In different clinical trials, anti-PD1 therapies such as Pembrolizumab or Nivolumab showed a relatively safe profile, with a low incidence of major adverse effects (drug-related grade 3 or 4 toxic effects only in 14% of the patients), being those related with pneumonitis the most severe of them.[10] These adverse reactions related with immune-checkpoints inhibitors have been named as immune-related adverse events (irAEs). When focusing on the skin irAEs, non-specficic macular papular rash and pruritus have been described as the most common ones. Interestingly, vitiligo has also been reported, but only in patients with melanoma. Urticaria, alopecia and mucosal involvement are other frequently described skin irAEs.[1–4]

The exacerbation of preexisting autoimune disorders related to immunotherapies has also been reported. These disorders include psoriasis, sarcoidosis, bullous pemphigoid and subacute 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.

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http://dx.doi.org/10.1016/j.ad.2016.07.013

0001-7310/

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 enfermdad 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

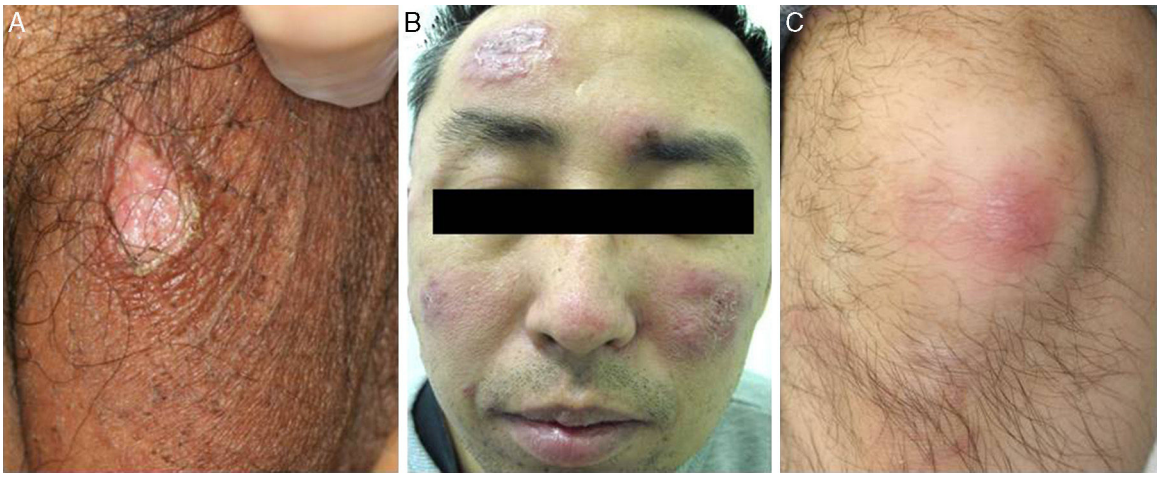

Figure 1 In 2006, the patient developed solitary scrotum ulcer (a), along with oral ulcers, folliculitis, and erythema nodosum-like lesions. In 2011, the patient developed tender, infiltrative erythematous plaques on the forehead and cheeks (b), and erythema nodosum-like lesion on the knee (c).

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' syndrome; symptoms of Sweet's syndrome appear representing a flare or in 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.

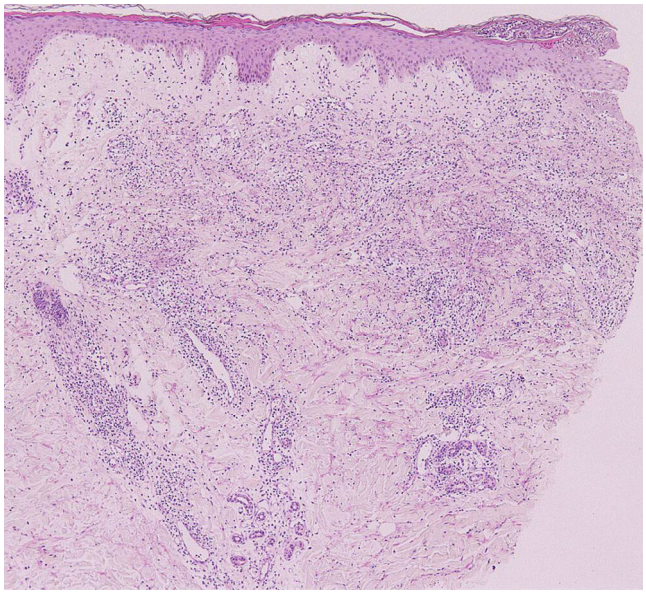

Figure 2 Histopathology showing dense inflammatory cell infiltrates through the dermis, mainly composed of neutrophils (hematoxylin and eosin stain, original magnification ×40).

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.

Conflicts of interest

None declared.

Funding sources

None.

