

Upper Respiratory Infection Followed by Concurrent Sweet's Syndrome and Erythema Nodosum

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ABSTRACT:

Sweet's syndrome (SS) is a rare inflammatory condition presented with fever, leukocytosis, erythematous, tender plaques and histology evidence of dense neutrophilic infiltration in the dermis. It appears mostly in women between age 30-60 years. Erythema nodosum (EN), a form of panniculitis, is manifested as erythematous painful rounded lumps and occurs 3-5 times more often in female patients in all age groups, but mostly between the second and the fourth decades of life. Although rare, concurrent occurrence of Sweet's syndrome and erythema nodosum is described and may be associated with autoimmune disorders, certain malignancies, gastrointestinal disease or upper respiratory tract infections. Here, we described 34-year-old saleswoman who developed concurrent Sweet's syndrome and erythema nodosum seven days after upper respiratory tract infection onset. During upper respiratory infection, she was treated with three-days azithromycin therapy, together with ibuprofen and paracetamol. Later, when she developed concurrent SS and EN, she was treated initially with clindamycin and prednisone 40 mg, followed by 60 mg of prednisone after which the patient becomes afebrile with gradual rash regression. There is limited knowledge on concurrent SS and EN, their etiopathogenesis and association with different diseases, infections and/or medications. Concurrent SS and EN in our patient was probably triggered by the upper respiratory tract infection. Although, there is no evidence that azithromycin may induce SS or EN or both, it could be considered as a possible trigger alone or together with the upper respiratory tract infection.

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KEYWORDS: upper respiratory infection, pharyngitis, Sweet's syndrome, erythema nodosum, azithromycin

SAŽETAK:

RESPIRATORNA INFEKCIJA GORNJIH DIŠNIH PUTOVA PRAĆENA ISTOVREMENO SWEETOVIM SINDROMOM I NODOZNI ERITEMOM

Sweetov sindrom (SS) rijetko je upalno stanje koje se manifestira vrućicom, leukocitozom, eritematoznim, nježnim plakovima i histološkim dokazom guste neutrofilne infiltracije u dermisu. Pojavljuje se uglavnom u žena u dobi od 30-60 godina. Nodozni eritem (EN), oblik panikulitisa, očituje se bolnim, eritematoznim, zaobljenim potkožnim čvorovima i javlja se 3-5 puta češće u bolesnica u svim dobnim skupinama, ali uglavnom između drugog i četvrtog desetljeća života. Iako je rijetka, istodobna pojava Sweet-ovog sindroma i nodoznog eritema opisana je i može biti povezana s autoimunim poremećajima, određenim malignim bolestima, gastrointestinalnom bolešću ili infekcijama gornjih dišnih puteva. Ovdje smo opisali 34-godišnju prodavačicu koja je razvila istodobni Sweetov sindrom i nodozni eritem sedam dana nakon početka infekcije gornjih dišnih puteva. Tijekom infekcije gornjih dišnih puteva, liječena je trodnevnom terapijom azitromicinom, zajedno s ibuprofenom i paracetamolom. Kasnije, kad je razvila istodobno SS i EN, liječena je u početku klindamicinom i prednizonom od 40 mg, a zatim sa 60 mg prednizona, nakon čega bolesnica postaje afebrilna s postupnom regresijom osipa. Malo se zna o istodobnom SS i EN, njihovoj etiopatogenezi i povezanosti s različitim bolestima, infekcijama i/ili lijekovima. Istodobni SS i EN u naše bolesnice vjerojatno je potaknut infekcijom gornjih dišnih puteva. Iako nema dokaza da azitromicin može izazvati SS ili EN ili oboje, moglo bi se pretpostaviti da bi mogao biti okidač sam ili zajedno s infekcijom gornjih dišnih puteva.

KLJUČNE RIJEČI: infekcija gornjih dišnih puteva, faringitis, Sweetov sindrom, nodozni eritem, azitromicin

INTRODUCTION

Upper respiratory tract infections (URI) include the infection in nose, sinuses, pharynx, larynx, and the large airways and are leading cause of morbidity. Usually, they are caused by different viruses, mostly rhinoviruses, but also the influenza virus, adenovirus, enterovirus, and respiratory syncytial virus. Bacterial infections are also common and often pharyngitis could be caused by *Streptococcus pyogenes*, a Group A streptococcus^{1,2}.

