

lupus erythematosus.⁵⁻⁷ To the best of our knowledge, this would be the first case of morphea relapsing due to any cancer immunotherapy treatment.

In conclusion, attending to the nature of this kind of immunotherapies, totally different from traditional chemotherapy, dermatologists should be aware not only of their typical irAEs, but also of the possibility of exacerbation or relapse of previously controlled skin diseases, especially immune-related ones. This will probably represent a new challenge for dermatologists in the future, as these treatments are being used more and more often. More experience is needed in order to conclude the exact relation of cancer immunotherapy and the relapse of these diseases.

Conflict of interests

The authors declare no conflict of interest.

Acknowledgement

A C. M. García del Real for his collaboration.

References

1. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med*. 2012;366:2443–54.
 2. Macdonald JB, Macdonald B, Golitz LE, LoRusso P, Sekulic A. Cutaneous adverse effects of targeted therapies: Part II: inhibitors of intracellular molecular signaling pathways. *J Am Acad Dermatol*. 2015;72:221–36, quiz 237–8.
 3. Sibaud V, Meyer N, Lamant L, Vigaros E, Mazieres J, Delord JP. Dermatologic complications of anti-PD-1/PD-L1 immune checkpoint antibodies. *Curr Opin Oncol*. 2016;28:254–63.
 4. Belum VR, Benhuri B, Postow MA, Hellmann MD, Lesokhin AM, Segal NH, et al. Characterisation and management of dermatologic adverse events to agents targeting the PD-1 receptor. *Eur J Cancer*. 2016;60:12–25.
 5. Johnson DB, Sullivan RJ, Ott PA, Carlino MS, Khushalani NI, Ye F, et al. Ipilimumab therapy in patients with advanced melanoma and preexisting autoimmune disorders. *JAMA Oncol*. 2016;2:234–40.
 6. Kato Y, Otsuka A, Miyachi Y, Kabashima K. Exacerbation of psoriasis vulgaris during Nivolumab for oral mucosal melanoma. *J Eur Acad Dermatol Venereol*. 2015.
 7. Matsumura N, Ohtsuka M, Kikuchi N, Yamamoto T. Exacerbation of psoriasis during Nivolumab therapy for metastatic melanoma. *Acta Derm Venereol*. 2016;96:259–60.
 8. Fett N, Werth VP. Update on morphea: part I. Epidemiology, clinical presentation, and pathogenesis. *J Am Acad Dermatol*. 2011;64:217–28, quiz 229–30.
 9. Peroni A, Zini A, Braga V, Colato C, Adami S, Girolomoni G. Drug-induced morphea: report of a case induced by balicitib and review of the literature. *J Am Acad Dermatol*. 2008;59:125–9.
 10. Nishino M, Sholl LM, Hodi FS, Hatabu H, Ramaiya NH. Anti-PD-1-related pneumonitis during cancer immunotherapy. *N Engl J Med*. 2015;373:288–90.
- A. Alegre-Sánchez,* P. Fonda-Pascual, D. Saceda-Corralo, E. de las Heras-Alonso
- Dermatology Service, Ramon y Cajal Hospital, Madrid, Spain*
- * Corresponding author.
E-mail address: adrian.alegresanchez@gmail.com (A. Alegre-Sánchez).
- 1578-2190/
© 2016 Elsevier España, S.L.U. and AEDV. All rights reserved.

Sweet's syndrome-like eruption in association with the exacerbation of Behçet's disease after the Great East Japan Earthquake



Erupción tipo síndrome de Sweet asociada al empeoramiento de la enfermedad de Behçet después del Gran terremoto de Japón oriental

Dear Editor:

We herein report a case of Behçet's disease (BD), which was stable until the Great East Japan Earthquake, but deteriorated thereafter and presented with Sweet's syndrome-like facial erythemas, along with exacerbation of other mucocutaneous conditions.

