



Case Report

Psoriatic arthritis and Hashimoto's thyroiditis in a patient presenting with major depression and subclinical hyperthyroidism: A case report

Lita Diah Rahmawati^{1*}, Bagus Aulia Mahdi²

1) Division of Rheumatology, Department of Internal Medicine, Medical Faculty of Airlangga University

2) Department of Internal Medicine, Medical Faculty of Airlangga University

ARTICLE INFO

Submitted : 17th February 2023

Accepted : 01st August 2023

Published : 25th January 2024

Keywords:

Arthritis, psoriasis, Cushing, thyroiditis, Secukinumab

***Correspondence:**

rahmawati.litadiah@gmail.com

This is an Open acces article under the CC-BY license



ABSTRACT

Psoriatic arthritis (PsA) is a chronic, deforming arthritis associated with psoriatic skin lesions. Numerous patients with PsA carry other co-existing chronic diseases, adding to their overall disease burden and affecting the patient's quality of life. Depression is a common illness known to coexist in about 20% of patients with PsA. Long-term inflammation conditions can make patients more depressed and make the treatment more difficult. Cushing Syndrome (CS) is a complication of long-term treatment due to the exposure of glucocorticoids given to turn the hypothyroid condition into hyperthyroid because hypercortisolism in humans lowers TSH secretion and TSH pulse amplitude. When PsA combines with depression and CS, it will create complex conditions and treatments. The complexity is all about how we control the disease activity of PsA and the vicious circle of an inflammatory process that is difficult to control. Conventional treatment will fail, and targeted therapy with monoclonal antibodies such as anti-IL-17 Secukinumab, is needed. Secukinumab as an anti-IL-17 will block the inflammation pathway from interleukin-17, decrease the inflammation process, and improve the symptoms of PsA. We report a patient with psoriatic arthritis and Hashimoto's thyroiditis (HT) with a major depressive episode with CS and subclinical hyperthyroidism successfully treated with Secukinumab.



QANUN MEDIKA

JURNAL KEDOKTERAN FKUM SURABAYA

<http://journal.um-surabaya.ac.id/index.php/qanunmedika>



INTRODUCTION

Psoriatic arthritis (PsA) is a chronic, deforming arthritis associated with the psoriatic skin lesion. A co-occurring chronic illness impacts the quality of life and contributes to the overall disease burden for many PsA patients. About 20% of PsA patients are also known to have depression, which is a prevalent condition. In psoriatic arthritis, inflammation frequently results in depressive problems. Recent studies in the field have shown that several aspects of depression, such as the inability to experience joy, the loss of intellectual abilities, and the inability to recognize and express emotions, may contribute to the condition as a whole (Armstrong & Read, 2020; Coates et al., 2016; Mathew & Chandran, 2020).

Psoriasis is a chronic, inflammatory and T-cell mediated autoimmune disease of the skin with worldwide prevalence reaching 2-3%. During the active phase of Cushing's syndrome (CS), skin lesions may improve as a result of the immunosuppressive effects of hypercortisolemia and may worsen following treatment. Researchers stated that an individual with one autoimmune condition, such as psoriasis or psoriatic arthritis, may have a higher likelihood of developing another autoimmune condition, such as Hashimoto's thyroiditis (HT) and depression (Haddad et al., 2017; Santos et al., 2021).

Metabolic consequences in CS frequently appear. Hypercortisolism may affect the axis of the other endocrine system. Inappropriate cortisol secretion can damage the hypothalamus-pituitary-thyroid axis, which determines the clinical and biochemical characteristics of "hypothyroidism." In susceptible patients, the "immunological tolerance" provided by the hypercortisolism during active CS can conceal the onset of autoimmune thyroid disorders, which become

more common once the hypercortisolism resolves. However, this phenomenon is likely caused by a variety of factors, including deiodinase-impaired function, in addition to the immunological process. CS may also indirectly affect thyroid function given that some drugs used to treat hypercortisolism are associated with modifications in the thyroid function test. The importance of monitoring thyroid function in CS patients both during the illness' active phase and after it has gone into remission is demonstrated by these considerations (Barbot et al., 2020; Nieman, 2015; Paragliola et al., 2021).

