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重型病毒性肝炎血小板聚集功能的初步研究

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提 要 采用Born法对35例重肝病人进行了血小板聚集率（PAR）的动态观察，设急黄肝、慢活肝病人和正常人为对照组。结果表明，重肝病人PAR显著降低，降低程度依次为晚、中、早期，PAR与血清总胆红素及凝血酶元活动度分别呈显著负相关和正相关，提示其PAR降低与肝功能损害程度有一定平行关系，故对病情严重程度的判断有一定价值；交叉试验的结果提示重肝的PAR降低系血小板本身缺陷所致。文中对有关重肝体内外血小板状态进行了讨论。

关键词 重型病毒性肝炎；血小板聚集；血小板

肝病的血小板功能不全早就受到注意，但由于方法学方面的限制，其研究进展缓慢。70年代以后Born法开始被应用于测定肝病的血小板聚集（PA）功能，从而推动了其血小板功能的研究。有关病毒性肝炎（肝炎）的PA功能则至今尚未见较大系列观察的报道。为此，我们在35例重型肝炎（重肝）病人中进行了PA测定，目的是了解重肝的血小板功能变化，并对其机理作一初步探讨。

材料与方法

一、一般资料

1. 对象：重肝35例，其中亚急性重型11例，慢性重型24例，男28例，女7例；年龄15～56岁，平均36.9岁。对照组：正常人43例，平均年龄27.4岁；急性黄疸型肝炎（急黄肝）30例，平均年龄25.5岁；慢性活动性肝炎（慢活肝）35例，平均年龄30.9岁。对照组男女比例大致与重肝组相同。病人诊断皆符合1983年全国病毒性肝炎防治方案的标准。重肝中30例，慢活肝中25例有肝组织病理学检查依据。肝炎病例系我科1984年5月至1985年6月住院病人，正常人标本也在相应期间内采集。

2. 观察期间：（1）重肝组分五期：①早期：拟诊早期重肝且以后确诊为重肝者；②中期：重肝诊断明确，并出现明显并发症者；③好转期：病人症状、体征及实验室检查明显好转；⑤恢复期：上述指标接近正常或正常。（2）急黄肝、慢活肝于病程极期及恢复期各做一次。

二、检查指标

1. PA：采用PAM-2型PPP自动平衡血小板聚集仪[1]，系光电比浊法（Born法）。磷酸缓冲液为0.1M，pH7.4；抗凝剂为3.6%枸橼酸钠；重肝时血小板数往往降低，故适当增加取血量及采用较低速度离心以尽量使富血小板血浆（PRP）中血小板数不至太低，并以同样数量作对比标准；受检病人除2例晚期重肝病人检测期间用过小剂量丹参注射液（8 ml/日，静滴）外，其余病人检测期间均未使用过抑制PA的药物。聚集剂：肾上腺素（Adr）、二磷酸腺苷（ADP）。终浓度Adr为5 μM和1.25 μM两种，ADP为1 μm。血小板聚集率（PAR）指标有：I相聚集率（I相，系Adr加入后1分钟或ADP加入后40秒的PAR）、5分钟聚集率（5′A）及最大聚集率（MAR，系聚集剂加入后5分钟内最大聚集率）。交叉试验（cross-over experiments）[2]：要求病人MAR在20%以下，对照为正常人，PAR在正常范围以内，聚集剂为Adr 5 μm。

2. 其他：血小板计数、纤维蛋白原（Fbg）、凝血酶原活动度（PTA）和血清总胆红素（TB）均为常规方法，只在重肝组中测定。

结果

一、PAR

1. 各组标本分别以ADP和Adr为聚集剂所作PAR测定的结果（见表1）表明，除正常组I相外，各组Adr和ADP所致PAR均呈非常显著的相关（$P<0.001$），其中I相以ADP较高，MAR以Adr较高，但差异不显著（$P>0.05$）。

2. I相、5′A及MAR（见表2）均以重肝组最低，除5′A、MAR于重肝组早期与

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表1 Adr和ADP所致PAR的比较 (X±SD)

例次	相关系数*	I 相		相关系数	MAR	
	r	Adr 5μM	ADP 1μM	r	Adr 5μM	ADP 1μM
重 肝 31	0.806(p<0.001)	16.2±9.4	19.3±10.1	0.908(p<0.001)	32.4±17.2	28.3±15.6
急、慢肝 40	0.798(p<0.001)	27.9±12.3	30.3±10.5	0.909(p<0.001)	53.0±18.9	47.2±19.7
正 常 25	0.226(p>0.05)	30.2±11.9	37.1±9.6	0.784(p<0.001)	63.2±14.7	60.4±16.3

注：系将同一标本分别以Adr和ADP为聚集剂检测PAR，并对结果进行相关分析

慢活肝组差异不显著 (P>0.05) 外，各指标于各期与对照组均有非常显著差异 (P<0.001)；慢活肝组与正常组相比也显著降低 (P<0.05，P<0.01)；急黄肝组则无明显改变 (P>0.05)。重肝组动态观察结果（见表3）表明，各指标于中期与各期均无显著差异 (P>0.05)，晚期则较早期、好转期和恢复期低 (P<0.05，P<0.01)。急黄肝、慢活肝组极期和恢复期相比各指标均无显著差异 (P>0.05) （见表4）。

表2 重肝组各期PAR与对照组的比较 (X̄±SD)

