

## Stability of a Lupus Nephritis Case after One Year of Integrated Therapy

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### Abstract

This case report revealed that how a stable condition of the patient with LN experienced accidentally with thrombocytopenia on early July 2019, which it is the most severe comorbidity of systemic lupus erythematosus and the patient's platelets increased from  $11 \times 10^3 \mu\text{L}$  to  $186 \times 10^3 \mu\text{L}$  after receiving the integrated pulse-prednisolone therapy plus core CHM treatment, composed of "Jia-Wei-Xiao-Yao-San" (6g), "Yin-Chen-Hao-Tang" (6g), "Xie-Fu-Zhu-Yu-Tang" (6g), "A-Jiao" (0.25g), "Dan-Shan" (0.25g) and "Gou-Teng" (0.25g). Over the same 28 day period, her alanine transaminase (ALT) and aspartate transaminase (AST) also decreased from 103 U/L, and 116 U/L to 62 U/L and 89 U/L, respectively; and her dosage of prednisolone was reduced from 50 mg to 5 mg per day. This case report follow-up wants to clarify the stability of a LN case after continuous one year of integrated conventional medicine with core Chinese herbal medicine. And it also could provide some clues for treating the severe comorbidity in systemic lupus erythematosus patients, it will provide the whole and comprehensive views for this following-up case. However, the comorbidity of systemic lupus erythematosus should be clarified with a comprehensive view in the future.

**Keywords:** Systemic Lupus Erythematosus; Lupus Nephritis; Traditional Chinese Medicine; Integrated Medicine; Thrombocytopenia

## Introduction and Case Report

### Patient Information

As reported in 2018 [1] treatment of an adult female lupus nephritis (LN) patient with an integrated combination of Chinese herbal medicine (CHM) and Western medicine resulted in the alleviation of both her subjective symptoms - including leg edema, frequent and foamy urine, and constipation - and objective signs such as urinary micro total protein (M-TP) and serum total cholesterol, and triglyceride levels. Six months after the initial publication of her case, the patient was still receiving the integrated treatment, her condition was well controlled and her M-TP of 113.1 mg/24 hours was within the normal range.

### Clinical findings and diagnostic assessment

The LN patient noticed some bruising on all four limbs in July 2019 and was admitted after it was found that her platelet count (PLT) was only  $11 \times 10^3 \mu\text{L}$ . After she received steroid-pulse therapy, her PLT increased to  $97 \times 10^3 \mu\text{L}$ , but it decreased again to  $13 \times 10^3 \mu\text{L}$

after 2 days. A urinary tract infection was diagnosed and treated with two 500 mg ciprofloxacin tablets per day and continuous pulse-prednisolone therapy for one week, after which the patient’s PLT rose to  $49 \times 10^3 \mu\text{L}$ . During the same admission, the patient was asked not to take any CHM; hence, after she was discharged, she sought treatment from the Center for Traditional Medicine at Taipei Veterans General Hospital on August 2, 2019.