Sweet's syndrome (SS) is a rare inflammatory condition presented with fever, leukocytosis erythematous, tender plaques and histology evidence of dense neutrophilic infiltration in the dermis. Different diseases, including infectious diseases, malignancies and medications are associated with SS. It appears mostly in women between age 30-60 years^{3,5}. There are major and minor criteria for diagnosis of SS (Figure 1)^{6,7}. For the treatment of patients with Sweet's syndrome systemic corticosteroids have been considered the primary option, but iodide or colchicine can also result in rapid resolution symptoms and lesions. In case that corticosteroids are contraindicated, indomethacin, clofazimine, dapsone, and cyclosporine can be administered^{3,4}.

Erythema nodosum (EN), a form of panniculitis, is manifested as erythematous painful rounded lumps, 1-6 cm in diameter and occurs 3-5 times more often in female patients in all age groups,

but mostly between the second and the fourth decades of life. EN is usually located symmetrically on the anterior surface of the lower extremities, but can also spread to the upper extremities and neck. It does not ulcerate and resolves without scarring. Streptococcal pharyngitis is the most common trigger of EN, which appears 2-3 weeks after infection resolution. *Mycoplasma*, *Chlamydia*, *Mycobacterium*, *Yersinia* spp., *Coccidioides* and *Histoplasma* caused infections could be followed by EN as well. Other medical conditions, which could be linked to EN development are: sarcoidosis, medication including antibiotics, inflammatory bowel diseases and sometimes pregnancy. If an infectious agent triggered EN, antibiotic therapy can be administered and non-steroidal anti-inflammatory agents are usually given. In case that some medication was responsible for the occurrence of EN, it should be stopped. The most common drugs that cause erythema nodosum are: oral contraceptives, sulfonamides and penicillin. However, despite investigation, no underlying cause is found in most erythema nodosum patients⁸.

Although rare, concurrent occurrence of Sweet's syndrome and erythema nodosum is described and may be associated with autoimmune disorders, certain malignancies, gastrointestinal disease. A case of a young male with a recent streptococcal infection was also described⁹⁻¹⁶.

