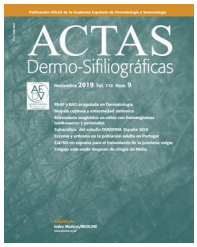
ACTAS Dermo-Sifiliográficas 114 (2023) 366–369

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

ACTAS
Dermo-Sifiliográficas

Full English text available at
www.actasdermo.org



CASE AND RESEARCH LETTER

Erythrodermic Psoriasis Has Become Less Frequent: Results From the Biobadaderm Registry

La psoriasis eritrodérmica es cada vez menos frecuente: resultados del registro Biobadaderm

Dear Editor,

Erythrodermic psoriasis (EP) is a rare and severe form of psoriasis characterized by erythema in 75–90% of the body surface[1,2] with high morbidity and increased mortality and considered a dermatological emergency.

EP's prevalence is less than 3% of all cases of psoriasis.[3] Although, its pathophysiology is largely unknown, it is thought to differ from that of plaque psoriasis (PP). EP may have a certain TH2 activation with Ig E, IL13, IL4 and IL10, while sharing TNF and IL-17A pathways with PP and genetics with pustular psoriasis, having found family mutations of CARD14 gene in EP.[4] Alternatively, EP could represent a worsening of the other types of psoriasis (such as plaque or generalized pustular psoriasis).

EP patients can present systemic symptoms, such as fever, CHILLS, dehydration, arthralgia, asthenia and lymphadenopathy. Environmental triggers often precipitate erythrodermic flares, including steroid withdrawal, systemic infections, drug exposure such as lithium, and emotional stress.[1]

Treatment of EP is challenging and usually based on clinical experience, in part due to its low incidence and need for urgent management. Conventional treatments, such as glucocorticoid, cyclosporine, acitretin, and methotrexate are frequently ineffective and their discontinuation may cause flares. Recommendations for biologic therapy have limited evidence, but it seems to be well-tolerated and with positive results.[5] Due to the need to obtain a rapid clinical response, the best therapies will be those with a faster onset of action, avoiding the more immunosuppressive agents given the high frequency of bacteraemia and sepsis in EP.[4] Biologics as infliximab or IL-17 antagonist could be the first line, followed by IL-23 antagonist, anti-IL12/23 or other anti TNF.[6] Interestingly, Th17 was found to be the second-most predominant T-cell type after Th2 in EP lesions, supporting the use of anti-IL-17 agents when rapid control is needed.[1]

We aimed to evaluate and compare the demographic characteristics, comorbidities and treatment prescription for EP with PP. To achieve this, we extracted data from the Biobadaderm from October 2008 to December 2021. The characteristics of the registry have been previously described.[7]

68 patients with inclusion diagnosis of EP were compared with 3930 patients with plaque psoriasis (PP). EP patients were older, had higher PASI and higher use of CsA when entering the cohort. No differences in comorbidities were observed, even when considering cancer and infection (Table 1).

Our most interesting finding has been a gradual reduction of EP cases included in the registry through the follow up time (Table 2). This may reflect the better disease control achieved recently in psoriatic patients due to advances in treatment. And it supports the idea that EP in some patients is a severe stage of other types of psoriasis, thus a greater control would result in a reduction of EP frequency.

When analysing the first treatment after entry in the cohort we found that the most prescribed treatments in EP compared with PP were Cyclosporine, Etanercept, Ustekinumab, Ixekizumab and Risankizumab (Table 1). When analysing all treatments used during follow up, the most frequently used in EP where Cyclosporine and anti-TNF due to their longer time of availability and that the majority of EP patients analyzed were included in the first eight years of the registry.

The limitation of our study is that in Biobadaderm, patients are classified with the diagnosis at the moment of inclusion, thus patients who developed EP after their inclusion in the registry were not analyzed. Moreover, treatment options changed during follow up period, which explains why the first treatment in several patients is no longer the current option for management of EP, as etanercept.

In conclusion, our study confirms that EP patients have a higher mean age, greater disease severity (higher base PASI and more frequent previous use of cyclosporine), and the decreasing frequency of this type of psoriasis.

https://doi.org/10.1016/j.ad.2022.12.001

Table 1 Demographic characteristics, comorbidities and previous therapies in plaque psoriasis, vs erythrodermic psoriasis and first drug used after entry in the cohort and all drugs used over follow-up.

