

急性白血病患者辨证分型与血象、骨髓象及血、尿环核苷酸关系的临床观察

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内容提要 把59例急性白血病患者分为温毒瘀血、痰热癥瘕、气阴两虚三型，观察其血象、骨髓象和血、尿环核苷酸变化，发现各型与正常人比较均有显著差异，但程度并不一致。对32例患者治疗前后观察，气阴两虚型的缓解率较高，而温毒瘀血型较差。实验认为急白中医分型具有分子病理学基础。

在肿瘤的防治中，急性白血病(简称急白)的研究是引人瞩目的课题，国内不少学者研究认为：急白患者血浆和外周白细胞内cAMP降低、cGMP升高、cAMP/cGMP比值降低^(1~3)，但尚未见急白中医辨证分型与血象、骨髓象及环核苷酸含量关系的报道。本文试图通过辨证分型，探索中医辨证的血象、骨髓象及分子学意义，为中医药治疗急白提供实验基础。

材料与方法

一、病例选择：正常人29例，男14例，女15例；年龄21~50岁。急白患者59例，男36例，女23例，年龄13~59岁。根据1982年8月全国中西医结合血液病学术会议制订的辨证分型标准，辨证为温毒瘀血型14例、痰热癥瘕型17例，气阴两虚型28例。59例急白患者其中32例进行治疗前后观察，男14例，女18例，年龄15~59岁，辨证为温毒瘀血7例、痰热癥瘕10例、气阴两虚15例。

二、治疗方案：急淋用VMP方案，个别疗程曾以MTX、Adr替代6-MP，急非淋用HAT或HCT方案，5天一疗程，个别患者曾用HOAP及COAP治疗，每次化疗间隙部分患者服用中药，住院期间除某些化疗规定用一定时间的肾上腺皮质激素外，尽可能避免使用其他药物。

每个疗程结束后5~7天复查血象、骨髓象和血、尿环核苷酸。

三、实验方法：取患者午前血、尿和骨髓作血象、骨髓象及血、尿环核苷酸测定。血浆环核苷酸测定采用EDTA钠盐抗凝取血，离心后取上层血浆，分别用3倍体积无水乙醇和2倍体积75%乙醇沉淀蛋白，合并二次上清置65℃水浴蒸干、测定时用pH4.75醋缓冲液复溶。尿cGMP测定25倍稀释，cAMP测定100倍稀释。cAMP和cGMP分别用“竞争蛋白结合分析法”和“放射免疫分析法”测定，药盒由北京原子能所提供。

结 果

见表1、表2。

表1 急白患者辨证分型与血象、骨髓象的关系(M±SD)

	血红蛋白 g% (n)	血小板 万/mm ³ (n)	骨髓原+早 幼稚细胞% (n)	骨髓 白细胞/红 细胞(n)
正常值	11~15	10~30	<5	3~5:1
温毒瘀血型	6.76±3.05 (14)	2.87±1.69 (14)	69.4±23.8 (14)	56.8±51.1 (13)
痰热癥瘕型	8.15±2.56 (17)	9.52±8.25 (17)	67.3±26.8 (17)	59.2±71.7 (17)
气阴两虚型	6.89±2.51 (28)	5.48±4.49 (28)	57.16±24.8 (28)	26.7±32.4 (23)

* 与痰热癥瘕型比较P<0.01, ** P<0.05, Δ与温毒瘀血型比较P<0.05

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表2 急白患者辨证分型与血、尿 cAMP、cGMP 及cAMP/cGMP比值的关系 (M±SD)