When PsA combines with depression and CS, it will be difficult to treat. Advanced treatments are needed with targeted therapies when conventional therapies are failed (Coates et al., 2022). The authors report a patient with psoriatic arthritis and HT with a major depressive episode, CS, and subclinical hyperthyroidism achieving improvements after Secukinumab.

CASE REPORT

A woman, 44, experienced excessive sadness and sleeping issues in the last five days before the admission. The patient found trouble falling and staying asleep as she only slept for 1-2 hours almost every day. She also felt unenergetic and unenthusiastic doing daily activities. She also withdrew herself from the society and didn't feel like doing anything. She felt useless and extremely pessimistic and also lost her focus and appetite. Moreover, she perceived several whispers telling her to cause trouble whenever she got emotional, though she did not communicate and follow the command of that certain whisper. The patient denied extreme mood fluctuations, excitement, or ghost sightings. All of these events began when her husband was slandered for causing a fire in the warehouse near their house.

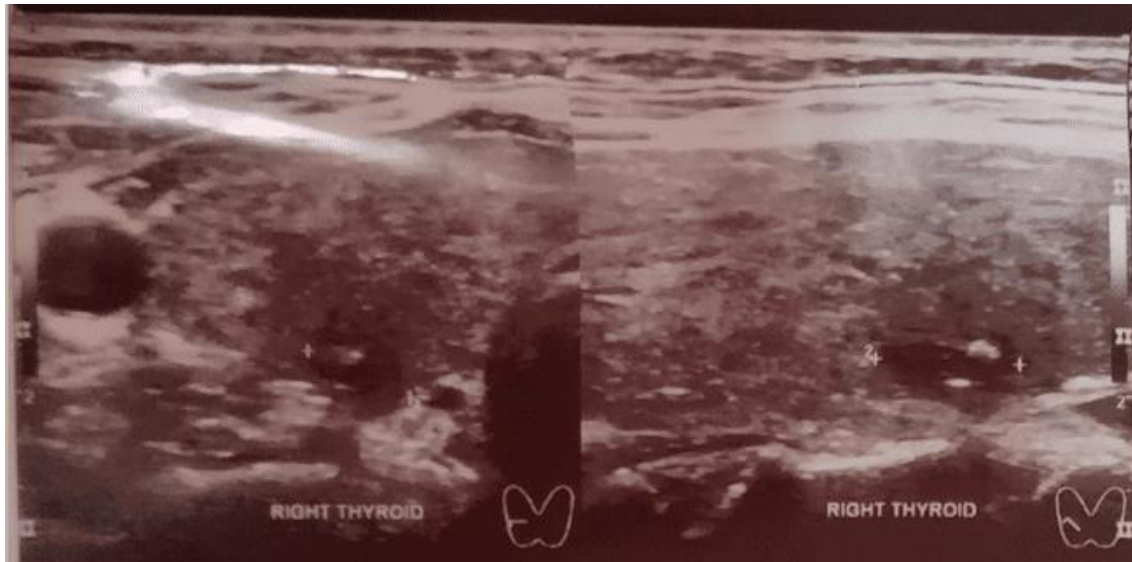


Figure 1. Heterogenous thyroid parenchymal ultrasound with decreased vascularity.

