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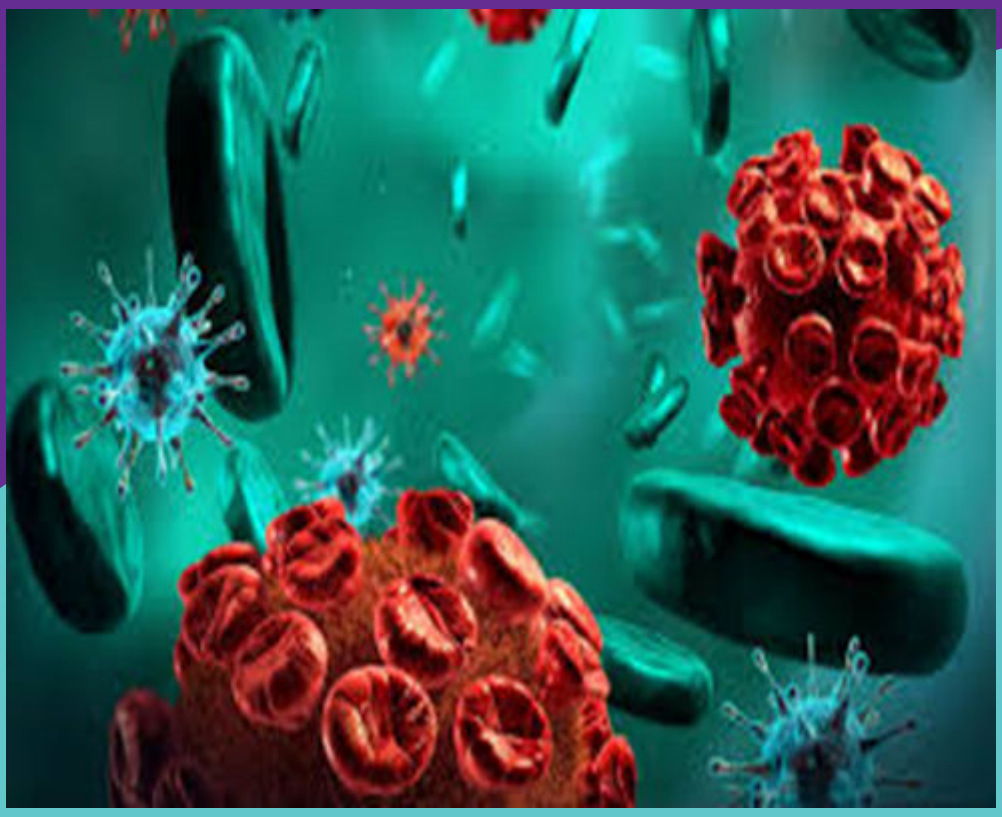

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ERAD, 2022, Volume 1, Issue 3, pages 1-3

Commentary

The effect of anti-rheumatic drugs in reducing the risk of Parkinson's disease in patients with rheumatoid arthritis

Running title: risk of PD and anti-rheumatic drugs

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Abstract

This commentary highlights the major points raised by a recent study investigating the effect of anti-rheumatic drugs used for the treatment of rheumatoid arthritis (RA) in reducing the risk for Parkinson's disease (PD). Several studies in the past have assessed the effect of anti-rheumatic drugs used for the treatment of RA in lowering the risk of incident PD, but the results have been inconsistent. Those studies left unanswered the question as to whether the reported risk reduction is independent of treatment with disease modifying anti-rheumatic drugs (DMARDs) or not. Several of the reported data indicate that DMARDs appear to further reduce this risk. We raise several points that we think must be taken into account in future studies and emphasize the need for continuous research to explore the underlying mechanism, which could be responsible for the presumed reduced risk for PD development in RA patients treated with specific biologics.

(Submitted 19 March 2022; revised 17 April 2022; accepted 24 April 2022)

Keywords- Alzheimer's disease; anti-TNF inhibitors; autoimmunity; biologics; disease modifying drugs; prevention; rheumatoid arthritis; risk

I. INTRODUCTION

A wealth of data explored in the recent past the effect of anti-rheumatic drugs used for the treatment of rheumatoid arthritis (RA) in reducing the risk of Parkinson's disease (PD) and Alzheimer's disease (AD)(1-4). Other studies have yielded conflicting results and RA *per se* (irrespectively of its treatment) has been associated with either lower of higher risk for those diseases (5). Nevertheless, a recent study has found that patients with rheumatoid arthritis have a lower risk of PD (6). To reach this conclusion the investigators of this nationwide case-control study analyzed data from the Finnish Parkinson's Disease (FINPARK) cohort, which includes 22,189 Finnish patients with clinically overt PD diagnosed in a 20-year period (1996 to 2015)(6). More precisely, the investigators analyzed cases with PD diagnosed during 1999 to 2015 and rheumatoid arthritis diagnosed >3 years before the diagnosis of PD. Each case was matched with up to 7 controls by age, sex, duration of rheumatoid arthritis, and geographical region. Overall, 315 cases with PD and 1,571 matched controls were included in the final analysis. As it was expected, the majority of the patients were female