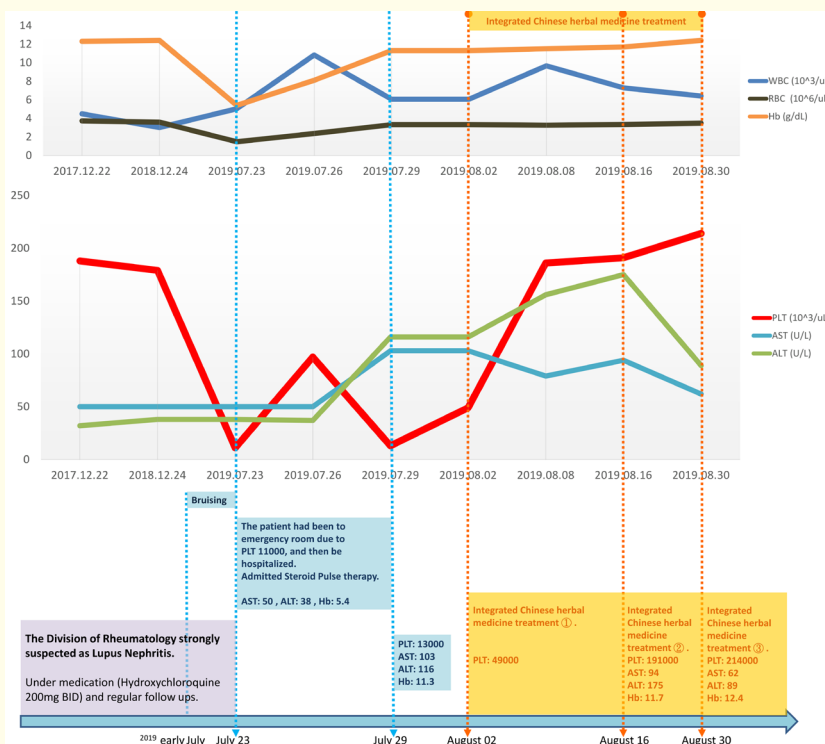


Figure 1: Timeline of changes in the symptoms and treatments of a patient with lupus nephritis and low platelet levels, July to August 2019.

### Therapeutic intervention

In the traditional Chinese medicine (TCM) clinic, the patient complained of fatigue, dizziness, and a greatly increased area of bruising to her four limbs. It was also noted that the heavy doses of prednisolone she had received (i.e. pulse prednisolone during her recent admission, and 50 mg/day after her discharge) were causing edema and flushing. TCM tongue diagnosis revealed a red tongue color, thin white tongue fur, red spots, dental impressions, and sublingual vessel stasis; and the TCM pulse diagnosis was of a combination of string-like pulse and rough pulse. At this point, the patient’s PLT, alanine transaminase (ALT) and aspartate transaminase (AST) were  $42 \times 10^3 \mu\text{L}$ , 103 U/L, and 116 U/L, respectively (Table 1).

The patient was prescribed a modified form of her previous daily core CHM treatment, composed of “Jia-Wei-Xiao-Yao-San” (6g), “Yin-Chen-Hao-Tang” (6g), “Xie-Fu-Zhu-Yu-Tang” (6g), “A-Jiao” (Colla corii asini) (0.25g), “Dan-Shan” (Salvia miltiorrhiza Bge.) (0.25g) and “Gou-Teng” (Uncaria rhynchophylla (Miq.) Jacks) (0.25g). After one week, i.e. on August 09, 2019, her PLT increased to  $186 \times 10^3 \mu\text{L}$ . On August 16, 2019, it reached  $191 \times 10^3 \mu\text{L}$ , and two weeks later,  $214 \times 10^3 \mu\text{L}$ . Over the same 28 day period, her AST and ALT also decreased,

→Lupus nephritis patient received integrated therapy from October 14, 2016			→ The patient had been to emergency room due to PLT: 11 (10 <sup>3</sup> / $\mu$ L) and then hospitalized during July 23~29, 2019 Admitted Pulse Prednisolone therapy.				→Integrated Chinese herbal medicine treatment from August 02, 2019		
Laboratory data	Normal Range	2018.12.24	2019.07.23	2019.07.26	2019.07.29	2019.08.02	2019.08.08	2019.08.16	2019.08.30
Platelets (10 <sup>3</sup> / $\mu$ L)	130 - 400	179	11	97	13	49	186	191	214
White blood cell (10 <sup>3</sup> / $\mu$ L)	4.0 - 11.0	3.01	5.04	10.83	6.06		9.66	7.29	6.41
Red blood cell (10 <sup>6</sup> / $\mu$ L)	3.8 - 5.5	3.59	1.48	2.37	3.32		3.27	3.33	3.48
Hemoglobin (g/dL)	12.0 - 16.0	12.4	5.4	8.1	11.3		11.5	11.7	12.4
Complement 3 (mg/dl)	90.0 - 180.0	91.6	56.6	58.4					
Complement 4 (mg/dl)	10.0 - 40.0	3	< 2	< 2					
AST (U/L)	< 40				103		79	94	62
ALT(U/L)	< 41	38	38	37	116		156	175	89
M-TP (mg/dl)	< 15.0	5.8							
M-TP (mg/24hrs)	< 140	113.1		130.7					
Blood urea nitrogen (mg/dl)	6.0 - 20.0			21	20				
Serum creatinine (mg/dl)	0.5 - 0.9	0.6	0.6	0.5	0.6		0.6		0.6
GFR (mL/min/1.73 m <sup>2</sup> )	> 60	110	110	136	110		110		110

**Table 1:** Laboratory data from before and during the administration of integrated therapy to a lupus nephritis patient with low platelet levels, July to August 2019.

to 62 U/L and 89 U/L, respectively; and her dosage of prednisolone was reduced from 50 mg to 5 mg per day. Her fatigue, dizziness, edema, flushing and bruising all improved, as did the red spots, dental impressions and sublingual vessel stasis. On September, the patient's prednisolone treatment ceased, and had not resumed as of the time of writing.