A 36-year-old male visited our hospital, complaining of fever, genital ulcer, folliculitis-like lesions, and erythema nodosum (Fig. 1a), and had been diagnosed previously with incomplete type BD six years ago. He received treatment with minocycline, colchicine, and his symptoms were under control. However, his

symptoms recurred along with a fever of up to 39°C and throat pain following the Great East Japan Earthquake in March 2011 when he was evacuated from home and placed at a shelter. Physical examination revealed multiple oral ulcers, folliculitis on the back, tender subcutaneous erythematous nodules on the knee, and tender infiltrative erythematous plaques with surface scales on the cheek, forehead, and neck (Fig. 1b and c). A biopsy specimen taken from his face showed dense neutrophil infiltration throughout the dermis (Fig. 2). Laboratory examination showed elevated levels of white blood cell counts (12,200/μl with 80% neutrophils), C-reactive protein (11.44 mg/dl), and erythrocyte sedimentation ratio (41 mm/h). Antistreptolysin O (ASO) level was within normal ranges. HLA typing was negative for HLA-B51, but positive for HLA-A2, A24, B54, and B62. He was successfully treated with oral prednisolone (20 mg/day).

The present case developed infiltrative erythemas on the face mimicking Sweet's syndrome, along with other cutaneous symptoms such as folliculitis and erythema nodosum. A biopsy specimen from the face revealed dense neutrophil infiltration throughout the dermis. Patients with BD rarely present with Sweet's syndrome-like infiltrative erythema.¹ On the other hand, several cases have been reported as a co-existence of BD and Sweet's syndrome; symptoms of Sweet's syndrome appear representing a flare or in

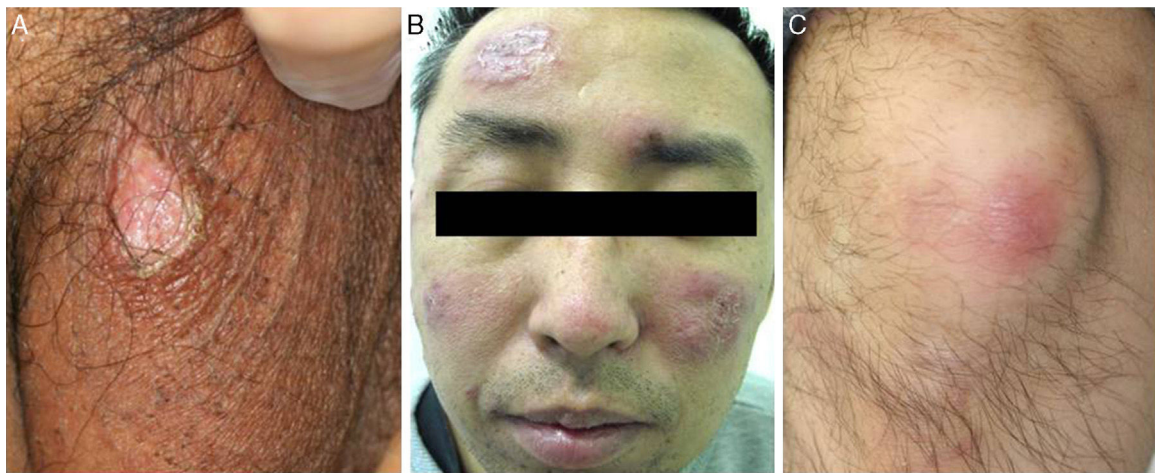


Figure 1 In 2006, the patient developed solitary scrotum ulcer (a), along with oral ulcers, folliculitis, and erythema nodosum-like lesions. In 2011, the patient developed tender, infiltrative erythematous plaques on the forehead and cheeks (b), and erythema nodosum-like lesion on the knee (c).

the acute phase of BD.² BD and Sweet's syndrome share common pathogenesis such as neutrophil activation, and Th1 type cytokines contribute to the pathogenesis of both disorders. We prefer to interpret our case as Sweet's syndrome-like eruptions that developed along with other symptoms such as oral ulcers, folliculitis, and erythema nodosum-like lesions in the exacerbation of BD, rather than the co-existence of Sweet's syndrome with BD, although the criteria of Sweet's syndrome are fulfilled. There were no other apparent triggers such as upper airway or gastrointestinal infections and the use of new drugs for the induction of Sweet's syndrome-like eruptions. Although the frequency is low, BD may be one of the underlying diseases susceptible for developing Sweet's syndrome-like eruptions. We have followed-up the patient for almost 10 years, and although he has had the occasional

worsening of BD, the Sweet's syndrome-like eruption occurred only once. Our patient has HLA-B54, which may be an important genetic background in the development of Sweet's syndrome-like eruption.

