Reverse Isotopic Phenomenon in Drug Reaction with Eosinophilia and Systemic Symptoms☆

Fenómeno isotópico inverso en el síndrome de reacción por drogas con eosinofilia y síntomas sistémicos

To the Editor:

Reverse isotopic phenomenon, or isotopic non-response, is an extremely rare phenomenon characterised by the absence of a skin disease at the site of another unrelated skin disease which is already healed.[1] Sparing occurs at the healed site of an inflammatory disease. Most reports of reverse isotopic phenomenon show the sparing of the skin previously involved in herpes zoster.[2]

We describe a case of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome due to carbamazepine with isotopic non-response at the site of healed herpes zoster.

A 60 year male presented to us with complaints of fever, breathlessness and red itchy rash over body since 7 days. The patient had developed herpes zoster on the lower part of the right chest around two months back, and was prescribed Tab Carbamazepine by a local physician for the residual pain.

On examination, the patient was found to have generalised swelling, particularly prominent over the periocular areas. He was febrile (100.6 F) and had tachycardia (heart rate-110/min) and tachypnea (respiratory rate-22/min). The abdomen was distended and bowels sounds were not heard. There was mildly tender lymphadenopathy in inguinal and axillary areas. Cutaneous examination revealed erythematous maculopapular lesions predominantly distributed over the face, trunk and proximal extremities with tendency to coalesce such that the whole of the trunk was involved except the right T9 dermatome which was characteristically spared. [Fig. 1] The skin of the right T9 dermatome showed hyperpigmented scars of the healed herpes zoster. [Fig. 2] The rest of the cutaneous and systemic examination was normal.

Investigations revealed leucocytosis (TLC- 15500/ cu mm; normal- 4000-11000/ cu mm) with eosinophilia (AEC- 1580/ cu mm; normal- 40-440/ cu mm). There was elevation of liver enzymes (SGOT- 660 IU; normal- 7-40 IU, SGPT- 590 IU; normal- 7-56 IU) and increased blood urea (120 mg/dl; normal- 10-40 mg/dl) and serum creatinine (1.9 mg/dl; normal- 0.3-1.2 mg/dl). The patient had a normal chest radiograph and a gas filled distended bowel suggestive of paralytic ileus. The patient had hyperamylesemia (260 U/l; normal- 40-140 U/l) suggestive of pancreatitis. He subsequently developed fatal acute respiratory distress

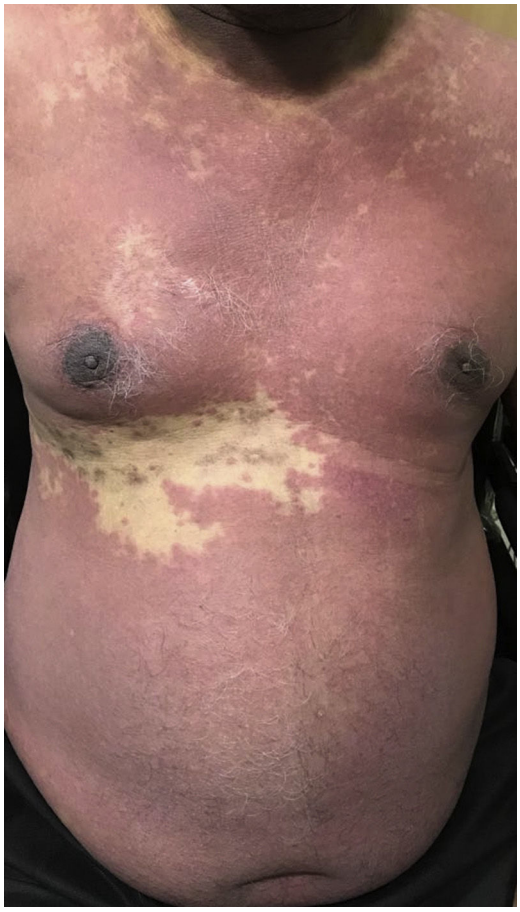

Figure 1 Confluent erythematous maculopapular lesions over the chest and abdomen with sparing of the right T9 dermatome.