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(>60%) (6); RA is more common in women than in men. The major finding of this large, well-executed study was that the use of DMARDs is not significantly associated with risk of PD, the only exception being chloroquine/hydroxychloroquine. Hence, no effect on the risk of other DMARDs, such as methotrexate, sulfasalazine, immunosuppressants and gold preparations, were noted. It must be noted though that a 3-year lag period exercised between exposure and outcomes (6). Chloroquine/hydroxychloroquine was indeed associated with decreased risk (adjusted odds ratio [OR] 0.74, 95% confidence interval [CI] 0.56-0.97) i.e a 26% lower risk of PD. The Authors' conclusion was that "this study provides Class II evidence that in individuals with rheumatoid arthritis using DMARDs, only chloroquine/hydroxychloroquine was associated with a potentially decreased risk of developing PD" and that the lower risk of PD in RA patients treated with chloroquine/hydroxychloroquine must be assessed further in terms of the potential underlying mechanisms (6).

This study had several limitations. For example, during the study period the number of patients on biological DMARDs (bDMARDs) was small and therefore it is not clear whether the sensitivity analysis of the effect of bDMARDs failed to find any association due to the small number of users. We must point here that the investigators included an endless list of anti-rheumatic drugs categorized separately ranging from sulfasalazine, chloroquine or hydroxychloroquine, gold preparations, including auranofin and sodium aurothiomalate, leflunomide and immunosuppressants. In the latter list several drug regimens were included consisting of azathioprine, certolizumab pegol, ciclosporin, mycophenolic acid, as well as biological DMARDs (bDMARDs)(6). In the list of bDMARDs the following biologics were included: abatacept, adalimumab, anakinra, etanercept, golimumab. As the authors pointed out, methotrexate was studied separately because of its common use but it is not clear whether RA patients treated with combination of methotrexate and bDMARDs were sub-analyzed. The same also applies for corticosteroids covering prednisolone, prednisone, and methylprednisolone. What is surprising us that the investigators did not assess dose-response or duration of treatment analyses. They argue that that was due to limitations caused by the sample size (6).

Another limitation of the study was the inability to analyze data related to smoking use. This would be of particular interest as smoking is a known modulator of an increased risk of RA in animal and clinical studies, while is associated with a reduced risk of PD. The authors speculated that if there was an effect this would be evident in the analysis of smoking-associated comorbid conditions, including cancer but this was not the case.

Genome wide association studies have suggested common immunogenetic pathways are shared by RA and PD (7). Also, several recent studies assumed that immune-mediated inflammatory processes noted in RA are also involved in the development of PD (8). That implies the potential of immunoregulatory drugs (used in the treatment of RA) in reducing the risk for future development of PD in successfully treated RA patients (9). However, if that was true and the dysregulation of the immunomodulatory inflammation had a significant impact in the development of PD, it would be expected that those anti-rheumatic drugs with the strongest anti-inflammatory potential would had the most significant effect in the reduced risk of PD, and that was not noted.

In our opinion these findings may not be merely explained by chance and may indeed bear a pathophysiological meaning given that data in animal studies have found that some of those immunomodulatory drugs have also an anti-PD potential effect. The reduced risk associated with chloroquine/hydroxychloroquine must be explored further. Hydroxychloroquine appears to be able to improve motor functions in an experimental model of PD (10). Also, chloroquine, in general, protects dopaminergic neurons against neurotoxins (11). Those experimental data must be treated with caution, as clinical data are not supporting an effect of hydroxychloroquine in reversing the progression of dementia in patients with AD(12). The authors have also speculated that the association between chloroquine/hydroxychloroquine and reduced risk of PD could be explained by a survival bias since both chloroquine and hydroxychloroquine are old drugs, and RA patients treated with those drugs have are arguably less severe disease and better overall health status than those treated with other DMARDs (6).

II. CONCLUSION

There is an increasing body of evidence indicating a reduced risk for PD in patients with RA but is not clear whether the effect of the reported risk reduction is independent of treatment with disease modifying anti-

rheumatic drugs (DMARDs) or not. Several of the reported data indicate that DMARDs appear to further reduce this risk. In a recent study such an effect appears to be exerted by chloroquine/hydroxychloroquine, a finding, which requires further investigation, in view of the reported anti-PD effect of those regimens.

