Severe psoriatic arthritis patient being managed by anti IL-17A inhibition therapy in 108 Military Central Hospital

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Summary

The article would like to introduce a psoriatic arthritis (PsA) patient in the Department of Rheumatology of 108 Military Central Hospital. This case of PsA had the secondary tuberculosis infection after Tumor necrotic factor inhibitor (TNFi) treatment, nevertheless the articular destruction caused by PsA still went on. The next management in these patients is always a controversy among the rheumatologists because the lack of international and national recommendation of management step-by-step. In addition, there were not many articles mentioning about this problem. After doctors-patient discussion, patient decided to be administered with Interleukin 17A inhibitor (IL-17Ai) (four doses secukinumab 300mg SC) plus methotrexate, then the disease remission (Minimal disease activity) was achieved without burden of tuberculosis. This success could contribute to the clinical experiences of biologic therapy in patients with severe side effects of TNFi treatment which becomes the more and more popular and causing many difficulties for clinicians.

Keywords: Psoriatic arthritis, Interleukin 17A inhibitor.

1. Background

Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with psoriasis, manifesting most commonly with peripheral arthritis, dactylitis, enthesitis, and spondylitis. The incidence of PsA is about 6 per 100.000 per year, and the prevalence is 1 - 2 per 1000 in the general population [1]. With the development of biotechnology, there are more and more options for adequate disease control, including biologic therapies. Up to present, there are two mains biologic options for PsA patients in Vietnam: TNF alpha inhibitor (TNFi) and IL-17A inhibitor (IL-17Ai). The TNFi could lead to secondary infection as the major side effect, especially tuberculosis. This problem is not very rare, however there was no international and national recommendation for management of these cases step-by-step. In additionally, the IL17i recently presents, hence there was not many publications about its usage in Vietnam.

This article would like introduce a special PsA clinical case Department of Rheumatology of Military Central Hospital 108 who had the secondary tuberculosis caused by previous management of TNFi, and the continuous articular destruction lead to complete disability. The IL-17Ai, Secukinumab, was administered with close observation, and the optimal outcome was shown. For this intention, all the patient files from April to June, 2020 was referenced. For each administration of Secukinumab, the clinical data was collected according to the target of

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treatment “Minimal disease activity MDA” (Table 1) such as tender joint count (TJC), swollen joint count (SJC), Psoriasis area severity index (PASI), Patients global disease activity VAS (2), Health assessment questionnaire (3), tender entheseal points. The subclinical data was collected such as: Renal and hepatic functions, erythrocyte sedimentary rate, serum iron, ferritin and transferrin in order to investigate the complications of medication. For the first administration, the necessary data for diagnostic confirmation is also included in the article.

2. Case presentation

Chief complaint

42 years old patient was hospitalized at the Department of Rheumatology, 108 Military Central Hospital in August 2020 with the chief complaint of poly-articular pain caused disability.

Personal and family history

He had no history of cardiovascular, pulmonary and digestive disease. No history of articular pain at the adolescence.

There was no family member diagnosed with musculoskeletal and dermatologic diseases at early age. No family history of psoriasis.

History of illness

Male patient diagnosed with the guttate and vulgar psoriasis since 11 years, partial response with methotrexate (MTX) 15mg/week treatment for 4 years.

From 2013, he has been attacked by symmetric polyarthritis (shoulder, wrist, metacarpal, metacarpophalangeal, ankle, knee joints). Then, methotrexate was withdrawn and TNF alpha inhibitor (Enbrel) was commenced as diagnosis of psoriatic arthritis (PsA). Partial response was recorded regarding the pain score and skin lesion.

In 2019, he was treated with other TNF alpha inhibitor (Simponi) combined with MTX 7.5mg/week in only the next 5 months because of newly diagnosed of pulmonary tuberculosis. Hence, Simponi and MTX had been stopped for beginning of tuberculosis treatment. 3 months before the hospitalization (April, 2020), he had symmetric polyarthritis, light fever, fatigue and anorexia without cough (still on the 5th month of tuberculosis treatment - maintenance phase – well response).

