Portuguese Journal of Dermatology and Venereology

Permanyer

Check for updates

Port J Dermatol and Venereol.

CASE REPORT

Sweet's syndrome and erythema nodosum following simultaneous COVID-19 and influenza vaccination: a report of two cases

Síndrome de sweet e eritema nodoso após vacinação simultânea contra a COVID-19 e a gripe: relato de dois casos

Jéssica F. Freitas[1], Gabriela C. M. Alé[1], Daniela K. Stolnicki[1], Marcus Trovó[1], Danielle C. Quintella[2], Fernando M. Belles[2], and Tullia Cuzzi[2]*

[1]Department of Dermatology; [2]Department of Pathology. Institute of Dermatology Professor Rubem David Azulay – Santa Casa da Misericordia do Rio de Janeiro, Rio de Janeiro, Brazil

Abstract

Sweet syndrome (SS) and erythema nodosum (EN) are dermatoses triggered by factors such as vaccination. We report two cases of EN and SS simultaneously, following vaccination against COVID-19 and influenza, in female patients, in their fourth decade of life, presenting with painful erythematous papules on the upper limbs, painful nodules on the lower limbs, and fever, with no relevant laboratory alterations. Histopathological examination of the lesion on the arm confirmed SS and, on the leg, EN. Treatment with systemic corticotherapy induced complete resolution of the conditions. Postvaccination cutaneous reactions are rare and can occur in association with the vaccine or the adjuvant. We cannot infer whether the cases were due to the influenza vaccination, the COVID-19 vaccination, or a combination of both vaccines. However, as these are the cases of two concomitant dermatoses after simultaneous vaccination, something not reported in the literature, the communication of these cases is relevant in the current global health situation.

Keywords: Sweet syndrome. Erythema nodosum. Vaccine. Case report.

Resumo

A síndrome de sweet (SS) e o eritema nodoso (EN) são dermatoses que podem ser desencadeadas por fatores como a vacinação. Relatamos dois casos de EN e SS que ocorreram em simultâneo, após vacinação contra COVID-19 e influenza, em duas doentes do sexo feminino, na quarta década de vida, apresentando pápulas eritematosas dolorosas nos membros superiores, nódulos dolorosos nos membros inferiores e febre, sem alterações laboratoriais relevantes. O exame histopatológico de lesão do braço confirmou SS e da perna EN. Foi instituído tratamento com corticoterapia sistêmica com resolução completa do quadro. As reações cutâneas pós-vacinação são raras e podem ocorrer em associação com a vacina ou seu adjuvante. Neste caso não podemos inferir se os casos foram decorrentes da vacinação contra a gripe, contra a COVID-19 ou da combinação de ambas as vacinas. No entanto, por se tratar de algo não relatado na literatura, a comunicação destes casos é relevante na atual situação de saúde global.

Palavras-chave: Síndrome de sweet. Eritema nodoso. Vacina. Relato do caso.

Correspondence:
Jéssica F. Freitas
E-mail: jeffreitas@hotmail.com

Received: 07-06-2024
Accepted: 05-10-2024
DOI: 10.24875/PJDV.24000056

Available online: 21-03-2025
Port J Dermatol and Venereol. 2025;83(1):60-63
www.portuguesejournalofdermatology.com

Introduction

We report the first two cases in the literature of patients who developed both erythema nodosum (EN) and Sweet syndrome (SS), following simultaneous vaccination against COVID-19 with the Comirnaty Bivalent BA. 1 vaccine (Pfizer) and influenza with the trivalent vaccine provided by the Brazilian Unified Health System.

Case report

Case 1: a 49-year-old healthy female presented with petechiae over an erythematous plaque on the digital pulps, a single painful erythematousedematous papule with a vesicle-like appearance on the left arm –at the site of one of the vaccines, an aphthous lesion on the jugal mucosa of the lower lip, and painful erythematous-violaceous nodules on the lower limbs (Fig. 1), which appeared simultaneously 2 weeks after COVID-19 and influenza vaccination. The condition was associated with a maximum fever of 38.3 °C. Laboratory studies showed no alterations; serologies for hepatitis and sexually transmitted infections were negative. Incisional biopsies were performed on the arm and the left leg, and the histopathology report confirmed SS and EN.

Case 2: a 41-year-old healthy female presented with painful erythematous-edematous papules and plaques with a vesicle-like appearance on the upper limbs, as well as painful erythematous-violaceous nodules on the lower limbs (Fig. 2) that appeared 1 week after COVID-19 and influenza vaccination, associated with fever (max 38.3 °C) and arthralgia. The patient had no alterations in serologies and other blood tests, except an elevated ESR (38 mm/h) and protein electrophoresis with asymmetrical distribution of the γ fraction. Histopathology of one of the lesions on the forearm confirmed the hypothesis of SS. Lower limb lesions were clinically diagnosed as EN.