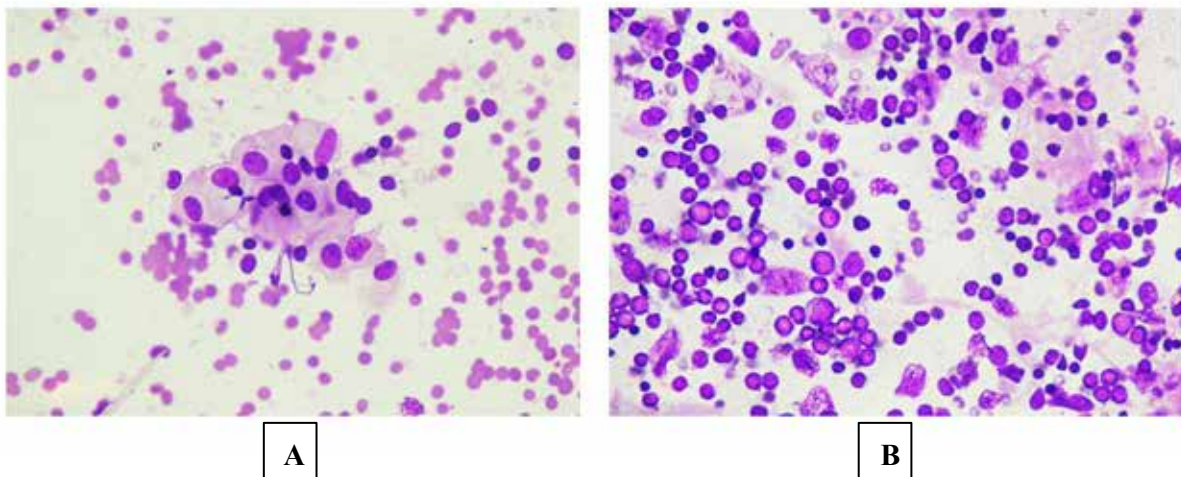


Figure 2. Histopathology of thyroid gland showing thyroid lymphocytic thyroiditis. A) oxyphil cell/hurthle cell; B) fire flare/ marginal vacuoles in the cytoplasm of the follicle

Previously, the patient had been diagnosed with HT in 2016 with anti-TPO results showing 301.1 IU/ml. The diagnosis was supported by the ultrasound imaging stating heterogeneous thyroid parenchymal ultrasound with decreased vascularity (Figure 1). The fine needle aspiration biopsy (FNAB) showed thyroid lymphocytic thyroiditis (Figure 2). The patient was treated routinely with oral levothyroxine 5mg once

daily. Seven months ago, due to palpitations and FT4 levels of 13.2 ng/dl, the patient was advised to stop having levothyroxine and take oral propranolol 10 mg twice daily. TSH and FT4 levels were within normal limits during the follow-up 2 months ago (Table 1).

The patient also had a history of psoriatic arthritis, dyspepsia, and hypertension. She



QANUN MEDIKA

JURNAL KEDOKTERAN FKUM SURABAYA

<http://journal.um-surabaya.ac.id/index.php/qanunmedika>



Table 1. Laboratory monitoring

| Parameters | During hospitalization | 1 month after hospitalization | Evaluation after 1 st Secukinumab | First month after 1 st Secukinumab |
|------------------------------|------------------------|-------------------------------|----------------------------------------------|-----------------------------------------------|
| Hemoglobin (g/dl) | 11.5 | 10 | 10.6 | 11.6 |
| White blood cell (/ μ l) | 7.820 | 7950 | 7330 | 11130 |
| Platelet (/ μ l) | 337.000 | 306.000 | 307000 | 347000 |
| Neu (%) | 65.2 | 64.8 | 81.2 | 73.6 |
| Lym (%) | 22.5 | 26.7 | 12.8 | 16.2 |
| ESR | 112 | | | |
| Glucose (mg/dl) | 121.4 | 75 | 108.2 | 110 |
| SGOT(U/L) | 15.2 | 19.4 | 19.6 | 12.7 |
| SGPT (U/L) | 9.1 | 13.5 | 17.5 | 8.1 |
| Alb (g/dl) | 4.25 | 3.73 | 3.73 | 4.32 |
| Bun (mg/dl) | 6 | 7.5 | 9.4 | 14.3 |
| Creatinine (mg/dl) | 0.7 | 0.713 | 0.77 | 0.8 |
| Na (mmol/L) | 138 | 139 | 138 | 137 |
| K (mmol/L) | 3.2 | 3.2 | 3.6 | 3.3 |
| Cl (mmol/L) | 107 | 108 | 109 | 107 |
| Ft4 (ng/dL) | 1.45 (0.89-1.76) | 0.93 | | |
| TSH (μ IU/mL) | 0.467 (0.55-4.78) | 0.790 | | |
| C-Reactive Protein (mg/dl) | 1.06 | 0.83 | | |