There was no remarkable of systemic symptoms at the admission. The musculoskeletal and dermatologic examination was presented in the Table 2. The skin lesion evaluation was demonstrated by the PASI score.

Treatment follow-up

The data of treatment assessment is briefly presented in the Table 2.

Before the first medication administration, regarding of the recommendation (American College of Rheumatology 2018) [1], patient was assessed before and after each dose of secukinumab 300mg SC by the Minimal Disease Activity (MDA) (Table 1). Because of current tuberculosis, he was also performed plain chest X-ray and strictly examined in order to rule out the possibility of reactivated infection. The current management of tuberculosis was respected as well. The markers of cancers (PSA, AFP, CEA, CA19-9, CA 72.4), and others common infections (HBV, HCV, HIV) were also requested, the negative results confirmed before the first dose. Patient was well explained before his decision, medication was administered under patient’s consent, and close discussion with bacteriologists and pulmonologists.

In the first administration, the subclinical results are shown in the Table 2. Patient was marked with anemia. The first dose of 300mg secukinumab was subcutaneously administered with 7.5mg methotrexate weekly and he was consulted for the second administration after 1 week.

The second admission was remarked with the lack of arthritis signs such as significant reduction of swelling in all examined joints, lower of morning stiffness (from 2 hour to 1 hours). As the optimistic result, the second same dose was given and methotrexate was also maintained with the dose of 7.5mg.

After the second and the third doses plus methotrexate as an oral small molecule, the remission was approached.

Table 1. Minimal disease activity for PsA

MDA is achieved when five of these seven criteria are met
Tender joint count ≤ 1
Swollen joint count ≤ 1
PASI ≤ 1 or BSA ≤ 3
VAS ≤ 15
Patient global disease activity ≤ 0.5
Health assessment questionaire ≤ 0.5
Tender entheseal points ≤ 1

Table 2. Investigating results of the patient

Assessment	**First admission**	**After the first dose**	**After the second dose**	**After the third dose**	**After the fourth dose**
WBC (G/l)	14.62	9.88	6.94	7.17	7.66
% Neu	86.1	68	72.3	49.5	52,1
RBC (T/l)	3.19	3.34	3.26	4.57	4.94
HGB (g/l)	82	91	88	131	147
PTL (G/l)	420	534	386	207	239
ERS (mm)	140mm	119mm	109mm	6mm	11mm
Urea (mmol/l)	7.35	10.48	9.78	12	8.66
Creatinine (µmol/l)	104	108	116	138	115
AST/GOT (U/l)	12	15	18	21	20
ALT/GPT (U/l)	6	7	9	21	20
Acid uric (µmol/l)	402	464	521	624	590
Anti-CCP (U/ml)	7				
Iron (umol/l)	2.7				
Ferritin (ng/mL)	736				
Transferin (g/L)	0.99				
MDA (Minimal disease activity)					
Tender joints count	13	13	2	2	2
Swollen joints count	10	5	0	0	0
PASI	40	30	21.3	9	5.8

Pts global disease activity VAS	80	60	50	10	10
HAQ	3	2	1.25	1	0.5
Tender entheseal points	6	6	4	2	0

3. Discussion

TNFi treatment is well-known with the risk of tuberculosis infection, especially in tropical country as Vietnam. Therefore, closely clinical and subclinical observation of tuberculosis in each re-examination is recommended. The current infection deprived the treatment of Golimumab in this patient even it well controlled the symptoms. Then, the next management is always challenging for most of rheumatologists. Even international and national recommendations have not well indicated in this situation [1, 4]

In the biologic scope, the role of T helper 17 (Th17 cells) and genetic associations of IL17 open more opportunities for the autoimmune diseases patients such as psoriasis, rheumatoid arthritis, Crohn disease and PsA [5]. Secucinumab is selective blockade agent of IL17A, it means the others interleukin 17 receptors and ligands among the IL17 family are intact, could help to control the immune-mediated inflammatory reactions (PsA pathology) but preserve the adaptive and innate immune cells function (immunity against bacteria) (Image 1). This characteristic is significant in the patients with high risk of infection thanks for the intact of defense ability. More interestingly, abundant of IL 17A-producing mast cells, neutrophils and T-cells have been identified in psoriatic skin lesion and inflamed synovial tissue. These evidences are supportive for the usage of IL17A blockade in the clinical scope of high risk infection and autoimmune chronic inflammatory disease targeting on the joint and skin especially the highly inflamed joint without enthesitis.