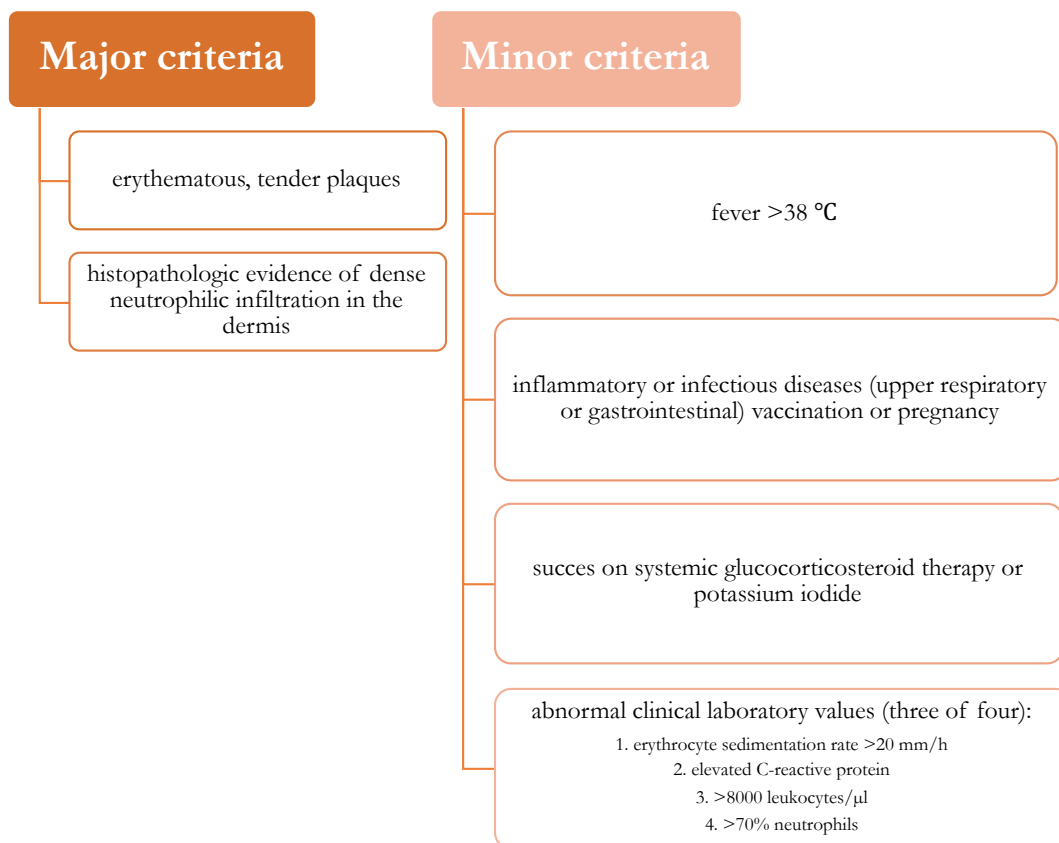


Figure 1. Major and minor diagnostic criteria for classic Sweet's syndrome based on fulfilling both major and two of the four minor criteria^{6,7}.

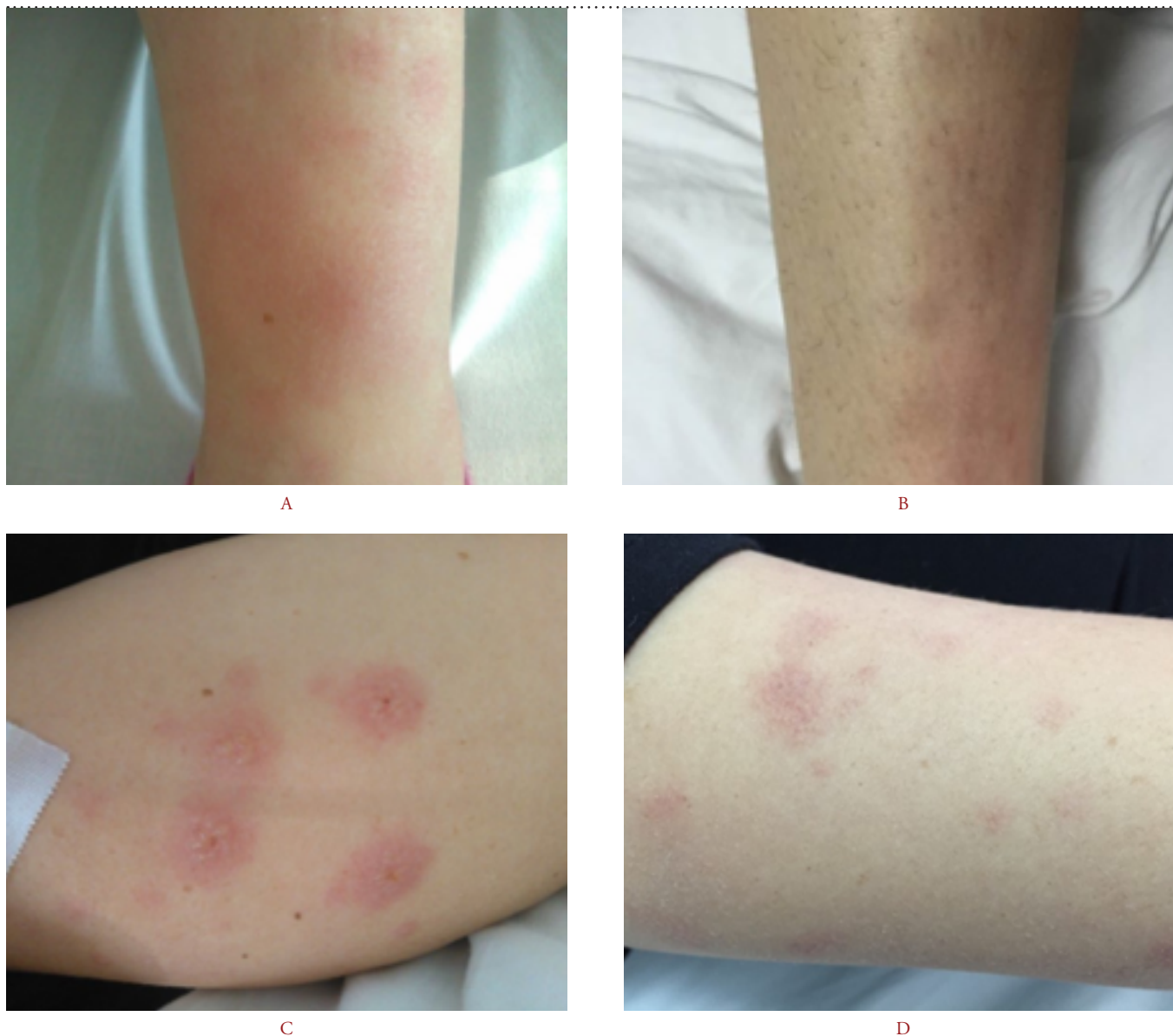


Figure 2. Rounded lumps (erythema nodosum) on the skin of the patient's lower leg, three (A) and ten days after the rash onset (B); Annular plaques and pustules developed on the skin of patient's forearm three (C) and ten days after the rash onset (D).