calcium lactate 500 mg once daily, folic acid once daily, antacids thrice a day, sucralfate 500 mg thrice a day, cyclosporin 100 mg twice a day, amlodipine 10 mg once daily, lisinopril 10 mg once daily, paracetamol 500 mg thrice a day, and methylprednisolone 4 mg once daily.

During this period of treatment, in addition to depression, the patient complained of palpitations accompanied by tremors in both hands. Vital signs showed blood pressure 130/80 mmHg, pulse 110/minute regular,

respiration rate 20/minute, axillary temperature 36.7°C, O₂ saturation 98% free air.

The patient had a moon face with a buffalo hump. Psoriatic plaques were visible on the scalp (Figure 3). The ECG shows a normal rhythm of 99 bpm (Figure 4).

AST, aspartate aminotransaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; TSH, thyroid stimulating hormone

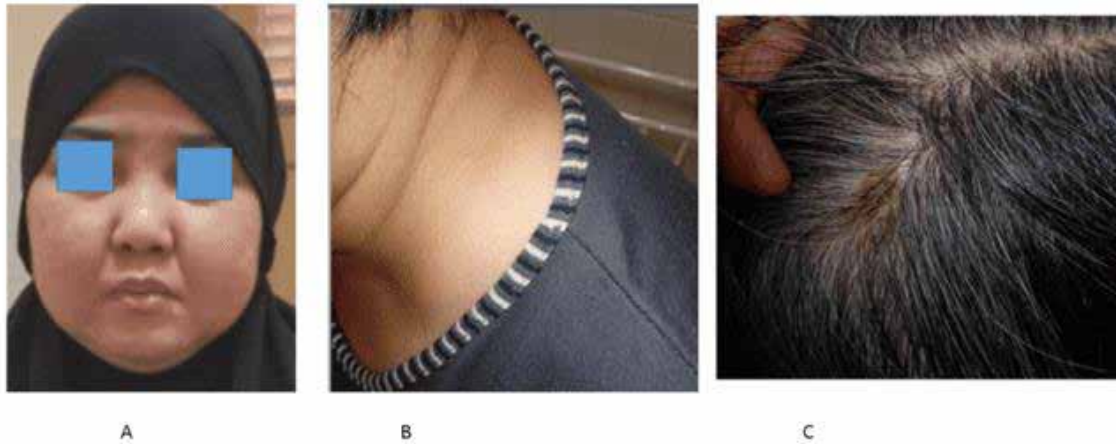


Figure 3. Clinical features of the patient. A) moon face; B) buffalo hump; C) psoriatic plaque on the scalp