Psychosocial stress has been reported to be a triggering and worsening factor of BD, and patients frequently develop a neurobehavioural syndrome, defined as 'neuro-psycho-BD'. Our patient's symptoms were possibly exacerbated by mental stress caused by the Great East Japan Earthquake. Mental health problems have affected many residents of evacuation zones in Fukushima,³ although there are no studies of the deterioration of BD examining a number of patients. Anxiety and depression are common psychiatric disorders in patients with BD and more numerous than in controls,⁴ and psychological stressors influence the onset and flare of BD and/or recurrent aphthoid stomatitis. Approximately 70% of patients with BD recognized a stress factor prior to the onset of the disease, and 80% of patients with BD declared stress in the relapse period.⁵ The hypothalamic-pituitary-adrenal axis affects the immune system, and thus in the present case the stress-induced immune alterations may have worsened the symptoms of BD.

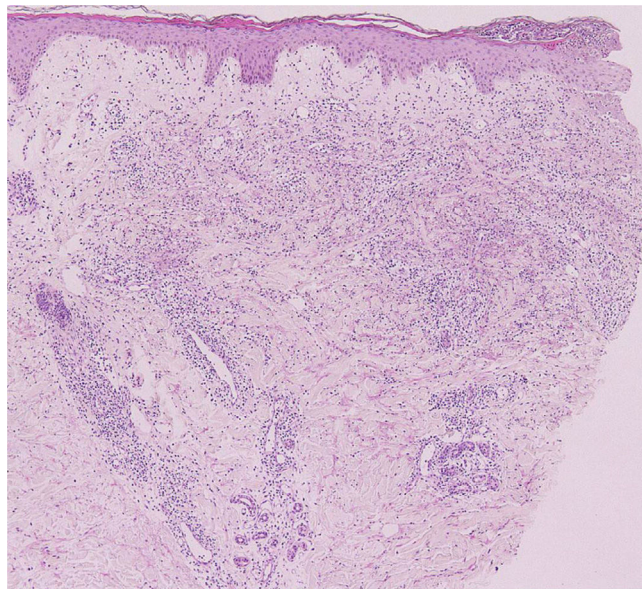


Figure 2 Histopathology showing dense inflammatory cell infiltrates through the dermis, mainly composed of neutrophils (hematoxylin and eosin stain, original magnification $\times 40$).

Conflicts of interest

None declared.

Funding sources

None.

References

1. Cho KH, Shin KS, Sohn SJ, Choi SJ, Lee YS. Behçet's disease with Sweet's syndrome-like presentation: a report of six cases. *Clin Exp Dermatol.* 1989;14:20–4.
2. Wu F, Luo X, Yuan G. Sweet's syndrome representing a flare of Behçet's disease. *Clin Exp Rheumatol.* 2009;27 Suppl.:S88–90.
3. Yabe H, Suzuki Y, Mashiko H, Nakayama Y, Hisata M, Niwa S, et al. Psychological distress after the Great East Japan Earthquake and Fukushima Daiichi Nuclear Power Plant accident: results of a mental health and lifestyle survey through the Fukushima Health

Management Survey in FY2011 and FY2012. *Fukushima J Med Sci.* 2014;60:57–67.

4. Calikoglu E, Onder M, Cosar B, Candansayar S. Depression, anxiety levels and general psychological profile in Behçet's disease. *Dermatology.* 2001;203:238–40.
5. Kartidag R, Unal S, Evereklioglu C, Sipahi B, Er H, Yologlu S. Stressful life events, anxiety, depression and coping mechanisms in patients with Behçet's disease. *J Eur Acad Dermatol Venereol.* 2003;17:670–5.

T. Miura, M. Ohtsuka, T. Yamamoto*

Department of Dermatology, Fukushima Medical University, Fukushima, Japan

* Corresponding author.

E-mail address: toyamade@fmu.ac.jp (T. Yamamoto).

1578-2190/

© 2016 Published by Elsevier España, S.L.U.

Congenital Plaque-type Glomuvenous Malformation: 11 Years of Follow-up and Response to Treatment With the Combined Pulsed-Dye and Neodymium:Yttrium-Aluminum-Garnet Laser[☆]



Malformación glomovenosa congénita en placas: 11 años de seguimiento y respuesta al tratamiento con láser combinado PDL/Nd: YAG

To the Editor:

Glomuvenous malformations (GVM), previously known as glomangiomas, show a familial tendency and are characterized histologically by the presence of vascular channels surrounded by a variable number of glomus cells. There is a rare form that presents as plaques. The treatment of these lesions has still not been standardized.