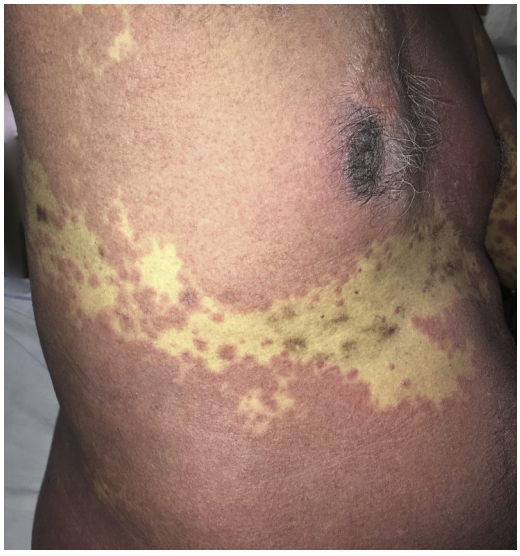

Figure 2 A closer view of the spared site shows hyperpigmentation and scars of healed herpes zoster with sparing of the T9 dermatome by the rash.

☆ Please cite this article as: Adil M, Amin SS, Dinesh Raj R, Tabassum H. Reverse Isotopic Phenomenon in Drug Reaction with Eosinophilia and Systemic Symptoms. Actas Dermosifiliogr. 2019;110:613–615.

Table 1 Details of cases of isotopic non-response reported in literature.

N.° de caso	Estudio	Edad/sexo	Enfermedad secundaria	Sitio de la preservación	Enfermedad primaria
1	Nuestro caso	60 años/varón	Síndrome DRESS	Tronco (dermatoma T9 derecho)	Herpes zóster
2	Tenea D[2] (2010)	39 años/mujer	Síndrome Stevens-Johnson	Lado derecho del tronco	Herpes zóster
3	Kannangara AP et al.[6] (2008)	53 años/mujer	Síndrome sobreposición SJS-TEN	Nervio craneal V1 izquierda	Herpes zóster
4	Kannangara AP et al.[6] (2008)	62 años/varón	Eritrodermia	C3-C4 izquierda	Herpes zóster
5	Park H et al.[7] (2008)	67 años/mujer	Eritema multiforme	Tronco (dermatoma T3)	Herpes zóster
6	Twersky JM et al.[5] (2004)	58 años/varón	Linfoma cutáneo células T	Tronco (dermatoma T8 izquierdo)	Herpes zóster
7	Jain R et al.[8] (2003)	ND	Lepra «borderline»	ND	Herpes zóster
8	Jain R et al.[8] (2003)	ND	Lepra «borderline»	ND	Herpes zóster
9	Okaya-Bayazit E et al.[9] (1999)	72 años/mujer	Granuloma elastolítico anular de células gigantes	Antebrazo izquierdo	Cicatriz quemadura
10	Nasca MR et al.[10] (1995)	53 años/varón	Acné esteroideo	Espalda	Sitio irradiación Rx
11	Huilgol SC et al.[11] (1995)	74 años/varón	Granuloma anular generalizado	Brazo izquierdo	Punto de vacunación

DRESS: drug reaction with eosinophilia and systemic symptoms; ND: no disponible; Rx: rayos X; SJS-TEN: Stevens-Johnson syndrome-toxic epidermal necrolysis.

syndrome. A diagnosis of DRESS syndrome was made based on the RegiSCAR criteria.[3]

DRESS syndrome is a rare idiosyncratic reaction reaction to a drug characterised by skin rash, fever, lymphadenopathy, eosinophilia and multiorgan involvement. It is commonly caused by anticonvulsant medications, allopurinol, minocycline and antiretroviral agents like abacavir. Pathogenesis is unclear but it is believed to occur in patients who metabolise the drugs and its active metabolites slowly. A genetic predisposition exists and Human Herpesviruses has been associated. The cross reaction of antiviral T cells with the culprit drug has been proposed to mediate this syndrome.[4] However, the sparing of the healed herpes zoster site casts doubt regarding this theory.