	Erythrodermic psoriasis $n = 68$	Plaque psoriasis $n = 3930$	*P* value for the difference
Sex, male (n, (%))	47 (69.1%)	2352 (59.8%)	0.1218
Current age (mean (sd))	62.8 (19.1)	53.6 (14.9)	**0.0000**
Age at entry in the cohort (mean (sd))	54.1 (16.9)	46.8 (14.5)	**0.0000**
Disease duration at entry in the cohort, years (mean (sd))	21 (13.9)	17 (13.4)	0.0137
PASI at entry in the cohort (mean (sd))	19.4 (13.7)	11.3 (7.4)	**0.0000**
Toxic habits			
Current or previous smoker (*n*, (%))	36 (63.2%)	1948 (63.1%)	0.9907
Current or previous alcohol drinking (*n*, (%))	33 (63.5%)	2143 (73.8%)	0.0947
	n (%)	*n* (%)	
Comorbidities			
Body mass index			0.5767
Normal (<25)	16 (31.4%)	1006 (32.7%)	
Overweight (25–29.9)	21 (41.2%)	1063 (34.5%)	
Obesity (>30)	14 (27.5%)	1009 (32.8%)	
Ischemic heart disease	2 (3.4%)	107 (3.1%)	0.8908
Heart failure	0 (0%)	35 (1%)	0.4339
Hypertension	22 (36.1%)	859 (24%)	0.0297
Diabetes	14 (23.3%)	447 (12.7%)	0.0144
Hypercholesterolemia	22 (35.5%)	1028 (28.9%)	0.2575
COPD	3 (5%)	115 (3.3%)	0.4717
Chronic haepatic disease	7 (11.1%)	318 (9.1%)	0.5918
Chronic renal failure	3 (5.1%)	50 (1.4%)	0.0227
Previous and current cancer	3 (5.2%)	147 (4.2%)	0.7245
Previous and current lymphoma	1 (1.7%)	11 (0.3%)	0.0765
HBV infection	3 (5.6%)	147 (4.6%)	0.7107
HCV infection	2 (3.6%)	70 (2.2%)	0.5750
HIV infection	1 (2.1%)	29 (1%)	0.7227
Psoriatic arthritis	12(17.6%)	559 (14.2%)	0.4238
	n (%)	*n* (%)	
Previous therapies			
Previous PUVA therapy	16 (23.5%)	711 (18.1%)	0.2491
Previous narrow band UVB therapy	7 (10.3%)	806 (20.5%)	0.0380
Previous therapy with methotrexate	32 (47.1%)	1523 (38.8%)	0.1637
Previous therapy with cyclosporine	39 (57.4%)	934 (23.8%)	**0.0000**
Previous therapy with acitretin	25 (36.8%)	867 (22.1%)	0.0039
	n (%)		*n* (%)
First drug used after entry in the cohort			
Cyclosporine	**14 (20.6%)**		337 (8.6%)
Etanercept	**14 (20.6%)**		390 (9.9%)
Adalimumab	8 (11.8%)		613 (15.6%)
Ustekinumab	**7 (10.3%)**		353 (9%)
Acitretine	7 (10.3%)		411 (10.5%)
Ixekizumab	**2 (2.9%)**		111 (2.8%)
Methotrexate	7 (10.3%)		986 (25.1%)
Secukinumab	1 (1.5%)		176 (4.5%)
Apremilast	1 (1.5%)		190 (4.8%)
Risankizumab	**1 (1.5%)**		40 (1%)
Tildrakizumab	0 (0%)		19 (0.5%)
Certolizumab pegol	0 (0%)		12 (0.3%)
Golimumab	0 (0%)		1 (0%)
Brodalumab	0 (0%)		26 (0.7%)

Table 1 (*Continued*)

	n (%)	*n* (%)
Dimethyl fumarate	0 (0%)	47 (1.2%)
Guselkumab	0 (0%)	64 (1.6%)
All drugs used over follow-up		
Methotrexate	50 (19.3%)	2248 (22.7%)
Cyclosporine	**37 (14.3%)**	706 (7.1%)
Adalimumab	30 (11.6%)	1602 (16.2%)
Etanercept	**29 (11.2%)**	977 (9.9%)
Ustekinumab	27 (10.4%)	1158 (11.7%)
Acitretine	**24 (9.3%)**	855 (8.6%)
Secukinumab	13 (5%)	511 (5.2%)
Infliximab	**13 (5%)**	207 (2.1%)
Ixekizumab	10 (3.9%)	419 (4.2%)
Guselkumab	**8 (3.1%)**	277 (2.8%)
Apremilast	5 (1.9%)	366 (3.7%)
Risankizumab	**5 (1.9%)**	167 (1.7%)
Dimethyl fumarate	2 (0.8%)	101 (1%)
Efalizumab	2 (0.8%)	86 (0.9%)
Golimumab	**2 (0.8%)**	20 (0.2%)
Brodalumab	1 (0.4%)	84 (0.8%)
Certolizumab pegol	1 (0.4%)	50 (0.5%)
Tildrakizumab	0 (0%)	62 (0.6%)

P values have been calculated using *t*-student or chi square. *P* values in bold are significant after Bonferroni correction for multiple testing (30 tests).

