

雷公藤流浸膏片治疗红斑狼疮的疗效观察

北京协和医院皮肤科 王宝玺 袁兆庄

内容提要 用雷公藤流浸膏片治疗23例红斑狼疮患者，并与同期仅用强的松治疗的19例系统性红斑狼疮(SLE)患者作对照。结果15例SLE患者症状得到控制，雷公藤组9/15例，对照组6/19例($P>0.10$)；消除关节痛，雷公藤组7/10例，对照组7/15例；消除盘状红斑，雷公藤组6/8例，对照组5/12例。8例盘状红斑狼疮(DLE)患者仅用雷公藤治疗，4例病情控制好转。雷公藤的副作用有外周血白细胞数下降，个别病例出现蛋白尿，表明雷公藤毒性作用与治疗有效量很接近，应用时应慎重，尤其对有肾脏损害的患者应注意。目前用雷公藤的适应症以DLE及无肾脏损害的SLE为宜。

雷公藤(*Tripterygium wilfordii* Hook.f.)属卫茅科植物，药用其去皮木质部分。近来本药被用于治疗多种自身免疫性疾病，都有一定疗效。现将我们近年来在门诊条件下用雷公藤流浸膏片治疗红斑狼疮23例的资料，总结报道如下。

临床资料

一、一般资料：雷公藤组为专科门诊治疗的初诊患者及曾用强的松治疗控制不满意或加重的复诊患者共23例。包括系统性红斑狼疮(SLE)15例，皆符合1982年ARA诊断标准^[1]；盘状红斑狼疮(DLE)8例，诊断依据临床表现、组织学检查及狼疮带试验结果。23例中男性5例(SLE 1例，DLE 4例)，女性18例(SLE 14例，DLE 4例)；年龄21~54岁，平均31.4岁；病程最长17年，最短15天，平均6.7年。对照组为同期专科门诊的19例SLE患者，其中男性3例，女性16例，年龄9~50岁，平均30岁；病程最长13年，最短50天，平均4.9年。

二、主要观察项目

1. 临床指标：(1)面部蝶状红斑或盘状红斑。(2)关节痛/炎。(3)发热。(4)乏力、纳差等中毒症状。

2. 实验室指标：(1)血常规包括血红蛋白、白细胞及血小板。(2)血沉。(3)抗核抗体(ANA)滴度。(4)抗DNA抗体。(5)补

体(CH_{50} 及 C_3)测定。(6)尿常规包括尿蛋白、尿中白细胞、红细胞及管型。(7)血清转氨酶检查等。

此外，雷公藤组中12例患者作了抗ENA抗体，抗平滑肌抗体(SMA)及抗RNP抗体检查，结果ENA阳性7例，SMA阳性1例，RNP阳性4例，对照组作检查的6例中，ENA阳性3例，RNP阳性1例，SMA均为阴性。有临床症状者进行胸部X线及心电图等检查。对照组8例患者胸透，发现1例有肺结核灶；7例中发现1例有窦性心律不齐与右束支不完全传导阻滞。雷公藤组7例患者胸透，发现1例双肺间质纹理增厚，左心室稍增大；1例有肺结核灶。5例心电图检查示2例心动过速，1例期前收缩，其余均正常。

治疗方法

一、雷公藤组：雷公藤流浸膏片(本院自制，每片0.5g，相当于生药5g)2片，每日口服3次。其中12例SLE患者维持原口服强的松不变(每日10~40mg)，其余3例SLE及8例DLE患者只服雷公藤片。皮损处同时外用氢化可的松霜或硅霜。

二、对照组：按常规给予强的松每日30~60mg口服，同时服用钾、钙等辅助药物。

治疗观察时间，雷公藤组最短15天，最长21个月，平均5.6个月；对照组最短20天，最长20个月，平均7.3个月。

结 果

一、疗效评定标准：治疗半个月后全面复查，综合分析，经治疗原异常项目中至少有上述2项临床及2项实验室指标恢复正常为病情控制；达不到此标准为无效；比原有异常项目增多为加重。