CASE REPORT

In 34-year-old saleswoman, the disease began eight days before admission to the hospital with a sore throat that lasted for the five days. On the sixth day after the upper respiratory tract symptoms onset, she became febrile up to 40 °C with chills and shivering. Next day she noticed a rash on the body and hands with mild pain and she was admitted to the hospital day after. Two days before admission she completed her three-days azithromycin therapy, taking ibuprofen and paracetamol as well. In childhood, she had contracted varicella and had lung tuberculosis at the age of 12. She had no chronic illnesses and was not taking therapy for chronic illnesses. Her daughter had a respiratory, possibly viral infection a week ago. She stated that she was allergic to amoxicillin clavulanic acid.

On admission, she is conscious, febrile (38.5 C), normotensive (110/70 mmHg), with neat pulse and respiratory frequency. Round-ed lumps, suggestive of erythema nodosum were observed on the skin of the lower legs of the patient, together with the annular plaques and pustules (0.5-1 cm in diameter) developed on the skin of patient's forearm (Figure 2 A, C) and very few at the trunk and neck. The conjunctival injection is recorded on both sides. Later, during the day, she became highly febrile up to 41 C.

She had high sedimentation rate (70 mm/h) and C-reactive protein (CRP) was 197 mg/l, with 8.800 leukocytes/ μ l. Chest X-ray was

normal and a slightly enlarged liver and polyp in the gallbladder were recorded on an abdominal ultrasound. On the second day of hospitalization, a skin biopsy was taken from the annular papule on the forearm and histopathologic evidence of neutrophilic infiltration in the dermis was confirmed later on. Initially, she was treated with clindamycin, and prednisone 40 mg. Three days later, sedimentation rate was 40 mm/h and CRP was 70 mg/l. Five days after admission, the patient was still febrile up to 38.5 and the prednisone dose was increased to 60 mg, after which the patient becomes afebrile with gradual rash regression (Figure 2 B, D).

DISCUSSION

Although etiology of SS or EN are not known, both syndromes could be triggered with upper respiratory infections or medications and associated with autoimmune or malignant diseases. Both are also reactive dermatoses with some similar clinical manifestations and histopathological findings, which could be successfully solved with corticosteroid therapy 3-5. Concurrent SS and EN are rare, but are described in the literature in connection with autoimmune or malignant diseases and also some respiratory, mostly streptococcal infections⁹⁻¹³.

Here we presented concurrent SS and EN in 34-years old, previously healthy woman with preceding upper respiratory tract infection

treated with azithromycin. We presumed that concurrent SS and EN in our patient was triggered with respiratory infection, but there is also possibility to be induced by antibiotic therapy. There is evidence in the literature that SS or EN are associated with some respiratory or gastrointestinal infections, including recent description of 29-year old Mexican who developed concurrent SS and EN possibly after the upper respiratory tract infection⁹⁻¹³. So far, there is no evidence in the literature that SS or EN could be induced by ibuprofen or paracetamol, which our patient took during the upper respiratory infection. Recent publication, however, described SS induced by an oral acetaminophen-codeine suspension and tablets, following repair of a facial fracture¹⁷. Also, no azithromycin therapy was associated with SS or/and EN so far and here we have no proof that this could be the case in our patient as well. Previously it was stated that tetracycline, minocycline, or clindamycin may be associated with SS^{18,19}. The therapy with oral prednisone was successful in our patient and skin rash was almost completely gone in three weeks of follow up.

CONCLUSION

There is limited knowledge on concurrent SS and EN, their etio-pathogenesis and association with different diseases, infections and /or medications. Here, we presented a concurrent SS and EN in 34-years old women, which was probably triggered by the upper respiratory tract infection. Although, there is no evidence that azithromycin may induce SS or EN or both, it could be considered as a possible trigger alone or together with the upper respiratory tract infection.

AUTHOR CONTRIBUTIONS:

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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