## Discussion

The severity level of thrombocytopenia, a potentially dangerous comorbidity in systemic lupus erythematosus (SLE) patients [2,3] can be a useful factor in the prediction of their survival [4,5]. Typically, corticosteroids and intravenous immunoglobulin are applied to treat primary and secondary immune thrombocytopenia [6]; however, they can have side-effects including edema, "moon face," and weight gain, leaving many patients dissatisfied with this approach [7]. Hence, the integration of CHM with conventional medicine as a treatment for thrombocytopenia-complicated SLE is well worth exploring.

One of the components of this paper's focal patient's core CHM prescription, "Jia-Wei-Xiao-Yao-San", is described as having the function "Course the liver and resolve depression", and is widely used as a treatment for chronic hepatitis B virus (HBV) [8,9] chronic hepatitis C virus (HCV) [10,11] and hepatocellular carcinoma (HCC) [9]. In the livers of rats, it has been found to inhibit superoxide-dismutase-like activity, lipid peroxidation and xanthine oxidase activity [12] and it has also been reported to have potential for reducing interleukin (IL)-6, IL-8 and macrophage inflammatory protein-1 $\beta$  [13]. "Yin-Chen-Hao-Tang", traditionally described as being able to "Clean heat and eliminate dampness", appears to alleviate oxidative stress [14,15], inflammation [16] and fibrosis [15,17] regulate lipid metabolism and the NF- $\kappa$ B/PPAR $\gamma$  signal pathways [18,19] and promote the mRNA expression of platelet-derived growth factor (PDGF) subunit B [20]. "Xie-Fu-Zhu-Yu-Tang" ("Quicken the blood and dispel stasis") may reduce TNF- $\alpha$  and IL-1 $\beta$  [21], reduce fibrosis [22] and release PDGF; while one study demonstrated that it could, more effectively than conventional medicine, restore PLT to the normal range, while decreasing IFN- $\gamma$ , IL-6, TNF- $\alpha$  and IL-18 and regulating the immune biomarkers of CD3+, CD4+, CD3+CD4+, CD8+ [23].

"E-Jiao" (Colla corii asini.), which has the traditional function "Enrich the blood and stop bleeding", appears to elevate and optimize Hb components during treatment for anemia [24]. "Dan-Shan" (Salvia miltiorrhiza Bge.) - "Clear heat quicken the blood and transform stasis" - could reduce both the phosphorylation of PDGF receptors [25] and fibrosis [26]. Lastly, "Gou-Teng" (Uncaria rhynchophylla (Miq.) Jacks), traditionally described as "Relieving convulsion and spasm", has been reported to modulate the phosphorylation of PDGF-R $\beta$  [27,28].

Based on the focal patient's lower PLT and higher AST and ALT following the CHM treatment described above, the prescription in question appears to have provided hepatic protection; had anti-inflammatory and anti-fibrosis effects; and promoted PDGF. It therefore might serve as a useful treatment for both thrombocytopenia (by elevating PLT), and hepatitis (by decreasing AST and ALT). However, large-scale investigations and further explorations of its biomedical mechanisms should be conducted before any firm conclusions are drawn.

## Conclusion

As well as thrombocytopenia, LN patients' comorbidities commonly include leukocytopenia, or poor liver function. Integration of the modified core CHM described above with prednisolone could alleviate their subjective symptoms as well as lead to improvement in objective signs such as PLT, AST and ALT. However, the safety of these CHMs and their efficacy for this purpose should first be tested via a well-defined randomized clinical trial.

## Conflicts of Interest

The authors declare that they have no competing interests.

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## Author's Contributions

WTT and HCL drafted the paper and amended the references. PHS, YYK and PWW edited the article and offered technical support. CMC conceived and conducted the entire study and edited the paper. All authors have read and approved the manuscript.

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