pruritični osipi na trupu i udovima dijagnosticirani su kao urtikarija. Smatralo se da pacijent boluje od akutnog stanja na temelju povišenih razina ESR-a, CRP-a, WBC-a i neutrofila, te zbog epizoda s le-

Therapy was begun intravenously with electrolyte fluid for transfusion (Solita-T3) 500 ml, prednisolone in physiological saline 40 mg/100 ml and d-chlorpheniramine (Polaramine) in glycyrrhizin (Neo-minophagen C) 100 mg/20 ml once daily, and penicillin in 5% glucose 1 g/100 ml twice daily for 2 days. After one day of treatment, cutaneous erythematous rashes disappeared, but he still had difficulty of breathing and periorbital edema. After 3 days, he was recovered and discharged, but he was given penicillin 500 mg 3 times/day for one week, d-chlorpheniramine 6 mg 2 times/day for ten days and diphenhydramine (Restanin) applied at affected areas. At 1-week follow-up, he had markedly relieved in edema and rashes and all symptoms appeared normal. The patient had not developed angioedema and urticaria during 3-year follow-up.

Discussion

Clinical findings of the patient characterized by sudden painless swelling of lips, tongue, face, periorbital tissue, and difficulty in breathing, speaking and fullness in the throat were related to angioedema, whereas erythematous pruritic rashes on his trunk, and extremities were diagnosed as urticaria. This patient is considered to have acute condition because levels of ESR, CRP, WBC, and neutrophil

zijama koje su trajale kraće od šest tjedana (2-4). U ovom smo prikazu predstavili pacijenta s urtikarijom i angioedemom u istoj epizodi. U jednoj ranijoj studiji Champion i suradnici (6) opisali su dokaze u prilog pojave urtikarije zajedno s angioedemom. Iz arhiva je jasno da je od 554 pacijenta s urtikarijom, njih 50 % imalo istodobno i angioedem i urtikariju, oko 40 % imalo je samo urtikariju, a 10 % samo angioedem.

U opisima raznih slučajeva urtikarije i angioedema, pokušali smo doznati etiologiju te pojave kod našeg pacijenta. Isključili smo povezanost urtikarije i angioedema s bolešću tiroide zbog normalnih rezultata testova funkcije štitnjače. Alergijska reakcija na lijekove može biti uzrok nastanka urtikarije i angioedema (23 %), posebice kod aspirina i sličnih salicilata (1, 7-8). Kod našeg su pacijenta bili negativni rezultati testa na preosjetljivost na vlastite lijekove. Taj test može ponekad dati i pogrešne rezultate, jer su lijekovi ispitani topikalno, a pacijent ih je primio oralno. Ipak, kako ih je bolesnik dugo uzimao, može se smatrati da se kod njega urtikarija i angioedem nisu razvili zbog alergijske reakcije. Drugi mogući razlozi - poput traume, emotivnog stresa i alergije na hranu - vjerojatno nisu uključeni u ovaj slučaj. Zato sve te pojave mogu biti vezane za reakciju preosjetljivosti, vjerojatno uzrokovanu infekcijom s HSV-om i to zbog izbijanja lezija koje podsjećaju na herpes labialis tijekom urtikarije i angioedema, iako vezikule nisu uočene prije erupcije ulkusa. U odsutnosti vezikula, nije bilo moguće obaviti izravnu imunofluorescenciju ni citološko ispitivanje struganjem baze vezikule te bojenjem Wrightovim, Giemsovim ili Papanicolaouvim bojama, kako bi se detektirala nazočnost multinukleiranih gigantskih stanica i intranuklearnih inkluzija (25). Dakle, u stadiju vezikula, preporučuju se izravna imunofluorescencija i citološka ispitivanja kako bi se dobila potvrda dijagnoze o infekciji HSV-om. No, oralne su lezije upućivale na herpes labialis, budući da je titar serumskih antitijela na HSV bio povišen na 1:32. Štoviše, ustanovili smo da su titrovi antitijela na coxsackie A i B virus, HBV i HCV dali negativne rezultate. Nažalost, serološke pretrage za HSV bile nisu dovršene, jer smo se poslužili metodom fiksacije komplementa kako bismo analizirali titar serumskih antitijela na HSV, a on nije bio specifičan za tipove HSV-a i klase imunoglobulina kao što su IgG i IgM. Zato na temelju rezultata seroloških ispitivanja nismo mogli klasificirati niti definirati vrstu HSV-a kod našeg pacijenta, ni kao tip 1 ni tip 2, a niti odrediti je li infekcija akutna ili kronič-