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http://dx.doi.org/10.1016/j.ad.2016.07.006
0001-7310/

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

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

Sra. Directora:

Las malformaciones glomovenosas (MGV), anteriormente conocidas como glomangiomas tienen una tendencia familiar y se caracterizan histológicamente por la presencia de canales vasculares rodeados por una cantidad variable de células glómicas. Existe una forma infrecuente en placas. El tratamiento de estas lesiones aún no está estandarizado.

Se trata de un recién nacido varón, producto de un embarazo gemelar, y parto pretérmino a las 34 semanas, con placas eritematosas localizadas en la espalda, presentes desde el nacimiento, sin historia familiar de lesiones similares. En la exploración física se apreciaron unas placas eritemato-violáceas, deprimidas, no pulsátiles en la espalda (fig. 1A). Con los posibles diagnósticos de una malformación capilar, miofibromas múltiples o necrosis grasa subcutánea, se practicó una biopsia de piel. La histopatología mostró un número aumentado de vasos ectásicos en la dermis y fue interpretada como una malformación capilar.

A los 6 meses, las placas habían adquirido un patrón anular, con halo eritematoso, centro deprimido azul-violáceo, vasos ectásicos y piel redundante (fig. 1B).

La falta de correlación clínico-patológica, motivó la toma de una nueva biopsia cutánea. En la histología se observó una dermis con estructuras vasculares, rodeadas por varias capas de células redondas monomorfas, de citoplasma eosinófilo (fig. 2A). La inmunohistoquímica mostró positividad de las células glómicas perivasculares para vimentina y α-actina, y fue negativa para desmina y S100 (fig. 2B). Con estos hallazgos se hizo el diagnóstico de una MGV congénita en placas.

Inicialmente se optó por un manejo conservador. Durante los años sucesivos, las placas se fueron extendiendo a la piel adyacente, adquiriendo un aspecto mayormente atrófico con vasos marcadamente dilatados y no se registró la aparición de nuevas lesiones.

A los 7 años, las lesiones continuaban siendo asintomáticas, sin embargo, su aspecto (fig. 1C) afectaba negativamente la autoestima del paciente lo que motivó la evaluación de las opciones terapéuticas. El tamaño de las lesiones limitaba su tratamiento quirúrgico. Se decidió iniciar un manejo con láser combinando PDL (595-nm) y Nd:YAG (1064-nm) (Cynergy modo Multiplex^{TM}, Cynosure, Westford, MA, EE.UU.), con un *spot* de 10 mm, una duración del pulso de PDL de 0,5 ms y una fluencia de 8,5-9 J/cm^2, seguido por un pulso de Nd:YAG con una duración de 15 ms y una fluencia de 50 J/cm^2. Simultáneamente se utilizó un sistema de enfriamiento para evitar el daño epidérmico. Las sesiones se realizaron bajo anestesia general, cada 2 o 3 meses. Las recomendaciones postratamiento incluyeron analgésicos orales y medidas de fotoprotección. Hasta la fecha el paciente ha completado 10 sesiones de láser con aclaramiento de las lesiones, reducción en el volumen de la lesión y del calibre de los vasos (fig. 1D). El tratamiento ha sido bien tolerado y no se ha reportado ninguna complicación.

Las MGV representan un 5% de las malformaciones venosas (MV) y se diferencian de las MV esporádicas y de las MV mucocutáneas hereditarias. Tienen una tendencia familiar (88%) con un patrón herencia autosómico dominante y una penetrancia incompleta (90%). Su etiología se ha relacionado con mutaciones en el gen de la glomulina (GLMN)[1]. Las MGV generalmente son múltiples y tienden a aparecer en edades tempranas. Se pueden presentar como lesiones pápulo-nodulares y/o en placas que pueden ser congénitas[2] o adquiridas[3].

Las MGV congénitas en placas, se presentan clínicamente como placas azuladas con una superficie en empedrado[1], o bien como placas atróficas con telangiectasias[2,4–9], como en nuestro paciente, y a menudo tienen una distribución segmentaria[5].

La histología se caracteriza por una proliferación, no encapsulada, de canales vasculares ectásicos rodeados por una o varias filas de células glómicas poligonales. La inmunohistoquímica expresa α-actina de músculo liso y vimentina, y es negativa para desmina[1–3].

La evolución de las MGV en placas es variable. Se ha descrito un engrosamiento y oscurecimiento progresivo de las lesiones, con tendencia a extenderse hacia áreas adyacentes no afectas[2], como se ilustra en nuestro caso.

El tratamiento de las MGV tiene como objetivos aliviar el dolor y mejorar aspectos tanto funcionales como cosméticos[6,7,9]. La cirugía constituye una alternativa para lesiones localizadas y de menor tamaño. En MGV múltiples o extensas se han empleado tratamientos como la escleroterapia y terapias ablativas con resultados variables[10]. También existen reportes de casos tratados con láser Nd:YAG con buenos resultados[9], y se ha descrito