二、结果

SLE患者治疗情况：临床指标：雷公藤组面部蝶形红斑消退2/4例，盘状红斑消退6/8例，关节痛缓解7/10例，发热消退2/5例，乏力消失4/7例；对照组分别依次为7/16、5/12、7/15、4/15及5/8例。因样本过少，未进行统计学处理。雷公藤组15例SLE患者中病情控制9例，无效4例，加重2例；对照组19例中分别为6、12、1例。两组对比 $P>0.10$ 。实验室指标：SLE患者治疗后实验室指标改变情况，见附表。各项目之间均因样本较少，未进行统计学处理。

附表 SLE患者治疗后有关实验室指标改变情况(例)

组 别	血 红 蛋 白	白 细 胞	血 小 板	尿 蛋 白	尿 白 细 胞	尿 红 细 胞	尿 管 型	转 氨 酶	血 沉	抗 核 抗 体	抗 DNA	狼 疮 细 胞	补 体 CH ₅₀	补 体 C ₃	
雷公藤	异常	5	8	3	9	7	6	2	6	8	12	10	3	12	10
	好转	2	5	1	3	2	2	1	5	4	3	6	3	3	6
对照	异常	2	10	4	10	11	9	2	3	10	16	15	4	13	14
	好转	2	3	3	2	1	6	0	3	7	7	11	1	4	7

DLE患者治疗情况：雷公藤组中8例DLE患者服用雷公藤，治疗观察方法同SLE患者。治疗后有4例红斑消退或显著减轻；2例有关节痛症状患者中的1例症状消失；2例伴有低热者均好转，1例仍有轻度乏力，1例无全身症状。实验室检查其中1例有ANA低滴度(低于1:20)反应，抗DNA抗体滴度增高，治疗前后无明显改变。

三、雷公藤的副作用：雷公藤组用药4周内出现外周血白细胞下降者7例，下降值至4000，其中2例降至4000以下。白细胞下降现象往往与症状好转相一致，尤其在DLE患者表现明显。2例患者服药4周后出现尿蛋白，而

此时病情未处于活动状态，并可除外其它因素。这些现象在停药后皆逐渐恢复正常。

讨 论

关于雷公藤治疗红斑狼疮的报道很多，如秦万章^[2]用雷公藤木质部分制成片剂或糖浆，治疗红斑狼疮患者103例，有效率91.2%，显效54.3%，说明经治疗后自觉症状、临床体征及各项化验指标都明显好转。本组病例用雷公藤和单纯用强的松治疗作比较，对SLE控制结果基本一致($P>0.10$)，说明雷公藤治疗也是有效的。特别在消除红斑及关节痛症状方面，雷公藤组似优于对照组。

关于雷公藤的药理作用，张益鹤^[3]报告雷公藤能够抑制新西兰小鼠局部异种移植物抗宿主反应过程，表现为延缓同种异体排斥时间及延缓抗原从尿中排泄时间，认为雷公藤有一定的免疫抑制作用。本组病例中出现白细胞降低、ANA及抗DNA抗体滴度下降，与此观点相符。临床观察到，雷公藤的治疗有效量似与中毒剂量很接近，如上述按常规剂量治疗的DLE患者，症状消退与白细胞下降基本上同时出现，若药物减量则疗效降低，再服仍有效，血白细胞值也同时下降。另外，雷公藤的肾脏毒性作用也应引起注意。曾有报道服用大剂量雷公藤致肾脏和多脏器损害，甚至死亡。本组患者中2例服药后出现尿蛋白，停药后症状消失。我们建议，成人用药量应控制在用生药(木质部分)每日30g以内，还要因人而异。目前雷公藤制剂很多，有效成份含量不尽相同，应研究规定统一的制剂。治疗期间应定期检查血像及肝肾功能。把DLE及肾脏损害不严重的SLE患者作为雷公藤的适应症较为适宜。

参 考 文 献

1. Tan EM, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25:1271.
2. 秦万章, 等. 雷公藤治疗103例系统性红斑狼疮. *中华皮肤科杂志* 1982; 15(3):141.
3. 张益鹤. 雷公藤中毒的大鼠实验病理研究. *中西医结合杂志* 1983; 3(6):360.