AUTHORS CONTRIBUTION

ED and DPB scripted the draft. The Authors approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

References

1. Bacelis J, Compagno M, George S, Pospisilik JA, Brundin P, Naluai AT, et al. Decreased Risk of Parkinson's Disease After Rheumatoid Arthritis Diagnosis: A Nested Case-Control Study with Matched Cases and Controls. J Parkinsons Dis. 2021;11(2):821-32.
2. Li C, Ou R, Shang H. Rheumatoid arthritis decreases risk for Parkinson's disease: a Mendelian randomization study. NPJ Parkinsons Dis. 2021;7(1):17.
3. Rugbjerg K, Friis S, Ritz B, Schernhammer ES, Korbo L, Olsen JH. Autoimmune disease and risk for Parkinson disease: a population-based case-control study. Neurology. 2009;73(18):1462-8.
4. Sung YF, Liu FC, Lin CC, Lee JT, Yang FC, Chou YC, et al. Reduced Risk of Parkinson Disease in Patients With Rheumatoid Arthritis: A Nationwide Population-Based Study. Mayo Clin Proc. 2016;91(10):1346-53.
5. Chang CC, Lin TM, Chang YS, Chen WS, Sheu JJ, Chen YH, et al. Autoimmune rheumatic diseases and the risk of Parkinson disease: a nationwide population-based cohort study in Taiwan. Ann Med. 2018;50(1):83-90.
6. Paakinaho A, Koponen M, Tiihonen M, Kauppi M, Hartikainen S, Tolppanen AM. Disease-Modifying Antirheumatic Drugs and Risk of Parkinson Disease: Nested Case-Control Study of People With Rheumatoid Arthritis. Neurology. 2022;98(12):e1273-e81.
7. Witoelar A, Jansen IE, Wang Y, Desikan RS, Gibbs JR, Blauwendraat C, et al. Genome-wide Pleiotropy Between Parkinson Disease and Autoimmune Diseases. JAMA Neurol. 2017;74(7):780-92.
8. Storelli E, Cassina N, Rasini E, Marino F, Cosentino M. Do Th17 Lymphocytes and IL-17 Contribute to Parkinson's Disease? A Systematic Review of Available Evidence. Front Neurol. 2019;10:13.
9. Tan EK, Chao YX, West A, Chan LL, Poewe W, Jankovic J. Parkinson disease and the immune system - associations, mechanisms and therapeutics. Nat Rev Neurol. 2020;16(6):303-18.
10. Hedya SA, Safar MM, Bahgat AK. Hydroxychloroquine antiparkinsonian potential: Nurr1 modulation versus autophagy inhibition. Behav Brain Res. 2019;365:82-8.
11. Kim CH, Han BS, Moon J, Kim DJ, Shin J, Rajan S, et al. Nuclear receptor Nurr1 agonists enhance its dual functions and improve behavioral deficits in an animal model of Parkinson's disease. Proc Natl Acad Sci U S A. 2015;112(28):8756-61.
12. Van Gool WA, Weinstein HC, Scheltens P, Walstra GJ. Effect of hydroxychloroquine on progression of dementia in early Alzheimer's disease: an 18-month randomised, double-blind, placebo-controlled study. Lancet. 2001;358(9280):455-60.

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Clinical Image

Discoid Lupus Erythematosus like eruption after mRNA SARS-CoV-2 Vaccination

Running title: Skin eruptions and vaccination

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Keywords- Adverse reactions; discoid lupus erythematosus; vaccine; skin eruptions; mRNA SARS-CoV2 vaccination

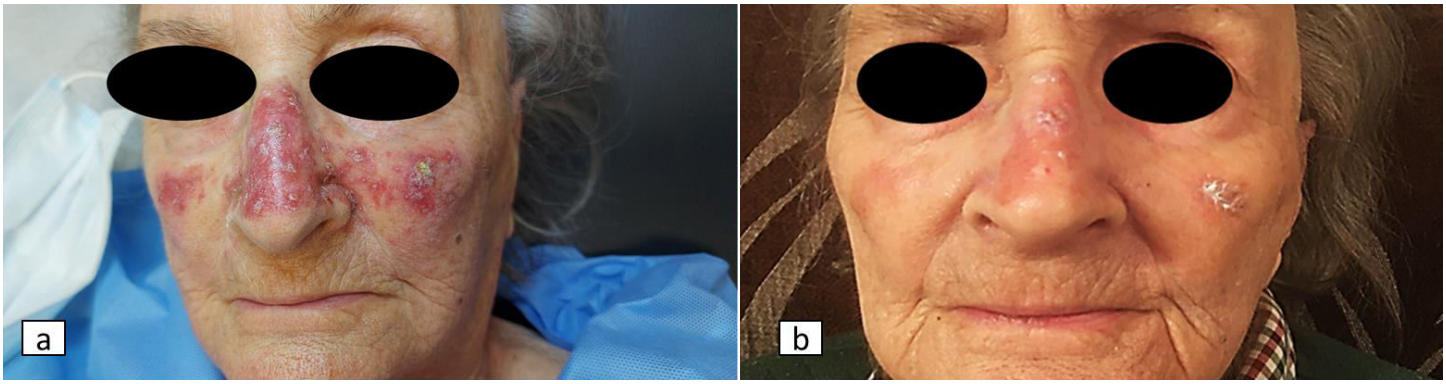

Fig. 1 A 78-year-old woman presents to the clinic with a scaly erythematous butterfly rash with patches and plaques on her nose and cheeks appearing 10 days after the second dose of BNT162b2 vaccination (Fig. 1a). The patient had no medical history of any autoimmune disease in the past. Histological examination showed dense chronic and acute inflammatory accumulations. A complete immunoassay was performed that was negative for autoimmune diseases. The lesions improved significantly in 10 days (Fig. 1b) and subsided completely 15 days after the topical application of methylprednisolone aceponate 0,1% cream twice per day. Previous reports have supported the emergence of lupus erythematosus skin lesion following mRNA SARS-CoV-2 vaccination (1-4).