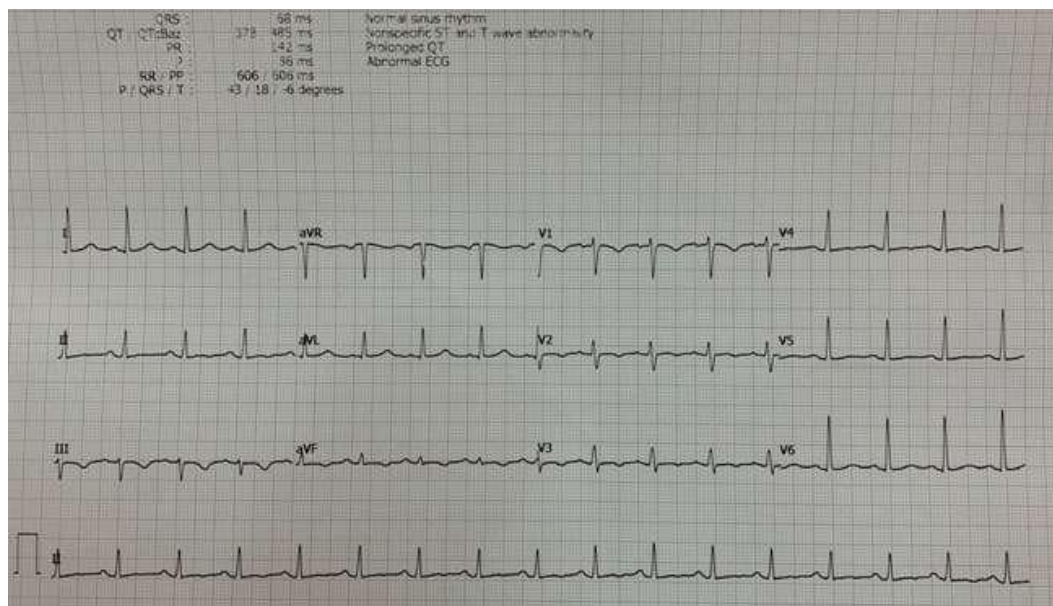


Figure 4. ECG showing normal sinus rhythm

Our patient was diagnosed with psoriatic arthritis with periods of major depression, CS, and subclinical hyperthyroidism. The follow-up was executed in the rheumatology outpatient clinic 1 month after her discharge. She complained of shoulder and back pain, and swollen, painful feet for 2 weeks as well, hence the patient had difficulty walking. Clinical evaluation showed high disease activity (DAPSA Score

58.83). The patient was then given intravenous methylprednisolone 40 mg once daily for three days, oral methotrexate 17.5 mg once daily for one week; oral sulfasalazine 1000 mg twice daily for 30 days. The regimen was followed by secukinumab 150 mg. Later on, swollen and painful legs subdued. The next follow-up was performed 1 month after secukinumab before the administration of the second secukinumab.



QANUN MEDIKA

JURNAL KEDOKTERAN FKUM SURABAYA

<http://journal.um-surabaya.ac.id/index.php/qanunmedika>



After the administration of two cycles of secukinumab, the pain and swelling in the feet resolved.

DISCUSSION

Psoriatic arthritis (PsA) is a chronic disease mediated by the immune system. PsA can induce chronic inflammation bringing about physical and psychological burdens. Depression is one of the psychological impacts found in PsA patients due to the disease activity and the long-term treatment. However, uncontrolled depression may trigger a dysregulation of the immune system, both adaptive and innate, which in turn aggravates the PsA (Coates *et al.*, 2016, Beurel *et al.*, 2020). Several studies have declared the elevation of acute phase proinflammatory cytokines in depressed patients, such as IL-6, TNF, C-reactive protein, and IL-17A (Beurel *et al.*, 2020; Köhler-Forsberg *et al.*, 2019).

Previously, researchers stated that patients with autoimmune disorders, such as psoriasis or psoriatic arthritis, may likely develop another concomitant condition, such as HT (Haddad *et al.*, 2017). Thyroid cell injury on HT was precipitated by cytokines from the lymphocytic infiltrate. It's capable of inducing the production of pro-inflammatory mediators from thyroid cells, which amplifies and maintains the autoimmune response. Previous research has demonstrated that HT, like many other autoimmune illnesses, is associated with an increase in thyroid and blood Th17 cells that secrete IL-17. However, a recent study revealed that IL-17 was also present in the thyroid follicular cells of HT (Weetman, 2021).