were increased, as well as episodes of lesions lasted less than 6 weeks (2-4). In this report, we demonstrated the patient with urticaria and angioedema at the same episode. In previous study, Champion et al (6) reported the evidence that urticaria could occur accompanied with angioedema by the records of 554 patients with urticaria, that 50% of patients had both angioedema and urticaria, approximately 40% had only urticaria and 10% only angioedema.

In addition to various causes of urticaria and angioedema, we attempted to find out the etiology in this patient. We excluded the association of urticaria and angioedema with thyroid disease because of normal results of thyroid function tests. Allergic drug reaction can cause urticaria and angioedema (23%) especially aspirin and related salicylates (1,7-8). This patient had negative results of scratch test for hypersensitivity to his medications. Scratch test may sometimes fail exact results because these drugs were tested topically whereas the patient took these drugs by oral administration. However, he had taken these drugs for a long time; it may be considered that he did not develop urticaria and angioedema from allergic drug reaction. Other possible causes, such as trauma, emotional stress and allergy to food were unlikely involved in this case. This patient thus may relate to a hypersensitivity reaction that was probably caused by HSV infection due to the outbreak of herpes labialis-like lesion at the time period of urticaria and angioedema, although vesicles were not obviously examined before ulcer eruption. In the absence of vesicles, we could not perform direct immunofluorescence or cytologic examination by scraping the base of vesicles and staining with Wright, Giemsa or Papanicolaou's stain to detect the presence of multinucleated giant cells and intranuclear inclusions (25). Thus, in vesicle stage, direct immunofluorescence and cytologic examination were recommended to confirm the HSV infection. However, oral lesions were indicated to herpes labialis since serum antibody titer for HSV was elevated at 1:32. Moreover, we found that the antibody titers for coxsackie A and B virus, HBV and HCV revealed negative results. Unfortunately, the serology of HSV was not completed because we used the complement fixation method to analyze the serum antibody titer for HSV, which did not specify for the HSV types and immunoglobulin classes as IgG or IgM. Thus, by our serological results, we could classify neither the definite type of HSV in this patient as type 1 or type 2 nor timing of the infection as acute or chronic. However, by clini-

na. Ipak, kliničke su manifestacije na donjoj usni, ali i njihova svojstva, upućivale na dijagnozu oralnih lezija prouzročenih infekcijom HSV-om tipa 1.