AUTHORS CONTRIBUTION

The author prepared the manuscript and the artwork. The author approves the final version of the manuscript.

CONFLICT OF INTEREST

The Author declares no conflict of interest

References

1. Baez-Negron L., Vila. Luis M. New-Onset Systemic Lupus Erythematosus after mRNA SARS-CoV-2 Vaccination. Case Reports in Rheumatology. 2022, Article ID 6436839, 4 pages, https://doi.org/10.1155/2022/6436839
2. Nune A., Iyengar K.P., Ish P., Varupula B, Musat C.A., Sapkota H.R. The Emergence of new-onset SLE following SARS-CoV-2 vaccination. QJM: An International Journal of Medicine; 2021.p.739–740
3. Aron-Maor A., Shoenfeld Y.Vaccination and systemic lupus erythematosus: the bidirectional dilemmas. Lupus. 2001; 10: 237-240.
4. Moyon Q, Sterlin D, Miyara M,et al. BNT162b2 vaccine-induced humoral and cellular responses against SARS-CoV-2 variants in systemic lupus erythematosus. Ann Rheum Dis.2022;81:575–583.

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Clinical Image

Primary sternal osteomyelitis: a rare clinical entity

Running title: primary sternal osteomyelitis

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Keywords- Costochondritis; culture; fever; microbes; MRI; osteomyelitis; sternum; treatment

A 40-year-old lady presented in the Department of Rheumatology and Clinical Immunology of our Hospital with low grade fever over a two months period and tenderness over the sternum, initially thought to be costochondritis by a general practitioner.
Contrast enhanced sagittal T2-weighted magnetic resonance imaging (MRI) of chest showed high signal intensity of bone marrow at the angle of Louis (sternal angle) the upper part of the body of the sternum and the lower half of the manubrium. Inflammatory tissue with enhancement was also seen at anterior – presternal region.
While bacteriological culture results were pending, antibiotic therapy with *Staphylococcus aureus* coverage were initiated empirically for treating primary sternal osteomyelitis. The aetiologic agent was *Staphylococcus hominis* and no apparent risk factor was detected. Primary sternal osteomyelitis is a rare clinical entity.

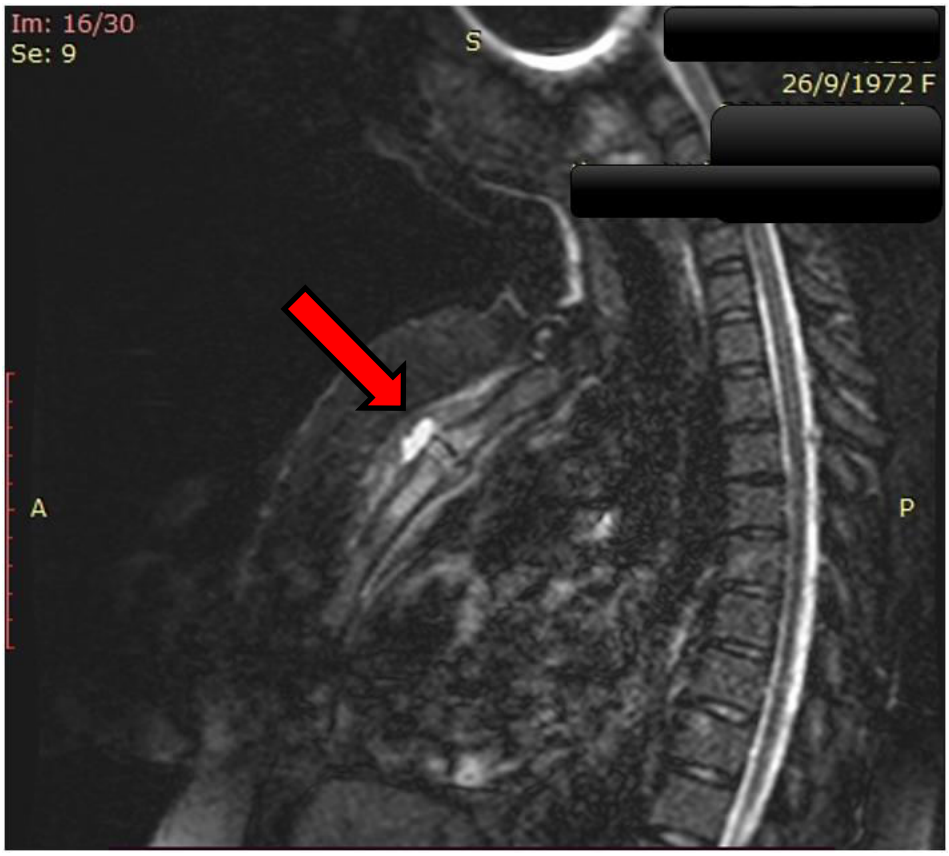

Fig. 1 Contrast enhanced sagittal T2-weighted magnetic resonance imaging (MRI) of chest showed high signal intensity of bone marrow at the angle of Louis (sternal angle) the upper part of the body of the sternum and the lower half of the manubrium (red arrow).

