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Experience of a Single Academic Center Using IL-1 Inhibition for Rare Dermatologic Conditions

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INTRODUCTION

Evidence-based literature regarding management of rare and severe dermatologic disease is limited. Canakinumab and anakinra, two therapeutics used for inhibiting IL-1 pathways, have seen increased utilization for treatment of refractory dermatoses. We sought to better characterize the breadth of dermatologic conditions for which these medications could be utilized. This report is the first to describe a US tertiary care center's experience of IL-1 blockade for dermatologic use in 23 patients with rare dermatologic conditions as well as refractory adult-onset Still's disease, systemic sclerosis, Behçet's disease, and lupus erythematosus. One novel finding in our study is the use of anakinra for treatment of discoid lupus erythematosus in a patient with systemic lupus erythematosus (SLE), supporting IL-1 as a key contributor in the pathogenesis in cutaneous lupus erythematosus.[1]

Evidence-based, therapeutic modalities for rare, severe dermatologic are lacking. Both canakinumab and anakinra are therapeutics used for inhibiting IL-1 pathways and have seen increased utilization for treatment of refractory dermatoses. We sought to better characterize the breath of conditions for which these medications could be utilized in a tertiary care center. All patients with dermatologic consultation that were treated with anakinra or canakinumab at New York University Langone Health (NYULH) from 2007 to 2019 were evaluated. Patients were excluded if medications were not prescribed for cutaneous indications or insufficient documentation existed to assess response. 53 patients were identified and 30 were excluded. Response to therapy was defined as complete (>75%), partial (25%-75%), or no response (<25%) based upon patient-reported clinical symptoms, physician-identified physical findings, laboratory evaluation, and review of clinical photography.

Tables I and 2 summarize 14 patients treated with anakinra and 9 patients treated with canakinumab, respectively. The mean age was 44 years. The mean total duration of therapy on anakinra was 19.5 months and 15 months for canakinumab. Treatment with anakinra resulted in complete response in 9/14 patients (64%), partial response in 4/14 (29%), and no response in 2/14 (7%). For canakinumab, 7/10 (70%) patients demonstrated a complete response/remission of disease, while 2/10 (20%) exhibited a partial response and 1 patient was refractory to treatment. In the treatment of SS, AOSD, HIDS, and Behçet's disease, several patients were transitioned to canakinumab after unsuccessful trials of anakinra, resulting in significant response or resolution. Adverse events from anakinra or canakinumab were infrequent and mild; side effects were not significant enough to withhold therapy.

The mean number of medications prior to initiation of anakinra was 3, while the mean was 2 for canakinumab. The most common medications used concurrently with both anakinra and canakinumab were oral glucocorticoids, methotrexate, and colchicine. Glucocorticoid use changed after implementation of IL-1 blockade. Roughly 48% of patients were able to discontinue glucocorticoids, while 13% required maintenance of >10mg/day, 34% required 5-10mg/day, and 65% required brief courses for flares.

One novel finding in our study is the use of anakinra for treatment of discoid lupus erythematosus in a patient with systemic lupus erythematosus (SLE). IL-1 is key to pathogenesis in cutaneous lupus erythematosus.[1] IL-1RA production of cells in patients with SLE shows diminished spontaneous and stimulated responses, which may ultimately perpetuate disease.[2] Use of anakinra for SLE is supported by experiments demonstrating that IL-1 antiserum added to SLE monocyte cultures decreases spontaneous IgG synthesis and number of immunoglobulin producing cells.[3] It has also shown clinical benefit in treatment of SLE arthropathy.[4]

Literature regarding management of these rare and refractory dermatologic conditions is limited. This report is the first to describe a US tertiary care center's experience of IL-1 blockade for dermatologic conditions, supporting the utility of anakinra and canakinumab for rare dermatologic conditions as well as alternative therapies in those with refractory AOSD, SS, Behçet's disease, and lupus erythematosus.

TABLE 1.