	血浆环核苷酸 pmol/ml 血浆				尿环核苷酸 pmol/mg肌酐			
	n	cAMP	cGMP	cAMP/cGMP	n	cAMP	cGMP	cAMP/cGMP
正常人	29	14.40±2.75	3.75±1.02	4.13±1.40	29	4727±1147	657±188	7.42±1.62
温毒瘀血型	13	8.21±2.66 ^{**}	12.23±17.12 ^{**}	1.19±0.74 ^{**}	12	3406±1335 [*]	2252±1447 ^{**}	1.94±1.11 ^{**}
痰热瘀血型	14	10.66±5.03 [*]	5.99±3.08 ^{**}	2.19±1.50 ^{**△}	9	3005±1207 ^{**}	1137±784 ^{**}	3.08±1.01 ^{**△}
气阴两虚型	26	9.03±3.10 ^{**}	5.43±3.38 ^{**△}	2.14±1.37 ^{**△}	20	2695±1099 ^{**}	982±397 ^{**△}	3.22±2.09 ^{**△}

* 与正常人比较 $P<0.05$, ** $P<0.001$; △与温毒瘀血型比较 $P<0.05$

从表1见到, 气阴两虚型和温毒瘀血型血小板较低, 与痰热瘀血型比较有显著性差异; 而温毒瘀血型血小板降低更为明显, 与气阴两虚型比较亦有显著差异。骨髓白细胞与红细胞之比一项, 气阴两虚型比其它两型低, 与温毒瘀血型比较 $P<0.05$ 。

表2可见分型各组血、尿 cAMP 降低, cGMP 升高, cAMP/cGMP 比值降低, 与正常人比较均有显著性差异。分型各组比较, 温毒瘀血型 cGMP 比气阴两虚型高, 两组比较有显著差异; 温毒瘀血型与其它两型 cAMP/cGMP 比较, 亦有显著性差异。

讨 论

我们对急白患者进行临床辨证, 分为温毒瘀血、痰热瘀痕和气阴两虚三型, 实验发现所有患者血红蛋白、血小板、血、尿 cAMP 含量降低; 骨髓中原+早、白/红比及血、尿 cGMP 含量升高, 与正常人比较有显著性差异。但各型降低和升高的程度不一样。从辨证分析, 温毒瘀血型和痰热瘀痕型属实证或虚中夹实, 而气阴两虚型以虚为主。从实验结果比较, 气阴两虚型血红蛋白, 血小板均低于痰热瘀痕型, 骨髓中白/红比和血、尿 cGMP 含量亦低于其他两型, 反映了虚证的特征。由于气阴两虚型 cGMP 较温毒瘀血型低, 因此 cAMP/cGMP 比值高于温毒瘀血型, 说明气阴两虚型 cAMP 与 cGMP 的相对平衡较温毒瘀血型为佳。Frederick 认为肿瘤细胞 cAMP 降低, cGMP 增高⁽⁴⁾。如果 cAMP

降低、cGMP 升高、cAMP/cGMP 比值降低与肿瘤生长有关的话, 那么是否可以认为温毒瘀血型的病情较气阴两虚型为重为急。温毒瘀血型临床常伴有感染, 中医学认为温热之邪易侵入血分、迫血妄行, 导致血溢脉外, 临床上有关较严重的发热和出血倾向, 实验也发现温毒瘀血型血小板计数极度降低, 也证实了这一点。

我们进一步对32例急白患者治疗前后观察, 15例气阴两虚型, 其中11例缓解, 缓解率73%; 10例痰热瘀痕型, 其中6例缓解, 缓解率60%; 温毒瘀血型7例, 其中1例缓解, 缓解率14%。经 χ^2 检验, $P<0.05$ 。说明各型的疗效有显著差异。实验认为, 中医学辨证分型具有一定的客观性, 并且提示临床治疗气阴两虚型效果较好, 痰热瘀痕型次之, 温毒瘀血型较差。

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Abstracts of Original Articles

Three Kinds of Herbal Tablets in the Treatment of Acute Appendicitis: Result of 150 Cases