AUTHOR CONTRIBUTION

The author prepared the manuscript and the artwork. The author approves the final version of the manuscript.

CONFLICT OF INTEREST

The Author declares no conflict of interest

ERAD 2022, Volume 1, Issue 3, pages 7-8

Commentary

Neutrophil-mediated acute inflammatory response exerts a protective effect on chronic pain

Running title: Neutrophils, inflammation, and pain

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Abstract

Chronic pain constitutes a major problem for patients and physicians alike. Deciphering the mechanisms driving the evolution of acute pain into chronic may provide ways for preventing this entity. A recent study showed that neutrophil-driven inflammation in patients with acute pain was associated with pain resolution, while administration of non-steroid anti-inflammatory drugs (NSAIDs) in a mouse model led to prolonged pain in the longrun, as corroborated by a database analysis that showed an increased risk of chronic pain in patients having taken NSAIDs. The realization that neutrophil-driven inflammation may provide benefits has been shown in other medical settings as well; as such, abundantly administering anti-inflammatory compounds warrants more careful consideration and more studies like this are more than encouraged.

(Submitted 31May 2022; accepted 03 June 2022)

Keywords- chronic pain; neutrophils; inflammation; non-steroid anti-inflammatory drugs.

INTRODUCTION

Chronic pain (CP) is a particularly disturbing symptom that leads patients to repeatedly seek medical attention and from several different specialties, often to no avail. Deciphering the pathways that mediate a transition from acute pain to CP remains more relevant than ever, since it could potentially provide methods of preventing it. The treatment of acute pain consists of several strategies with various degrees of supportive scientific literature, with the medicinal mainstay remaining non-steroidal anti-inflammatory drugs (NSAIDs) (1).

Transcriptomics consists a relatively new field of research, which goes beyond the basic genetic markup of a cell and focuses on its function, by assessing the entirety of RNA transcribed by a cell or tissue (2). In a very interesting newly published study in *Science Translational Medicine* (3), Parisien et al. (2022) performed a transcriptome-wide analysis on samples from patients with acute pain, and followed them for 3 months. Considerable changes in transcription profiles were reported for patients whose pain resolved, but not for those who developed CP. In the relieved patients, a decrease in neutrophils and an upregulation of CD8+ T-cells was shown over time, while the most significant change in gene expression was again found in neutrophil-specific genes, reflecting an increase of inflammatory pathways and neutrophil degranulation in the acute phase. In a mouse model, NSAID administration during the acute phase led to prolonged

pain, as opposed to administration of other analgesics with no anti-inflammatory properties, while depletion of neutrophils led to prolonged pain as well. On the contrary, injection of neutrophils or neutrophil-expressed proteins prevented CP. Taking these findings one step further, the researchers analyzed data from a large database and found that patients taking NSAIDs had a 1.76-fold risk of developing CPs than those not taking NSAIDs.

CONCLUSION

This study comes to add itself to a growing body of evidence that claims that inflammation is not an ubiquitous villain; this multifaceted cascade of reactions seems to serve several good purposes, especially during the acute phase (4), and inhibiting it might indeed prove detrimental in the long run. As shown here, granulocytes seem to be of particular importance in this sense; for instance, though anti-inflammatory drugs used in multiple sclerosis seem to carry some promise in targeting neuroinflammation in ischemic stroke, inhibiting polymorphonuclear cells led to worse outcomes (5). Studies like this are more than important, since proper pain treatment is very relevant in everyday practice and avoiding drugs that may be associated with CP can eventually prevent it, and its effects on overall health and quality of life.

AUTHORS CONTRIBUTION

AMA conceptualized and wrote the manuscript.

DA performed the relevant literature search and reviewed the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Webster LR, Markman J. Medical management of chronic low back pain: efficacy and outcomes. Neuromodulation. 2014;17 Suppl 2:18-23.
2. Chambers DC, Carew AM, Lukowski SW, Powell JE. Transcriptomics and single-cell RNA-sequencing. Respirology. 2019;24(1):29-36.
3. Parisien M, Lima LV, Dagostino C, El-Hachem N, Drury GL, Grant AV, et al. Acute inflammatory response via neutrophil activation protects against the development of chronic pain. Sci Transl Med. 2022;14(644):eabj9954.
4. Sherwood ER, Toliver-Kinsky T. Mechanisms of the inflammatory response. Best Pract Res Clin Anaesthesiol. 2004;18(3):385-405.
5. Aloizou AM, Siokas V, Pateraki G, Liampas I, Bakirtzis C, Tsouris Z, et al. Thinking outside the Ischemia Box: Advancements in the Use of Multiple Sclerosis Drugs in Ischemic Stroke. J Clin Med. 2021;10(4).