Our patient was a newborn boy from a twin pregnancy, born preterm at 34 weeks, with erythematous plaques present on his back since birth. There was no family history of similar lesions. On physical examination, nonpulsatile, depressed erythematous-violaceous plaques were observed on the boy's back (Fig. 1A). We performed skin biopsy to clarify our differential diagnosis of capillary malformation, multiple myofibromas, or subcutaneous fat necrosis. Histopathology showed an increased number of ectatic vessels in the dermis and was interpreted as a capillary malformation.

At 6 months, the plaques had acquired an annular pattern, with an erythematous halo, depressed blue-violaceous center, ectatic vessels, and flaccid skin (Fig. 1B).

A further biopsy, performed because of the lack of clinical-pathological correlation, revealed a dermis with vascular structures surrounded by several layers of monomorphic round cells with eosinophilic cytoplasm (Fig. 2A). Immunohistochemistry showed the perivascular glomus cells to be positive for vimentin and α -actin and negative for desmin and S100 (Fig. 2B). Based on these findings, we made a diagnosis of congenital plaque-type GVM.

Initially we took a wait-and-see approach. Over the following years, the plaques extended to the adjacent skin and took on a more atrophic appearance, with very dilated vessels. No new lesions appeared.

At 7 years of age, the lesions were still asymptomatic, but their appearance (Fig. 1C) negatively affected the patient's self-esteem, leading us to evaluate the treatment options. The size of the lesions limited a possible surgical intervention. It was decided to start treatment with combined pulsed dye (PDL) (595 nm) and neodymium-doped yttrium aluminium garnet (Nd:YAG) (1064 nm) lasers (Cynergy MultiplexTM, Cynosure, Westford, Massachusetts, United States), with a spot size of 10 mm, a PDL pulse duration of 0.5 ms and fluence of 8.5–9 J/cm², followed by a pulse of Nd:YAG with a duration of 15 ms and fluence of 50 J/cm². A cooling system was used simultaneously to prevent epidermal damage. The sessions were performed under general anesthesia every 2 or 3 months. The post-treatment recommendations included oral analgesia and photoprotection. At the time of writing, the patient has received 10 sessions of laser therapy, with lightening of the color of the lesions and a reduction in lesion volume and in the caliber of the vessels (Fig. 1D). Treatment has been well tolerated and no complications have been detected.

GVMs account for 5% of venous malformations (VM) and are distinct from sporadic VMs and from hereditary mucocutaneous VMs. A familial tendency is detected in 88%, with an autosomal dominant inheritance pattern and incomplete penetrance (90%). Their etiology has been related to mutations in the glomulin gene (*GLMN*).¹ GVMs are usually multiple and tend to appear at an early age. They can present as papular-nodular lesions or as plaques, and may be congenital² or acquired.³

Congenital plaque-type GVMs present clinically as bluish plaques with a cobblestone surface,¹ or as atrophic plaques with telangiectasias,^{2,4–9} as in our patient. A segmental distribution is often observed.⁵

Histology is characterized by a nonencapsulated proliferation of ectatic vascular channels surrounded by 1 or several layers of polygonal glomus cells. Immunohistochemistry is positive for α -smooth muscle actin and vimentin and negative for desmin.^{1–3}

The clinical course of plaque-type GVMs varies. Progressive thickening and darkening of the lesions has been reported, as well as a tendency to spread into adjacent unaffected areas,² as was seen in our patient.

The objectives of treatment of GVMs are to relieve pain and improve function and cosmetic appearance.^{6,7,9} Surgery is an option for small localized lesions. Treatments such as sclerotherapy and ablative therapy have been used in multiple or extensive GVMs, but results have not been consistent.¹⁰ There are also descriptions of cases treated with Nd:YAG laser with good results,⁹ and PDL lasers have been reported to be useful for the more superficial component of the lesions.⁶ The dual laser (PDL/Nd:YAG) allows us to treat different depths of the skin using lower fluences and thus

[☆] Please cite this article as: Vargas-Navia N, Baselga E, Muñoz-Garza FZ, Puig L. Malformación glomovenosa congénita en placas: 11 años de seguimiento y respuesta al tratamiento con láser combinado PDL/Nd: YAG. *Actas Dermosifiliogr.* 2017;108:72–74.