Iako se u nekoliko studija opisuju odnos angioedema ili urtikarije te infekcija HSV-om, nema dokaza prema kojima je infekcija HSV-om uzrokovala angioedem ili urtikariju. Doeglas i suradnici (15) pronašli su znatno više titrove antitijela fiksacije komplementa za HSV kod pacijenata s urtikarijom, negoli kod kontrolne skupine ($P < 0,05$). Zingale i suradnici (5) otkrili su jednog pacijenta s angioedemom usne koji se ponovno pojavio nakon rekurencija HSV-a tipa 1, i to u 776 slučajeva s angioedemom. Moramo istaknuti da su se pacijenti s rekurentnom infekcijom HSV-om i istodobnom urtikarijom ili angioedemom, brzo oporavljali nakon primjene aciklovira (13, 24). Angioedem i urtikarija kod našeg pacijenta pojavili su se tri tjedna prije HSV lezija, što je opisano kod urtikarije šest tjedana prije infekcije HSV-om (24). Posljednja je erupcija HSV lezija možda indikativna za razdoblje inkubacije HSV-a ili na klinički asimptomatsku reaktivaciju. Ipak, precizna uloga HSV-a u patogenezi angioedema i urtikarije ostaje nepoznata, ali može ju se povezati s reakcijom preosjetljivosti. Ustrajne virusne infekcije, poput infekcija virusima HSV, EBV, ili CMV, bile su glavni uzrok angioedema i kroničnih urtikarija (13). Čak su površinski antigeni HBV-a pronađeni u imunim kompleksima na stijenkama krvnih žila urtikarijskih lezija, i čini se da aktiviraju sustav komplemenata (20, 26-27). Na taj su način mastociti mogli otpuštati kemijske posrednike poput histamina ili anafilotoksina, što je uzrokovalo dilataciju krvnih žila i propuštanje plazme iz lokalnih postkapilarnih venula, a to vodi prema razvoju kliničkih manifestacija angioedema i urtikarije (2, 4, 28). Iako smatramo da je kod opisanog pacijenta infekcija HSV-om možda potaknula urtikariju i angioedem, ne bi se smjelo zanemariti ni to da su oni možda idiopatske naravi, te da se slučajno javljaju zajedno s infekcijom HSV-a.

U svakom slučaju, akutna faza može zahtijevati liječenje, i to se obično čini oralnim antihistaminima. U težim slučajevima ili ako postoje znakovi i simptomi anafilakse, koriste se epinefrin subkutano, kortikosteroidi sustavne primjene te se pacijent smješta u bolnicu zbog opservacije, a može biti indicirano i promatranje te intervencija dišnih puteva (2-3, 29-30). Hrapav glas, poteškoće u gutanju ili kada se tek počinje govoriti, mogli bi predstavljati rane znakove edema ždrijela i grkljana (2, 4, 29). U opisanom slučaju pacijent je imao poteškoće s disanjem i govo-

cal manifestations of location at lower lip and characteristics of lesions, we diagnosed oral lesions as caused by HSV type 1 infection.

Although there have been a few studies to demonstrate the relationship of angioedema or urticaria and HSV infection, no convincing evidence exists in which HSV infection caused angioedema and urticaria. Doeglas et al (15) found significantly higher complement fixation antibody titers for HSV in urticaria patients than in the controls ($P < 0.05$). Zingale et al (5) revealed one patient with angioedema of lips relapsed upon recurrences of HSV type 1 among 776 cases with angioedema. Moreover, patients who had recurrent HSV infection as well as angioedema or urticaria at the same duration rapidly recovered from the angioedema or urticaria by trials of acyclovir (13, 24). Angioedema and urticaria in our patient appeared 3 weeks before the HSV lesions, that is similar to one previous report of appearance of urticaria before HSV infection for 6 weeks (24). The latter eruption of HSV lesions may be indicated to incubation period of HSV or clinically-asymptomatic reactivation. However, the exact role of HSV in the pathogenesis of angioedema and urticaria remains unclear but it may relate to a hypersensitivity reaction. Persistent viral infection including infection with HSV, EBV, or CMV has been a significant cause of angioedema and chronic urticaria (13). Moreover, HBV surface antigens were found in immune complexes on blood vessel walls of urticarial lesions and seem to activate the complement system (20, 26-27). By this way, mast cells could release chemical mediators such as histamine or anaphylatoxins, which caused blood vessel dilatation and leakage of plasma from local post capillary venules leading to development of clinical manifestations of angioedema and urticaria (2, 4, 28). Although we believe that HSV infection possibly induced the urticaria and angioedema in this patient, it could not be negligible that urticaria and angioedema may be of idiopathic cause and occur as coincidence with the HSV infection.