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Educational Note

Antigen-specific autoreactive T cell responses targeting the central nervous system

Running title: Autoreactive T cells and central nervous system

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Keywords- Autoimmuniity; Adverse reactions; autoimmunity; autoimmune rheumatic diseases; cyclosporine; gum hypertrophy; treatment

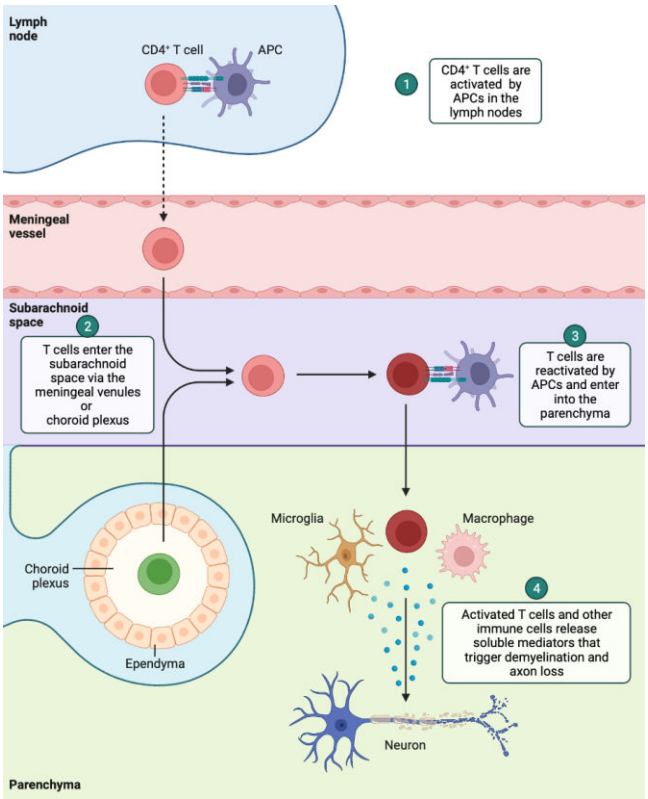

Fig. 1 Activation of antigen-specific autoreactive CD4+ T lymphocytes showing the possible paths of activated T cell entry Based on a consise review by (1). $CD4^+$ T cells are most likely primed in the periphery by professional antigen presenting cells (APC) i.e. dendritic cells (DCs), which present autoantigenic epitopes such as myelin or other disease-related epitopes (2). In turn, APCs residing in the central nervous system (CNS) can seize these autoantigens *in situ* and migrate them to the lymph nodes. Antigen-specific autoreactive $CD4^+$ T cells cross the blood–cerebrospinal fluid (CSF) barrier and enter the subarachnoid space.
Those T cells are re-activated within the subarachnoid space by HLA class II-expressing macrophages and DCs expressing various autoepitopes enter the subarachnoid space in the choroid plexus. Reactivated T cells and their immune counterparts release soluble mediators and trigger a series of events damaging the myelin sheath, ultimately leading to demyelination (1-5) (prepared using a template by BioRender under a license to DPB).

References

1. Goverman J. Autoimmune T cell responses in the central nervous system. Nat Rev Immunol. 2009;9(6):393-407.
2. Baron JL, Madri JA, Ruddle NH, Hashim G, Janeway CA, Jr. Surface expression of alpha 4 integrin by CD4 T cells is required for their entry into brain parenchyma. J Exp Med. 1993;177(1):57-68.
3. Florou DT, Mavropoulos A, Dardiotis E, Tsimourtou V, Siokas V, Aloizou AM, et al. Tetracyclines Diminish In Vitro IFN-gamma and IL-17-Producing Adaptive and Innate Immune Cells in Multiple Sclerosis. Front Immunol. 2021;12:739186.
4. Kivisakk P, Imitola J, Rasmussen S, Elyaman W, Zhu B, Ransohoff RM, et al. Localizing central nervous system immune surveillance: meningeal antigen-presenting cells activate T cells during experimental autoimmune encephalomyelitis. Ann Neurol. 2009;65(4):457-69.
5. Vasileiadis GK, Dardiotis E, Mavropoulos A, Tsouris Z, Tsimourtou V, Bogdanos DP, et al. Regulatory B and T lymphocytes in multiple sclerosis: friends or foes? Auto Immun Highlights. 2018;9(1):9.

AUTHORS CONTRIBUTION
The authors prepared the manuscript and the artwork. The authors approvesdthe final version of the manuscript.