Characteristics and Therapeutic Regimens of Patients Treated with Anakinra

Age	Gender	Diagnosis	Dose of Anakinra (Subcutaneous)	Concurrent Anti-inflammatory Therapy with Anakinra	Previous Therapies	Total Duration (Months)	Level of Response*	Side Effects
48	Male	AOSD	100mg daily	Hydroxychloroquine	Hydroxychloroquine	5	None	Transaminitis
40	Female	AOSD	100mg daily	Colchicine	Colchicine	5	Complete	Transaminitis
54	Female	AOSD	100mg daily	--	Methotrexate	5	Complete	None
62	Female	AOSD	100mg q48hours	Methotrexate	Methotrexate	29	Complete	None
51	Male	AOSD	100mg daily	Methotrexate	Methotrexate	7	Complete	None
37	Female	AOSD	100mg daily	--	Methotrexate	30	Complete	None
50	Male	AOSD†	100mg daily	--	--	6	Partial	Injection site reaction
24	Female	Behçet's Disease	100mg daily (200mg q8hours for flares)	--	Apremilast Azathioprine	2	Partial	None
30	Female	Behçet's Disease†	100mg daily	Methotrexate	Colchicine Methotrexate Hydroxychloroquine Mycophenylate mofetil Etanercept	6	Partial	Neutropenia, Transaminitis
60	Female	Discoid Lupus	100mg daily	--	Isotretinoin Hydroxychloroquine Chloroquine Dapsone Methotrexate Mycophenolate mofetil Azathioprine 6-mercaptopurine Cyclosporine Ustekinumab Apremilast Belimumab Leflunomide Thalidomide Lenalidomide	18	Partial	Transaminitis, lightheaded-ness, acute pancreatitis
28	Female	HIDS†	100mg daily, tapering to PRN	--	--	84	Complete	None
70	Male	SS	100mg daily	--	--	36	Complete	None
31	Female	TRAPS	100mg daily	--	Etanercept Certolizumab	20	Complete	None
32	Female	TRAPS	100mg daily, (300mg daily for flares)	--	Etanercept	20	Complete	None

†individuals trialed on canakinumab following anakinra due to lack of or insufficient response
*Response to therapy was defined as complete (>75%), partial (25%-75%), or none (<25%) based on patient reported clinical symptoms, physician-identified physical examination findings, and laboratory evaluation.

TABLE 2.

Characteristics and Therapeutic Regimens of Patients Treated with Canakinumab

Age	Gender	Diagnosis	Dose of Canakinumab (Subcutaneous)	Concurrent Anti-inflammatory Therapy with Canakinumab	Previous Therapies	Total Duration (Months)	Level of Response*	Side Effects
50	Male	AOSD†	300mg q28 days	--	Anakinra	9	Complete	None
19	Female	Behçet's Disease	300mg q28 days (150mg q1 week for flares)	Colchicine	Colchicine	4	Complete	None
53	Female	Behçet's Disease	300 - 450mg q28 days	Colchicine Azathioprine	Apremilast Colchicine Azathioprine	17	Complete	Transaminitis
30	Female	Behçet's Disease†	150mg q28 days	Colchicine Azathioprine	Colchicine Methotrexate Hydroxychloroquine Azathioprine Mycophenylate mofetil Etanercept Anakinra	20	None	None
24	Female	Behçet's Disease	300mg q28 days	--	Apremilast Azathioprine	5	Partial	None
28	Female	HIDS†	150mg q6 weeks	--	Anakinra	48	Complete	Periorbital swelling
63	Female	SS	150 q28 days	--	--	2	Partial	Exanthematous drug reaction
62	Male	SS	150mg q8 weeks	--	--	27	Complete	None
44	Male	SS	300 - 450mg q28 days	--	Colchicine	7	Complete	Urticarial drug reaction
31	Female	TRAPS	150mg q28 days	--	Colchicine Certolizumab	11	Complete	None

†individuals trialed on canakinumab following anakinra due to lack of or insufficient response
*Response to therapy was defined as complete (>75%), partial (25%-75%), or none (<25%) based on patient reported clinical symptoms, physician-identified physical examination findings, and laboratory evaluation.

DISCLOSURES

The authors have no conflicts of interest to declare.

REFERENCES

1. Robinson ES, Werth VP. The role of cytokines in the pathogenesis of cutaneous lupus erythematosus. *Cytokine.* 2015;73(2):326-334.
2. Hsieh SC, Tsai CY, Sun KH, et al. Defective spontaneous and bacterial lipopolysaccharide-stimulated production of interleukin-1 receptor antagonist by polymorphonuclear neutrophils of patients with active systemic lupus erythematosus. *Br J Rheumatol.* 1995;34(2):107-112.
3. Jandl RC, George JL, Dinarello CA, Schur PH. The effect of interleukin 1 on IgG synthesis in systemic lupus erythematosus. *Clin Immunol Immunopathol.* 1987;45(3):384-394.
4. Ostendorf B, Iking-Konert C, Kurz K, Jung G, Sander O, Schneider M. Preliminary results of safety and efficacy of the interleukin 1 receptor antagonist anakinra in patients with severe lupus arthritis. *Ann Rheum Dis.* 2005;64(4):630-633.

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