In any case, the acute phase may require treatment, which is usually satisfactorily accomplished with oral antihistamines. In severe case or accompanied by signs and symptoms of anaphylaxis, subcutaneous epinephrine, systemic corticosteroids, hospitalization for observation and airway management may be indicated (2-3, 29-30). Hoarseness, difficulty in swallowing, initiating speech may be early signs of pharyngeal and laryngeal edema. (2, 4, 29). In this case, the patient had difficulty in breathing,

rom, te je imao osjećaj ispunjenosti grla, a to može upućivati na uključenost ždrijela i grkljana te rizik od opstrukcije dišnih puteva (2,11,29). Zato mu je propisana terapija sustavnim kortikosteroidima i antihistaminima, kako bi se olakšalo njegovo ozbiljno stanje. Nismo primijenili antivirusne agense, budući da oralne lezije nisu bile u stadiju vezikula nego ulkusa s krastom tijekom šestoga dana njegova posjeta našoj klinici. Zanimljivo je da su Shelley i suradnici (13) postigli uspjeh s profilaktičkom primjenom aciklovira u napadu i na angioedem ili kroničnu urtikariju i na infekciju HSV-om, što govori u prilog relevantnosti virusne infekcije s angioedemom ili urtikarijom i terapijskog učinka antivirusnih lijekova suprimiranjem cirkulacije virusnog antigena.

U sažetku istaknimo da akutni angioedem i urtikarija kod opisanog pacijenta mogu biti prouzročeni virusno-potaknutom reakcijom, trigger je vjerojatno infekcija HSV-om ili može jednostavno biti istodobna pojava. Dakle, za točnu dijagnozu i plan liječenja potrebni su pacijentova povijest bolesti, klinička i laboratorijska ispitivanja te svijest o tome da mu je život u opasnosti, pa ga je nužno hitno zbrinuti.

Zahvale

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speaking, and fullness of throat that may be indicated to pharyngeal and laryngeal involvement and subsequent risk of airway obstruction (2,11,29), thus he received systemic corticosteroid and antihistamine to relieve this serious condition. We did not give him any antiviral agents since the oral lesions were not in vesicle stage but in crust ulceration stage when he visited our clinic on day 6, that appeared not necessary to give the antiviral agent. Interestingly, Shelley et al (13) succeeded with acyclovir prophylaxis of attack of both angioedema or chronic urticaria and HSV infection, suggesting the relevance of viral infection with angioedema or urticaria and the therapeutic effect of antiviral medication by suppressing circulating viral antigen.

To sum up, acute angioedema and urticaria in this patient may be relatively caused by virus-induced reaction, probably triggered by the HSV or may be concurrent. Thus, patient's medical history, clinical and laboratory examination are required for diagnosis and appropriate treatment including awareness and prompt treatment of the life-threatening condition.

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Abstract

We report a case of acute angioedema and urticaria, which is possibly induced by herpes simplex virus infection. A Japanese 58-year-old male patient presented urticaria including cutaneous erythematous rashes at extremities and trunk. He also developed angioedema which was characterized by swelling of lips, tongue, face, and periorbital tissue with difficulty in breathing, speaking, and fullness in throat. Six days later, crusted ulcers were detected on lower lip. Complete blood studies and biochemical screening examination, antibody titers for viral infections, urinalysis and scratch test for drug hypersensitivity have been investigated. Interestingly, serum complement fixation antibody titer for HSV showed high titer at 1:32. Accompanied by oral ulcerations, he was diagnosed as herpes labialis. The patient was admitted and treated intravenously with antihistamine, penicillin, and corticosteroid. After 3 days of treatment, his symptoms significantly improved. From 3-year follow-up, he had not developed angioedema and urticaria. This letter shows clinical pictures, treatment and possibility of the relation of angioedema and urticaria with herpes simplex virus infection. However, one should also consider the possibility of coincidence of herpes simplex virus infection.

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Key words

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