Treatment with oral prednisone –at a dose of 40 mg/day for 7 days followed by gradual weaning until completing

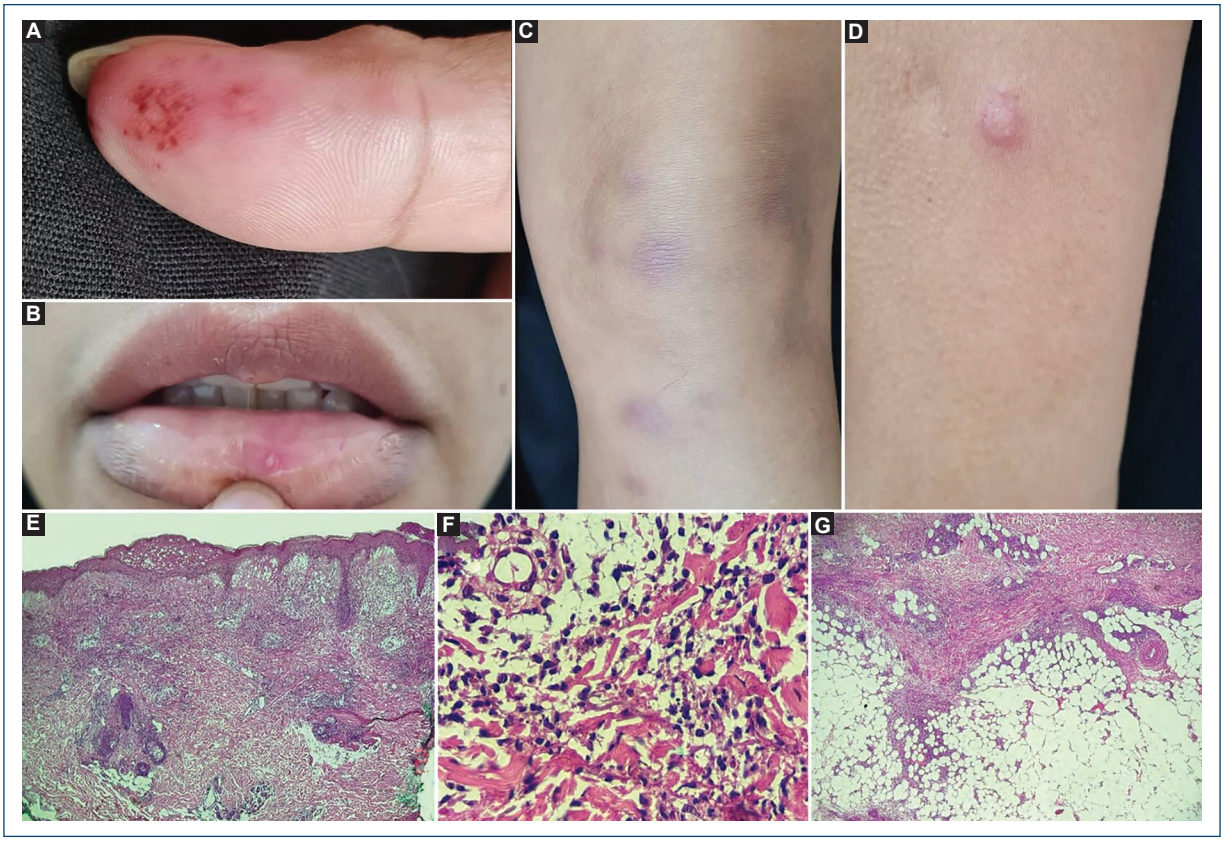

Figure 1. Patient 1 – petechiae over an erythematous plaque on the digital pulp of the first right finger **(A)**, single aphthous lesion on the lower lip **(B)**, erythematous-violaceous nodules on the lower limbs **(C)**, and erythematous papules with hypochromic center and central pseudovesiculation located on the left arm **(D)**. Histopathology from the arm with papillary dermal edema, perivascular and interstitial dermal infiltrate (H&E, 4×) **(E)**, predominantly with neutrophils and leukocytoclasis (H&E, 40×) **(F)**, and from the leg with septal panniculitis (H&E, 4×) **(G).**