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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Clinical Image

Systemic lupus erythematosus with only oral manifestations

Running title: Persistent buccal bilateral mucositis with discoid lesions

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Keywords- Autoimmune disease; autoimmunity; oral manifestations; rheumatic disease; tongue;

(submitted 30 June 2022; revised 02 July 2022; accepted 03 July 2022)

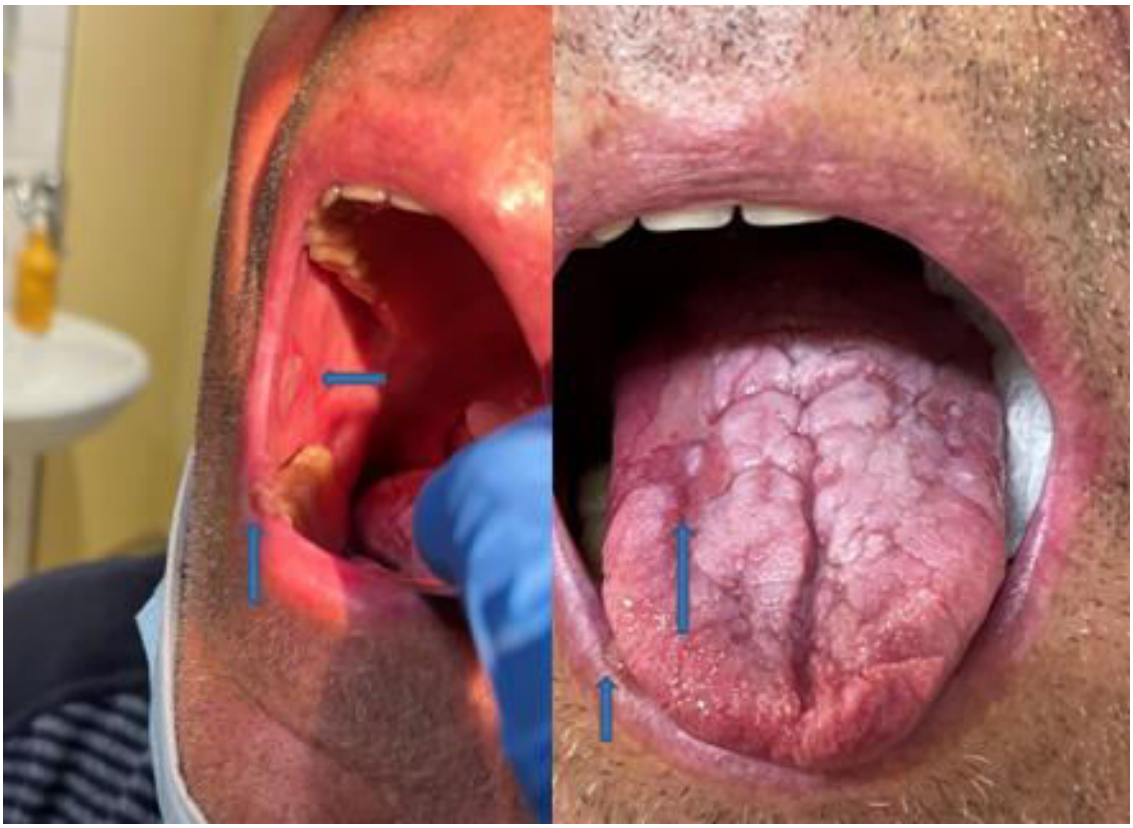

Image. Careful examination of the oral cavity discovered findings indicative primarily of a systemic disease. Our patient's, oral mucosa and tongue (blue arrows) had features of discoid lesions, characterized by a well-demarcated zone of erythema, silvery white, scarred plaques atrophy, ulceration accompanied by radiating striae. These lesions resemble those found in patients with erosive lichen planus. Also a discoid lesion was noted on the inferior lip vermilion and in the periodontal gingival mucosa and bilaterally on the buccal. Although many organs can be affected in patients with of systemic lupus erythematosus (SLE), cutaneous lesions are seen in the great majority. In our case, early oral manifestation was not accompanied with skin or other visceral manifestations. Serologic identification of anti-double stranded DNA (ds-DNA) and anti-Sm antibodies, the serological autoantibody markers of SLE, have assissted in the firm diagnosis of the autoimmune rheumatic disease.

AUTHORS CONTRIBUTION
The author prepared the manuscript and the artwork. The author approves the final version of the manuscript.

CONFLICT OF INTEREST
The Author declares no conflict of interest

ERAD, 2022, Volume 1, Issue 3, page 13-14

Clinical Image

Late diagnosis of extensive herpes zoster infection in a patient with granulomatois with polyangiitis

Running title: herpes zoster in an immunosuppressed GPA patient

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Keywords- ANCA; immunosuppression; infection; vasculitis; virus; Wegener's granulomatosis

(submitted 18 August 2022; accepted 22 August 2022)