Long-term PsA treatment using glucocorticoids (GCs) may underlie the occurrence of CS. It has been shown that hypercortisolism in humans lowers TSH secretion and TSH pulse

amplitude. The mean 24-h TSH levels are lower in CS patients than in controls, and the mean 24-h TSH pulse amplitude is also lower in CS patients. Hypothyroidism can become subclinical hyperthyroidism when the TSH level is out of homeostasis (Paragliola *et al.*, 2021; Petramala *et al.*, 2018).

GCs drastically alter the Th1/Th2 ratio and cause mature T cells to undergo apoptosis. Different cytokines and cellular interactions control how Th1/Th2 differentiation occurs. A major shift towards Th2 differentiation is caused by GCs' inhibition of the macrophage IL-1 system, one of the primary inducers of the Th1 shift. By preventing Th1 differentiation, the resulting generation of IL-4 enhances Th2 polarization (Hasenmajer *et al.*, 2020).

It's interesting to note that T cells' sensitivity to GC exposure reinforces Th2 polarization. Th1 cells are sensitive to both GC-induced apoptosis and cytokine release, whereas Th2 cells are only sensitive to the latter. The Th17 population, a different T cell fraction, appears to be resistant to both (Hasenmajer *et al.*, 2020).

A breakthrough medication called secukinumab which targets the protein IL-17A was invented to provide a therapeutic option for those with moderate to severe psoriasis. Secukinumab 300 mg rated higher than other agents such as brodalumab, ixekizumab, ustekinumab, guselkumab, tildrakizumab, and risankizumab in terms of short-term attainment of sPGA 0/1 or IGA 0/1 or PGA 0/1 (SUCRA = 98.1%) (Bai *et al.*, 2019).

This case discloses a phenomenon in which CS shifted the hypothyroid state in HT to subclinical hyperthyroidism. The depressive episodes aggravated PsA activity as seen from the DAPSA score during follow-up. Clinical improvement was achieved after the second administration of secukinumab.



QANUN MEDIKA

JURNAL KEDOKTERAN FKUM SURABAYA

<http://journal.um-surabaya.ac.id/index.php/qanunmedika>



CONCLUSION

PsA is an autoimmune disease accompanied by chronic inflammation generating serious physical and psychological burdens. Depression can exacerbate PsA activity. As a result of long-term steroid treatment, CS can shift the HT-related hypothyroid condition to subclinical hyperthyroid. All of this complexity may initiate clinical deterioration of PsA. Secukinumab promoted clinical improvements after its second administration.