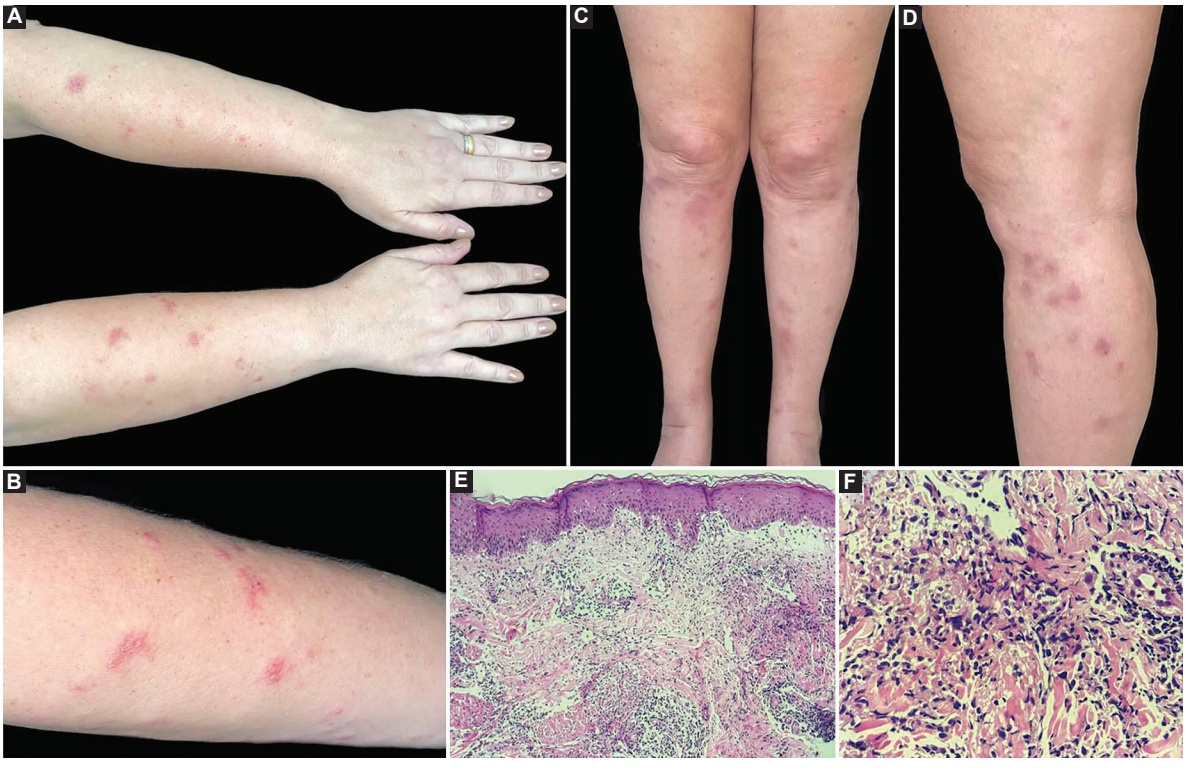

Figure 2. Patient 2 – erythematous papules and plaques with pseudovesiculation on the forearms **(A),** and left forearm **(B)**, and erythematous-violaceous nodules on the lower limbs **(C)**, and left leg **(D)**. Histopathology from a lesion on the forearm showing focal papillary dermal edema and dermal infiltrate (H&E, 10×) **(E)** predominantly composed of neutrophils (H&E, 40×) (**F**).

21 days of treatment – was initiated in both cases, with complete resolution in 14 days and no recurrence.

Discussion

SS occurs predominantly in middle-aged women following an infectious condition. Vaccinations can also trigger the syndrome[1], which can still be associated with inflammatory conditions such as EN[1,2]. Elevated erythematous plaques with vesicle-like appearance preferentially affect the face, neck, and extremities and may be accompanied by fever, general malaise, involvement of the eyes, joints, and oral mucosa[1]. It is associated with the pathergy phenomenon, with few reports in the literature, which may justify the appearance of a single lesion at the vaccine application site as shown in case 1[3].

The diagnosis includes the presence of two major criteria (abrupt onset of lesions and compatible histopathology –diffuse dermal and perivascular neutrophilic infiltrate, with leukocytoclasia and dermal edema) and at least two minor criteria (fever, constitutional symptoms, leukocytosis, good response to systemic corticotherapy, and presence of triggering factors such as medication, vaccination, neoplasm, pregnancy, and infectious/inflammatory diseases)[1]. Some authors also propose specific diagnostic criteria for the drug-induced form, requiring the presence of five criteria: abrupt appearance of typical cutaneous lesions, histopathology compatible with SS, presence of fever and constitutional signs and symptoms, temporal relationship between the onset of the medication and clinical manifestation or relapse after therapeutic testing with the drug, and temporal relationship between withdrawal of the medication or use of systemic corticosteroids and resolution of the condition[4].

SS responds quickly to systemic corticotherapy, which is the first line of treatment[1] –the therapeutic option adopted in the two cases reported. Laboratory tests can reveal leukocytosis with neutrophilia, elevated ESR, and transient IgA monoclonal gammopathy, which has also been described in the literature after Janssen's Ad26.COV2.S vaccine[3].