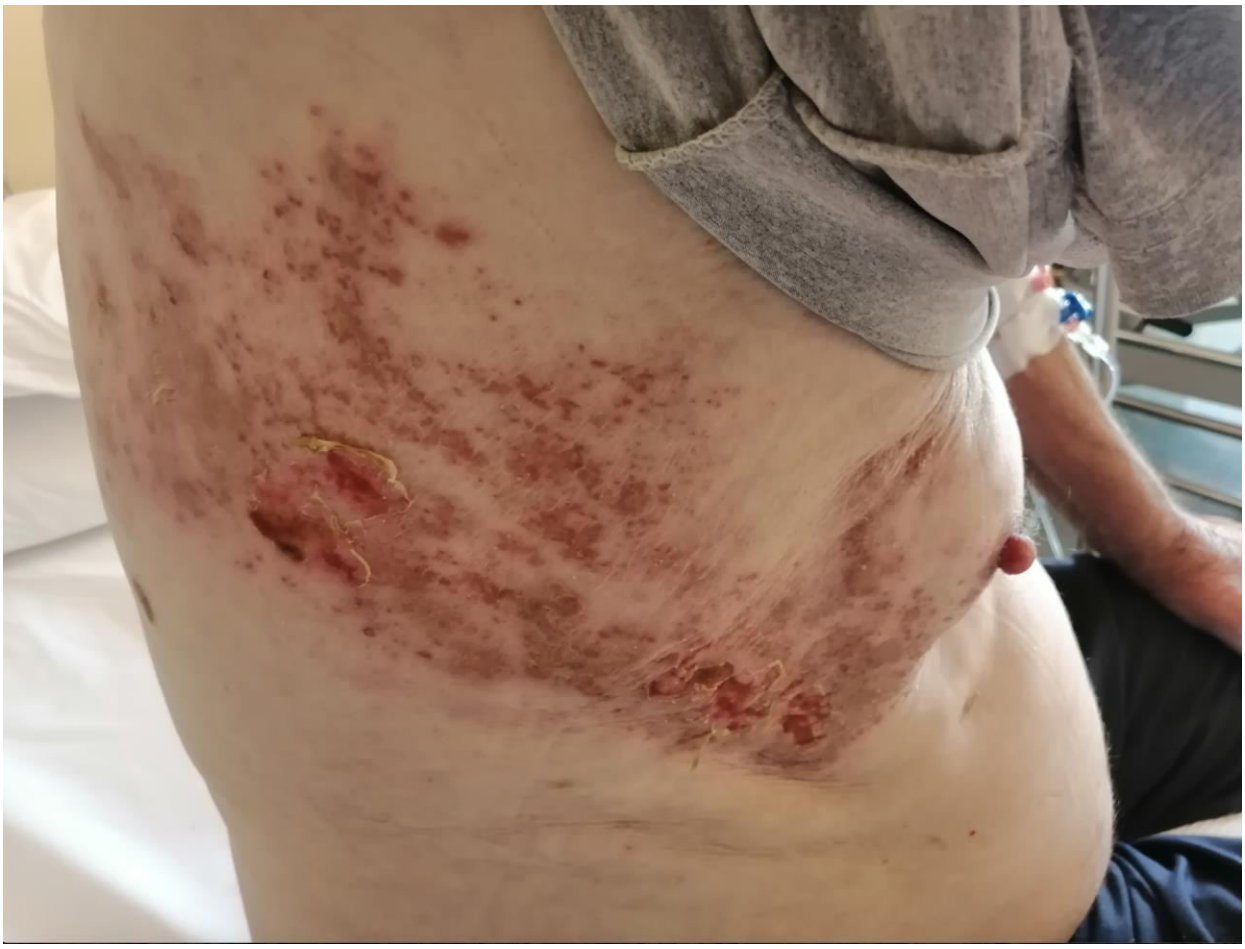

Image. Herpes zoster in a drug-induced immunosuppressed patient with c-ANCA positive vasculitis. This is the case of a 79-year-old man with a two-year history of granulomatosis with polyangiitis (formerly known as Wegener's disease) with both renal and lung involvement. At diagnosis, the patient presented with low grade fever, arthralgias, lung nodules and necrotizing glomerulonephritis. Laboratory tests revealed increased inflammation markers and the presence of c-ANCA and anti-PR3 antibodies at high titre. The patient

received methylprednisolone and cyclophosphamide pulses with sufficient response. Prior to his current admission, he was successfully treated with azathioprine. Last week, he presented to our department with significant erythematous rash with crusted vesicles extending
to a great area along the right T4 dermotome. The clinical image was firstly attributed to neglected herpes zoster infection in an immunosuppressed patient. Although the rash was typical of herpes zoster virus, the patient mentioned no excruciating pain or neuralgia. Analgesics, which he received for joint pain and arthralgia for the last 2 weeks, probably obscured pain and early diagnosis. Herpes zoster is usually self-limited. However, risk of serious infection increases with age, and with any condition or treatment causing severe immunosuppression. Our patient was treated with iv acyclovir (10 mg/kg) for ten days. With the initiation of treatment, the rash was significantly reduced and gradually receded without any complications.

AUTHORS CONTRIBUTION

The authors prepared the manuscript and the artwork. All authors approved the final version of the manuscript.

CONFLICT OF INTEREST

The Authors declare no conflict of interest