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Since 1978, three kinds of herbal tablets, namely, Qing Jie (清解) tablet, Hua Yu (化瘀) tablet and Ba Huang (巴黄) tablet, have been prepared and used clinically in this institute in the treatment of acute appendicitis. 150 cases of acute simple appendicitis and mild suppurative appendicitis were reviewed, of which, 139 patients (92.7%) were cured, 9 were improved, with an overall effective rate of 98.7%. The mean hospitalization was 7.05 days. The herbal tablets are advantageous in their simplicity in application, rapid and satisfactory effects, and in saving large amounts of herbs. The three kinds of tablets correspond to three principles of treatment based on the theory of traditional Chinese medicine, i.e., Antipyrexia with detoxication, activation of blood circulation with dispersing stasis, and purgation to end stasis. Thus treatment on the basis of differentiating syndromes can be efficiently given with new preparations of herbal medicine, the effective components of which are extracted by scientific methods. Pharmacological studies demonstrated that Qing Jie tablets were bacteriostatic in vitro to *E. coli* and *Pseudomonas aeruginosa*; Hua Yu tablets could increase the blood flow of rat intestinal wall and inhibit the formation of cotton granulation; Ba Huang tablets could markedly enhance the intestinal peristalsis, hence a potent purgation.

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The Treatment of Leucopenia with Inspissated Granula of *Epimedium Sagittatum* and Its Effects on Serum Zn, Cu and Mg

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Chronic leucopenia of unknown etiology was treated with inspissated granula of *Epimedium sagittatum* (15 g b.i.d. ~ t.i.d. for 30~45 days) and changes of serum contents of Cu, Zn and Mg were evaluated with atomic absorption spectroscopy method before and after treatment. The therapeutic results of 14 cases are: 3 cured, 4 very effective, 4 effective and 3 of no effect. Before treatment, the determination of Cu, Zn, Mg and Cu/Zn ($M \pm SD$) contents for 22 cases of leucopenia and 36 cases of normal for control are 86 ± 13 , 77 ± 11 , 2230 ± 183 , 1.1264 ± 0.21 and 137 ± 22 , 124 ± 21 , 2300 ± 172 , 1.1297 ± 0.22 respectively. The contents of Cu and Zn decreased very remarkably ($P < 0.001$), but that of Mg and Cu/Zn are not very significant. For the 14 experimental cases, the Cu, Zn, Mg and Cu/Zn ($M \pm SE$) are 85.4 ± 3.29 , 77.8 ± 2.63 , 2293 ± 44.9 , 1.09 ± 0.04 and 82.5 ± 2.80 , 65.7 ± 4.97 , 2103 ± 40.5 , 1.28 ± 0.09 before and after treatment respectively. The Zn and Mg are significantly decreased ($P < 0.05$) and Cu/Zn is significantly elevated ($P < 0.05$).

The authors consider that there may be some relationships between Zn and Mg changes and the pathogenesis of leucopenia and differentiation of symptoms. The therapeutic effect of inspissated granula of *Epimedium sagittatum* may be closely related to the utilization of serum Zn and Mg. It is not simply due to a supplement of Zn and Mg but rather due to the balance of Yin and Yang regulation of the body.

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Typology of Acute Leukemia According to Symptom Differentiation and Observation on Its Relation to Blood, Bone Marrow and Cyclic Nucleotides in Serum and Urine

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Acute leukemia was classified into three types according to symptom differentiation: (1) Heat toxins with stagnant blood, (2) Aggregation of phlegm and heat, (3) Deficiency of both Qi and Yin. The blood, bone marrow and cyclic nucleotides in serum and urine in the 59 patients were observed. The experiment has proved that all indices in each type are significantly different from that of the control, but present differences among one another. The hemoglobin and platelet were higher in aggregation of phlegm and heat than in other two types. The ratio of white cell/red cell of marrow was lower in deficiency of both Qi and Yin than in other two types. The cGMP in serum and urine were also reduced greatly than heat toxins with stagnant blood. However the ratio of cAMP/cGMP was higher than the first group. The change between pretreatment and post treatment in 32 patients was further observed. The percentage of remission was higher in deficiency of both Qi and Yin, but lower in heat toxins with stagnant blood. The experiment has indicated that the typology of acute leukemia into three types according to Chinese traditional medicine could serve as the base of molecular pathology.

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