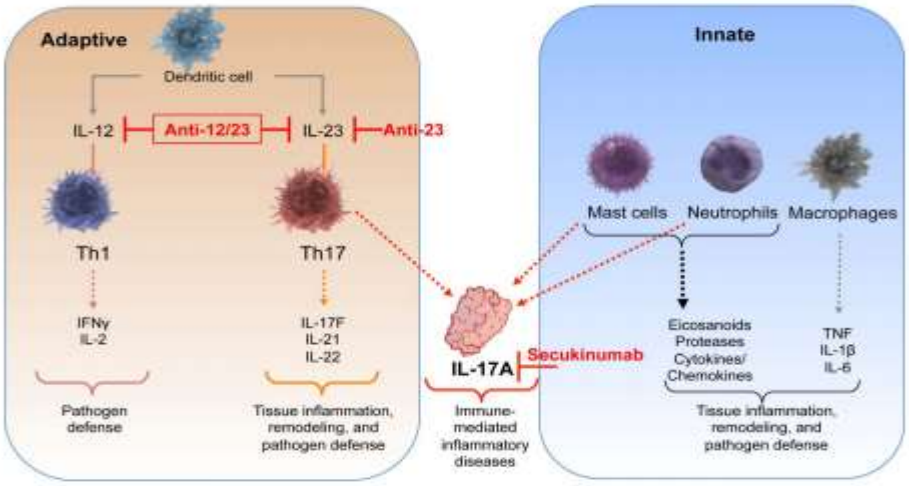

Figure 1. Anti-IL-17A inhibition impacts pro-inflammatory drive in autoimmunity, preserving other Th17 and innate immune cell functions. Targeting IL-17A has the potential to reduce autoimmune inflammation while leaving other immune functions undisturbed [1].

In the clinical scope, the IL17A inhibitor is recommended as the second line for biologic therapy (American College of Rheumatology 2018). And if the patient meets the contraindication of the first line, the second line will be the first priority. However, it is not clarified that when and how to manage the second line in this situation.

In American College of Rheumatology 2018 recommendation, the combination therapy (Oral small molecule and biologic agent) is highly recommended, especially with dominant skin lesion. Because of the optimal outcome in skin lesion, methotrexate is the choice encouraged.

With this patient with current tuberculosis infection and dominant skin lesion, the choice of IL17A could help to well control the inflammation but keep the defense of bacteria intact. The decision of start point set at the fifth months of tuberculosis treatment as discussed with pulmonologist and bacteriologist. In the situation of lacking national consensus, it is necessary to have the multidisciplinary consultations for proper beginning treatment decision rather than only based in rheumatologist opinion.

The outcome was apparently seen in the fourth dose (as the FUTURE trial showed) [6] with archived MDA without burden of tuberculosis or other infection. There was also no renal and hepatic toxicity. The anemia considered as the result of chronic inflammation was resolved after the third administration.

However the cause of hyperuricemia was ill-defined between adverse effect of tuberculosis treatment and concomitant disturbance of PsA. The molecular relationship between hyperuricemia and psoriatic arthritis was mentioned [7], however the exact mechanism has been unproven. In this patient, the concomitant treatment of tuberculosis could be a reason of unresolvable hyperuricemia.

4. Conclusion

In term of lacking international and national consensus of biologic treatment in patients with concomitant infection, especially tuberculosis, this psoriatic arthritis case is the necessary data for further recommendation of management of these situations. During the maintenance phase in good response patient, it should begin the biotherapy less aggressive (IL17Ai - Secukinumab) in order to inhibit the chronic inflammation of PsA, but preserve the innate and adaptive immune which are important for tuberculosis management. As result, this clinical case achieved disease remission without burden of infection. IL17A-i has been already available in Vietnam with limited usage. It needs more data to encourage its usage in Vietnam where the latent tuberculosis is widely common.

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