REFERENCES

- Armstrong, A. W., & Read, C. (2020). Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA: The Journal of the American Medical Association*, 323(19), 1945–1960. <https://doi.org/10.1001/jama.2020.4006>
- Bai, F., Li, G. G., Liu, Q., Niu, X., Li, R., & Ma, H. (2019). Short-Term Efficacy and Safety of IL-17, IL-12/23, and IL-23 Inhibitors Brodalumab, Secukinumab, Ixekizumab, Ustekinumab, Guselkumab, Tildrakizumab, and Risankizumab for the Treatment of Moderate to Severe Plaque Psoriasis: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. *Journal of Immunology Research*, 2019, 2546161. <https://doi.org/10.1155/2019/2546161>
- Barbot, M., Zilio, M., & Scaroni, C. (2020). Cushing's syndrome: Overview of clinical presentation, diagnostic tools and complications. *Best Practice & Research. Clinical Endocrinology & Metabolism*, 34(2), 101380. <https://doi.org/10.1016/j.beem.2020.101380>
- Beurel, E., Toups, M., & Nemeroff, C. B. (2020). The Bidirectional Relationship of Depression and Inflammation: Double Trouble. *Neuron*, 107(2), 234–256. <https://doi.org/10.1016/j.neuron.2020.06.002>
- Coates, L. C., FitzGerald, O., Helliwell, P. S., & Paul, C. (2016). Psoriasis, psoriatic arthritis, and rheumatoid arthritis: Is all inflammation the same? *Seminars in Arthritis and Rheumatism*, 46(3), 291–304. <https://doi.org/10.1016/j.semarthrit.2016.05.012>
- Coates, L. C., Soriano, E. R., Corp, N., Bertheussen, H., Callis Duffin, K., Campanholo, C. B., Chau, J., Eder, L., Fernández-Ávila, D. G., FitzGerald, O., Garg, A., Gladman, D. D., Goel, N., Helliwell, P. S., Husni, M. E., Jadon, D. R., Katz, A., Laheru, D., Latella, J., ... GRAPPA Treatment Recommendations domain subcommittees. (2022). Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nature Reviews. Rheumatology*, 18(8), 465–479. <https://doi.org/10.1038/s41584-022-00798-0>
- Haddad, A., Ashkenazi, R. I., Bitterman, H., Feldhamer, I., Greenberg-Dotan, S., Lavi, I., Batat, E., Bergman, I., Cohen, A. D., & Zisman, D. (2017). Endocrine Comorbidities in Patients with Psoriatic Arthritis: A Population-based Case-controlled Study. *The Journal of Rheumatology*, 44(6), 786–790. <https://doi.org/10.3899/jrheum.161274>
- Hasenmajer, V., Sbardella, E., Sciarra, F., Minnetti, M., Isidori, A. M., & Veneri, M. A. (2020). The Immune System in Cushing's Syndrome. *Trends in Endocrinology and Metabolism: TEM*, 31(9), 655–669. <https://doi.org/10.1016/j.tem.2020.04.004>
- Köhler-Forsberg, O., N Lydholm, C., Hjorthøj,



QANUN MEDIKA

JURNAL KEDOKTERAN FKUM SURABAYA

<http://journal.um-surabaya.ac.id/index.php/qanunmedika>



- C., Nordentoft, M., Mors, O., & Benros, M. E. (2019). Efficacy of anti-inflammatory treatment on major depressive disorder or depressive symptoms: meta-analysis of clinical trials. *Acta Psychiatrica Scandinavica*, 139(5), 404–419. <https://doi.org/10.1111/acps.13016>
- Mathew, A. J., & Chandran, V. (2020). Depression in Psoriatic Arthritis: Dimensional Aspects and Link with Systemic Inflammation. *Rheumatology and Therapy*, 7(2), 287–300. <https://doi.org/10.1007/s40744-020-00207-6>
- Nieman, L. K. (2015). Cushing's syndrome: update on signs, symptoms and biochemical screening. *European Journal of Endocrinology / European Federation of Endocrine Societies*, 173(4), M33–M38. <https://doi.org/10.1530/EJE-15-0464>
- Paragliola, R. M., Corsello, A., Papi, G., Pontecorvi, A., & Corsello, S. M. (2021). Cushing's Syndrome Effects on the Thyroid. *International Journal of Molecular Sciences*, 22(6). <https://doi.org/10.3390/ijms22063131>
- Petramala, L., Olmati, F., Conforti, M. G., Concistré, A., Bisogni, V., Alfieri, N., Iannucci, G., de Toma, G., & Letizia, C. (2018). Autoimmune Diseases in Patients with Cushing's Syndrome after Resolution of Hypercortisolism: Case Reports and Literature Review. *International Journal of Endocrinology*, 2018. <https://doi.org/10.1155/2018/1464967>
- Santos, A., Webb, S. M., & Resmini, E. (2021). Psychological complications of Cushing's syndrome. *Current Opinion in Endocrinology, Diabetes, and Obesity*, 28(3), 325–329. <https://doi.org/10.1097/MED.0000000000000633>
- Weetman, A. P. (2021). An update on the pathogenesis of Hashimoto's thyroiditis. *Journal of Endocrinological Investigation*, 44(5), 883–890. <https://doi.org/10.1007/s40618-020-01477-1>