The possible reason for the sparing of a skin lesion to a secondary insult is unclear. The rash of DRESS may result from alteration of the local immune response by a virus itself or by production of Th1 cytokines like TNF-alpha, IFN-gamma, IL-2 and IL-5.[2] The loss or hypoactivity of Langerhans cells at the site of herpes zoster has been demonstrated and may play a role in this sparing phenomenon.[5] Also, herpesvirus infected keratinocytes have decreased expression of MHC and ICAM-1, hindering their function as antigen presenting cells and inhibiting T cell response, thereby leading to the skin rash of DRESS.[6]

Isotopic non-response needs to be differentiated from isomorphic non-response or Renbök phenomenon. The site of another unrelated skin disease is spared in both of the above phenomenon. This disease is still active in Renbök phenomenon while it is healed in the isotopic non-response.[1]

Very few cases of reverse isotopic phenomenon have been reported in literature. There reports have shown the sparing of the sites of vaccination,[7] herpes zoster[2,5,6,8,9] and burn scar[10] that have occurred in diverse conditions like epidermal necrolysis,[2] erythema multiformae,[8] cutaneous lymphomas,[5] leprosy[9] and annular elastolytic giant cell granuloma.[10] [Table 1] Ours is probably the first case of reverse isotopic phenomenon in DRESS syndrome.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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https://doi.org/10.1016/j.adengl.2018.09.013
1578-2190/

Molluscum Contagiosum on the Palms: An Uncommon Location☆

Molusco contagioso palmar, una localización excepcional

To the Editor:

Molluscum contagiosum (MC) is a very common infectious dermatosis. It is caused by a double-strand DNA virus of the same name, which belongs to the *Poxviridae* family. Estimated prevalence is 7% in children and up to 18% in immunocompromised adults. The virus is transmitted by direct contact, fomites, or autoinoculation, and manifests clinically in the form of cupuliform umbilicated papules that the same color as the skin and generally asymptomatic. The papules infrequently appear on glabrous skin.[1]

A 43-year-old man with no past medical history of interest visited our department with 2 lesions on the right hand; the lesions caused discomfort when pressed or rubbed and had appeared a week earlier. Physical examination revealed 2 erythematous papules on the hypothenar region of the left palm, with diameters of 2 and 4 mm, respectively. Both lesions were slightly infiltrated to the touch and the larger lesion showed central hyperkeratosis and a perilesional erythematous halo (Fig. 1). The rest of the physical examination was normal. One of the lesions was excised and biopsied, and showed lobulation of the epidermis toward the dermis, and keratinocytes with intracytoplasmic inclusion bodies (Fig. 2). The diagnosis of palmar MC was established based on these findings and the other lesion was treated using cryotherapy. Both lesions resolved completely a month after treatment.

In children, infection by the MC virus tends to be located on the face, torso, and extremities. In adults, the most frequent site is in the genital region and surrounding areas.[2] Involvement of the palms and soles is exceptional regardless of age. The first case of plantar MC was published by

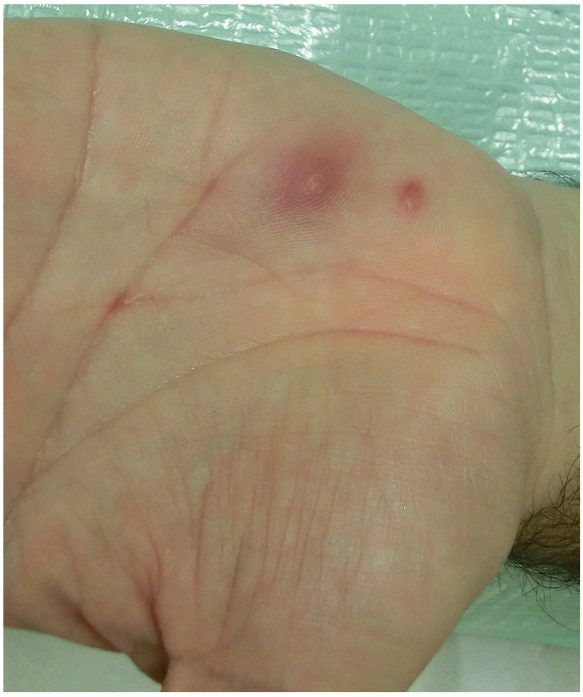

Figure 1 Two erythematous papules with diameters of 2 and 4 mm, respectively. The larger papule shows central hyperkeratosis and a perilesional erythematous halo.

☆ Please cite this article as: García-Montero P, Serrano-Pardo R, Ruiz-Rodríguez R, Sánchez-Carpintero I. Molusco contagioso palmar, una localización excepcional. Actas Dermosifiliogr. 2019;110:615–617.