Table 2 Percentage of erythrodermic patients at entry in the cohort in consecutive periods.

	2008–2012	2013–2017	2018–2021
Plaque psoriasis	1511 (97.6%)	906(97.5%)	1513(99.5%)
Erythroderma	37 (2.4%)	23 (2.5%)	8 (0.5%)

Changes over time are statistically significant ($P < 0.0001$).

Funding

Biobadaderm received funding from ''Agencia Española del Medicamento'' and Pharmaceutical companies (Abbott/AbbVie, Almirall, Amgen, Janssen, Leo Pharma, Lilly, MSD, Novartis, Pfizer and UCB). Funding industry has not participated in study design, data collection or management, nor manuscript writing or decisions about publication.

Conflict of interest

Dr. Rivera-Diaz acted as a consultant and/or speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including Janssen Pharmaceuticals Inc., Almirall SA, Boehringer, Lilly, AbbVie, Novartis, Leo-Pharma, and UCB.

The rest of authors do not declare any conflict of interest for this article.

Acknowledgements

We would like to thank Drs. Sahuquillo-Torralba, Antonio; Dauden, Esteban; de la Cueva Dobao, Pablo; Baniandrés, Ofelia; Belinchón, Isabel; Ruiz-Genao, Diana; Ferran Farrés, Marta; Flórez Menéndez, Ángeles and other members of the Biobadaderm registry for their collaboration.

References

1. Reynolds KA, Pithadia DJ, Lee EB, Liao W, Wu JJ. A systematic review of treatment strategies for erythrodermic psoriasis. J Dermatol Treat. 2019, http://dx.doi.org/10.1080/09546634.2019.1689228.
2. Yamada M, Kubo H, Kobayashi S, Ishizawa K, He M, Suzuki T, et al. The increase in surface CXCR4 expression on lung extravascular neutrophils and its effects on neutrophils during endotoxin-induced lung injury. Cell Mol Immunol. 2011;8:305–14.
3. Lebwohl M, Psoriasis. Lancet. 2003;361:1197–204.
4. Shao S, Wang G, Maverakis E, Gudjonsson JE. Targeted treatment for erythrodermic psoriasis: rationale and recent advances. Drugs. 2020;80:525–34, http://dx.doi.org/10.1007/s40265-020-01283-2.
5. Carrasquillo OY, Pabon-Cartagena G, Falto-Aizpurua LA, Santiago-Vazquez M, Cancel-Artau KJ, Arias-Berrios G, et al. Treatment of erythrodermic psoriasis with biologics: a systematic review. J Am Acad Dermatol. 2020;83:151–8.
6. Lo Y, Tsai T-F. Updates on the treatment of erythrodermic psoriasis. Psoriasis Targets Therapy. 2021;11:59–73.

7. Rivera R, Garcıa-Doval I, Carretero G, Daudén E, Sánchez-Carazo J, Ferrándiz C, et al. BIOBADADERM, the Spanish registry of adverse events associated with biological drugs in dermatology: first report. Actas Dermosifiliogr. 2011;102:132–41.

R. Rivera-Diaz[a,*], G. Carretero[b], J.M. Carrascosa[c], I. García-Doval[d]

[a] *Dermatology Department, University Hospital 12 de Octubre & Universidad Complutense, Madrid, Spain*
[b] *Dermatology Department, Universitary Hospital Gran Canaria Doctor Negrin, Gran Canaria, Spain*
[c] *Dermatology Department, H. Germans Trias i Pujol, Spain*
[d] *Academia Española de Dermatología y Venereología, Research Unit, Fundación Piel Sana & Complexo Hospitalario Universitario de Vigo, Servicio de Dermatologia, Spain*

[*] Corresponding author.
E-mail address: rriveradiaz@hotmail.com (R. Rivera-Diaz).