Tablet *Tripterygium wilfordii* in Treatment of Lupus Erythematosus

Wang Baoxi(王宝玺), Yuan Zhaozhuang(袁兆庄)

PUMC Hospital, Beijing

Twenty-three cases of lupus erythematosus, including 15 cases of SLE and 8 cases of DLE treated with *Tripterygium wilfordii* (TW, three tablets thrice a day, each tablet contains 5 gm of crude TW) were reported. As controls, 19 cases of SLE were treated with prednisone alone at the same time. 9/15 cases in the former group and 6/19 in the latter got improvement after treatment. There was no significant difference between the two groups ($P > 0.10$). However, TW had beneficial effects to remission of arthralgia (7/10 in the former group and 7/15 in the latter group) and erythematosus rash (6/8 in the former group and 5/12 in the latter). Clinically, four out of eight cases of DLE improved after treatment with TW. TW had some toxic effects, such as decrease of peripheral blood leukocyte and kidney damage. Since the toxic dose and effective dose could be quite close, special attention should be paid when the drug was being used, especially on those patients with nephropathy. So the authors suggested that the indication of TW could include the patients of DLE and SLE without nephropathy. (Original article on page 407)

NK Cell Activity in Patients with Insufficiency of the Kidney

Chen Xiaofeng(陈小峰), Wang Peixun*(王培训)

Fujian College of TCM, Fuzhou

*Guangzhou College of TCM, Guangzhou

Natural killer cell (NKC) plays an important role in anti-cancer, anti-virus and the regulation of immune reaction in human body. NK cell activities from the peripheral blood were determined with ^{51}Cr release method from the human erythroleukemia cell line K562 in 61 patients, who were selected in the light of the standard of deficiency syndrome in TCM with insufficiency of the Kidney in which 12 kinds of diseases in western medicine were included, and 60 healthy subjects as control group. The patients with insufficiency of the Kidney showed significantly decrease in NK cell activity compared to the control group (25.29 ± 10.20 vs 56.27 ± 16.72 , $P < 0.001$). NK cell activities in 20 out of 60 patients, with deficiency of Kidney-Yang(阳), were lower than 21 with deficiency of Kidney-Yin(阴) (19.38 ± 7.44 vs 26.60 ± 8.95 , $P < 0.01$) and 20 with deficiency of Kidney-Qi(气) (19.38 ± 7.44 vs 29.38 ± 11.30 , $P < 0.01$), respectively, while there was no difference between the deficiency of Kidney-Qi ($P > 0.05$). The authors also found that NK cell activities of healthy subjects were strongly inhibited by plasma from 43 out of 61 patients. These results suggested that decreased NK cell activity is one of the common characters in patients with insufficiency of the Kidney in TCM and there are some inhibitory substances against NK cell activity in plasma of ones. The fact that NK cell activity of patients with deficiency of Kidney-Yang was the lowest among three kinds patients with insufficiency of the Kidney. It supports the theory of Kidney-Yang playing much more important part in human body. It was proposed that the relationship of NK cell and the Kidney in TCM and the increase and regulation of NK cell activity with tonifying Kidney should be further studied.

(Original article on page 409)

Experimental Studies on Antagonistic Effect of Re Du Qing(热毒清)

on Endotoxin Induced Damage of Lysosomes and Mitochondriae

Li Mingzhen(李鸣真), Ye Wangyun(叶望云), Huangpu Yongmu*(皇甫永穆), et al

Institute of TCM-WM, *Dept. of Medical Molecular Biology, Tongji Medical University, Wuhan

A rabbit endotoxic DIC model was preliminarily performed. The structures of lysosomes and mitochondriae in liver cells were evidently destroyed as observed under electronic microscope, whereas those rabbits pretreated with Re Du Qing (RDQ, formerly named anti-inflammatory No. 6) — a mixture of Chinese traditional herbs providing antipyretic and detoxifying action, showed principally normal ultrastructure in liver cells. In lysosomal functional studies, the activity of the lysosomal marker enzyme—acid phosphatase (ACP) was $79.0 \pm 4.7\%$ ($M \pm SD$) in model group, higher than pretreated group ($54.01 \pm 4.0\%$, $P < 0.01$). Studies on the mitochondrial function showed that the significant criteria of the respiratory activity of mitochondria — respiratory control ratios (RCR) was 2.83 ± 1.08 in model group and markedly lower than pretreated group (5.46 ± 1.25 , $P < 0.01$). Mitochon-