EN is characterized by the presence of symmetrical, painful erythematous nodules located mainly in the pretibial region[5]. Like SS, it is more common in adult

women and has the same triggering factors, such as vaccinations[5]. The histopathology shows septal panniculitis with neutrophilic infiltrate in the acute phase and later an infiltrate with lymphocytes, histiocytes, and giant cells. Diagnosis is eminently clinical and treatment includes anti-inflammatory and symptomatic drugs[5].

Postvaccination cutaneous reactions are rare and can occur in association with the vaccine or the adjuvant[6]. With the COVID-19 pandemic, recent articles have discussed the association between either SS or EN and vaccination against SARS-CoV2[3,6]; however, the association of these disorders with vaccination is rare, with few case reports in the literature[6–10]. Until now, we found no case reporting the concomitance of both dermatoses after vaccination. Nevertheless, in the second case reported, we believe that two diseases, SS and EN, represent different manifestations of the same hypersensitivity reaction to the vaccine at two different body sites. However, in contrast to the first case, a biopsy of the cutaneous leg lesions was not performed and we cannot completely rule out the possibility of SS mimicking EM. Actually, some authors have described that SS can present on the legs with lesions that clinically resemble EN[11,12].

We cannot infer whether the cases were due to the influenza vaccination, the COVID-19 vaccination, or a combination of both vaccines. However, as these are concomitant cases of the two dermatoses after simultaneous vaccination, something not yet reported in the literature, the communication of these cases is relevant in the current global health situation. However, it is important to note that nonserious adverse events from vaccination, such as these two, should not discourage people from getting vaccinated.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Wojcik A de L, Nishimori FS, Santamaría JR. Síndrome de Sweet: estudo de 23 casos. Anais Brasileiros de Dermatologia [Internet]. 2011 Apr 1;86:265–71. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7938036
2. Bonamigo RR, Razera F, Olm GS. Dermatoses neutrofílicas: parte I. An Bras Dermatol. 2011 Feb;86(1):11–27.
3. Bechtold A, Owczarczyk-Saczonek A. Atypical presentation of Sweet syndrome with nodular erythema and oral ulcerations provoked by Ad26.COV2.S SARS-CoV -2 vaccination and review of literature. Dermatol Ther. 2022 Oct;35(12):e15923.
4. Joshi TP, Friske SK, Hsiou DA, Duvic M. New practical aspects of Sweet syndrome. Am J Clin Dermatol. 2022 May;23(3):301–18.
5. Pérez-Garza DM, Chavez-Alvarez S, Ocampo-Candiani J, Gomez-Flores M. Erythema nodosum: a practical approach and diagnostic algorithm. Am J Clin Dermatol. 2021 May;22(3):367–78. DOI: 10. 1007/s40257-022-00673-4.
6. Chahed F, Ben Fadhel N, Ben Romdhane H, Youssef M, Ben Hammouda S, Chaabane A, et al. Erythema nodosum induced by covid-19 pfizer-biontech mrna vaccine: a case report and brief literature review. Br J Clin Pharmacol. 2023 Feb;89(2):536–40. DOI: 10.1111/bcp.15351.
7. Jia Y, Fu B, Dong L, Zhao M. Sweet syndrome induced by SARS-cov-2 vaccines: a systematic review of patient-report studies. Hum Vaccin Immunother. 2023 Aug 1;19(2):2217076. DOI: 10.108021645515.2023.2217076.
8. Baker O, Chen KS, Kaminska I, Rajagopal V. Sweet syndrome following the chadox1-S vaccine. BMJ Case Rep. 2024 Jan 12;17(1):e257635. DOI: 10.1136/bcr-2023-257635.
9. Nikolaeva DG, Bogdanov IA, Kadurina MI, Tsankov NK. Erythema nodosum induced by the Pfizer-BioNTech vaccine. Skinmed. 2023 Aug 28;21(3):198–9.
10. Gonzalez-Canete M, Pinto-Pulido EL, Vega-Diez D, Rodriguez-Villa A, Moreno-Artero E, Andina Martinez D, et al. Erythema nodosum after COVID-19 vaccine: report of two pediatric cases. Pediatr Dermatol. 2023;40(4):660–3. DOI: 10.1111/pde.15205.
11. Cohen PR. Concurrent sweet syndrome and erythema nodosum. Baylor Univ Med Cent Proc. 2023 Dec 20;37(1):180–2. DOI: 10.1080/08998280.2023.2282859.
12. Dege T, Schmieder A, Kerstan A, Goebeler M, Goller SG. Concurrent sweet syndrome and erythema nodosum: two sides of the same coin? Eur J Dermatol. 2023 Apr 1;33(2):192–3. DOI: 10. 1684/ejd.2023.4468.