Clinical spectrum and supportive treatment of dermatologic adverse events associated with PD-1, PD-L1, CTLA-4 immune checkpoint inhibitors

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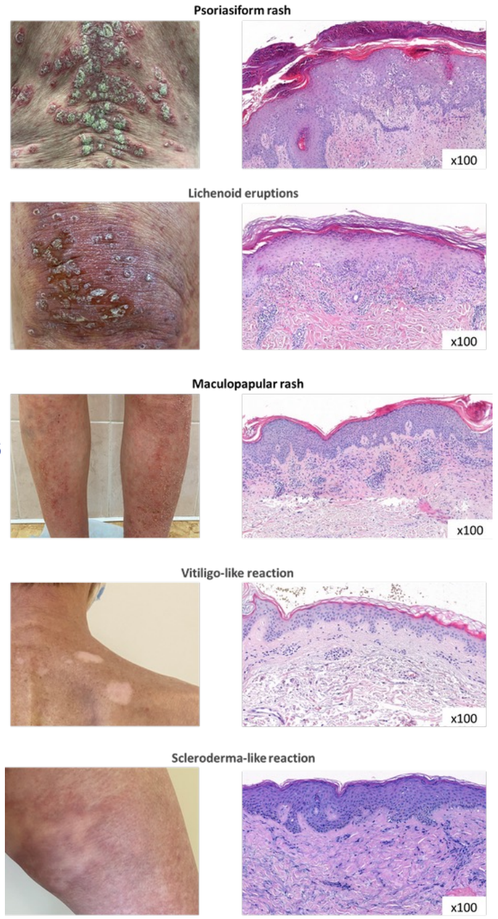
Background

Immune checkpoint inhibitors (ICIs) have shown exceptional efficacy in the treatment of many types of cancer. Reactivation of the immune response can reduce auto-tolerance and lead to the development of immune-related adverse events (irAEs). Dermatologic immune-related adverse events (dirAEs) account for 44% of all the adverse events. Assessing the clinical spectrum of dirAEs and providing effective supportive care remains an important interdisciplinary problem.

Materials and methods

The study included 57 patients with dirAEs associated with ICI therapy. The severity of dirAEs was assessed using Body Surface Area (BSA), CTCAE-NCI v5.0 and the Dermatology Life Quality Index (DLQI). The Psoriasis Area and Severity Index (PASI) score was assessed in patients with psoriasiform rash. Correlation analysis was performed to assess the impact of dirAEs on patients' quality of life.

Figure 1. Clinical and histological features of the immune-related dermatological adverse events



Results

The structure of the dirAEs evaluated is shown in Table 1. Clinical and histological features of the dirAEs are presented in Figure 1. According to the results of the correlation analysis, psoriasiform rash and pruritus had the greatest negative impact on patients' quality of life (Table 2). 12 patients had grade 2-3 psoriasiform rash and received supportive treatment with methotrexate at a dose of 20 mg q.wk for 5 weeks. There were significant improvements in BSA, PASI and DLQI scores at weeks 2, 4 and 6 (Figure 2). By week 6 of the therapy, 88% of patients had complete resolution of the psoriatic rash and 12% had CTCAE-NCI v5.0 grade 1 severity (Figure 3).

Table 1. Clinical structure and severity of dermatological adverse events in patients receiving ICI treatment

dirAEs	Number of patients n (%)	Period of occurrence, weeks	CTCAE, grade	n (%)	BSA, %	DLQI, scores	
Pruritis	37 (77,08%)	3 [2;5]	I	2 (5,4%)	-	I	3,8
			II	21 (56,75%)		II	7,9
			III	14 (37,83%)		III	9,3
Psoriasiform rash	20 (41,66%)	4 [3;6]	I	5 (25%)	28,1	I	5,2
			II	13 (65%)		II	16,3
			III	2 (10%)		III	28,5
Maculopapular rash	9 (18,75%)	3 [2;7]	I	3 (33,33%)	27,8	I	10,6
			II	5 (55,55%)		II	16,6
			III	1 (11,11%)		III	22
Lichenoid eruptions	7 (14,58%)	9 [7;11]	I	2 (28,57%)	19,2	I	7,5
			II	4 (57,14%)		II	9,75
			III	1 (14,28%)		III	18
Vitiligo-like reaction	5 (10,41%)	8 [7;9]	I	3 (60%)	8,3	I	2
			II	2 (40%)		II	1
			III	-		III	-
Bullous pemphigoid	2 (4,16%)	9	I	-	26,4	I	-
			II	-		II	-
			III	2 (100%)		III	30
Scleroderma-like reaction	1 (2,08%)	156	I	-	87	I	-
			II	-		II	-
			III	1 (100%)		III	30

Table 2. Correlation between the DLQI and clinical manifestation of immune-related dermatological adverse events

	Pruritus	Psoriasiform rash	Lichenoid eruptions	Maculopapular rash	Vitiligo-like reastions
DLQI, r	0,885	0,866	0,861	0,854	0,125
p	<0,05	<0,05	<0,05	<0,05	<0,05

Figure 2. Dynamics of indices during methotrexate therapy in patients with psoriasiform rash

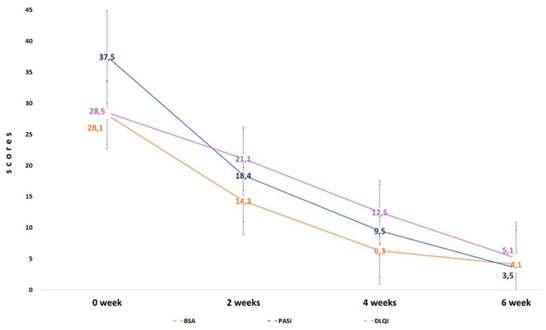
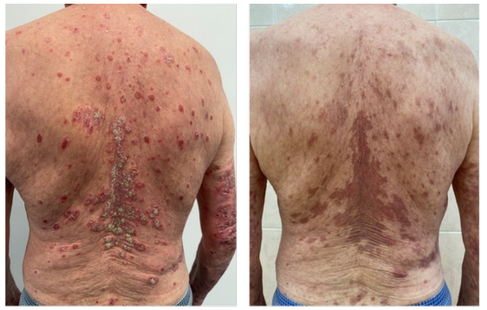


Figure 3. Patient with immune-related psoriasiform rash treated with methotrexate



BSA - 33 PASI - 28,5 DLQI - 27

0 week

BSA - 6 PASI - 1,8 DLQI - 3

6 week

Conclusion

ICI-associated psoriasiform rash and pruritus were the most common dirAEs and had the greatest impact on patients' quality of life. Methotrexate showed significant efficacy in the supportive treatment of psoriasiform dirAE. We are continuing the present study to confirm the results presented here and to evaluate the safety profile of methotrexate in patients with immune-related psoriasiform skin eruption.

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