例数	Adr 5μM			Adr 1.25μM		
	I 相	5′A	MAR	I 相	5′A	MAR
重肝早期 6	12.7±6.4	36.6±15.9	36.6±15.9	9.1±3.9	27.2±8.9	27.4±9.1
重肝中期 29	13.3±10.2	26.6±16.7	27.4±17.2	12.1±10.1	23.7±17.5	24.3±18.2
重肝晚期 19	8.1±4.9	18.6±13.3	18.9±13.2	6.6±4.9	17.2±12.8	17.4±12.7
急黄肝 29	28.1±12.5	57.6±18.8	57.6±18.8	22.1±9.0	52.8±18.0	53.2±18.0
慢活肝 33	19.8±10.2	40.6±17.1	41.2±16.8	16.3±9.1	37.3±19.5	37.8±19.5
正 常 43	27.6±9.9	60.3±17.1	60.3±17.1	23.6±8.8	51.1±19.9	54.1±19.9

注：除5′A、MAR于重肝组早期与慢活肝差异不显著 (P>0.05) 外，各指标于各期与各组均有非常显著差异

正常组于Adr1.25μM时检测例数为38

表3 重肝组各期PAR、血小板计数、Fbg的比较 (X̄±SD)

例数	PAR Adr 5μM			血小板计数	Fbg
	I 相	5′A	MAR	(万/mm³)	(mg/dl)
早 期 6	12.7±6.4	36.6±15.9$^{\Delta}$	36.6±15.9$^{\Delta}$	10.0±3.2	—
中 期 29	13.3±10.2	26.6±16.7	27.4±17.2	8.9±3.8	133±59
晚 期 19	8.1±4.9	18.6±13.3	18.9±13.2	7.2±3.5	101±25
好转期 11	19.0±9.8$^{\Delta\Delta}$	39.5±18.8$^{\Delta\Delta}$	40.6±18.2$^{\Delta\Delta}$	—	182±62$^{*\Delta\Delta}$
恢复期 11	20.3±8.7$^{\Delta\Delta}$	35.3±12.3$^{\Delta}$	36.2±12.7$^{\Delta}$	—	—

注：*、$^{\Delta}$ 分别表示该期与中、晚期差异显著 (P<0.05)，$^{**\Delta\Delta}$ 为差异非常显著 (P<0.01)

检测例数：血小板计数和Fbg于重肝中期为21，晚期为10；Fbg于好转期为6

3. 交叉试验：PRP与PPP（贫血小板血浆）交叉温育后，对照PPP加重肝病人PRP的PAR前后无显著变化 (t=0.474，P>0.05)；重肝病人PPP加对照PRP也未见

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表4 急黄肝、慢活肝组极期和恢复期PAR的比较（X±SD）

	病期	例数	I相	5′A	MAR
急黄肝	极期	25	29.3±13.4	59.2±18.8	59.2±18.8
	恢复期	25	24.0±7.6	56.1±11.3	56.2±11.3
慢活肝	极期	23	17.5±9.5	10.0±19.2	40.2±18.9
	恢复期	23	24.2±11.6	46.3±16.1	46.9±16.0

注：聚集剂为Adr 5μM

显著变化（t=1.226，P>0.05），但其中1例慢重肝病人PPP加入对照PRP后PAR明显增强，MAR从22.5%增高到65%。

二、血小板计数和Fbg

见表3。血小板计数随病情加重逐渐减少，但各期无显著差异（P>0.05）。Fbg于中、晚期与好转期分别有显著和非常显著差异（P<0.05，P<0.01）。

三、PAR与TB、PTA的关系

MAR与TB 60例次相关分析表明，二者呈非常显著负相关（r=-0.462，P<0.001）；MAR与PTA25例次呈显著相关（r=0.416，P<0.05）。

讨论

既往肝病的PA研究多以ADP为聚集剂，Adr很少使用。近年来有人提出临床研究可以Adr取代ADP。本实验对各组部分标本同时以ADP和Adr为聚集剂所作PA测定的结果表明，在肝炎的PA测定中完全可以Adr取代ADP。

本实验中PAR以重肝降低最显著，慢活肝次之，而急黄肝改变不明显；重肝组早期PAR即明显降低，以后随病情加重降低更著，并随病情好转而回升；MAR与TB、PTA分别呈非常显著负相关和显著正相关。这些都提示PAR降低与肝功能损害程度有一定平行关系，与Rubin等[3]在肝病患者中观察到的情况相似。这表明PAR测定对肝炎尤其是重肝病情严重程度的判断有一定价值。

肝病的PRP和PPP交叉试验国外已有少数报道。Thomas[4]首先观察到酒精性肝硬化病人PPP对正常人PRP有抑制效应，推测与血中FDP增高有关。但以后一些研究结果与之不一致，陆续发现肝病时血小板结构、功能和形态具有多种改变，故多数人认为，尽管FDP抑制有一定作用，但主要缺陷在血小板本身。我们对7例PAR显著降低的重肝病人所作交叉试验的初步结果提示，这些病人的血小板功能不全不能归咎于血浆因子的过多或不足。这也与Rubin等[2]、Owen等[5]在肝病中观察到的情况一致。其中1例PPP反而使正常人PRP的PAR增强，推测与该病人当时已处于低血压休克状态，血中致聚物（如血管活性物质）增高有关。由于本实验所作例数不多，其意义尚待进一步探讨。

已有一些研究表明重肝体内有明显的PA，如体内多种毒性物质的作用、DIC、单核细胞促凝血活性增高[6]、肝损害导致的血窦内皮细胞改变[7]以及红细胞聚集、血流速度降低所致的血小板受损等因素均可引起PA。最近Capel等[8]和Ingeberg等[9]均提出严重肝病时可有获得性血小板贮藏池病，表现为血小板在体内各种致聚物的作用下发生聚集、释放反应，导致δ颗粒空竭，从而使其功能降低。由此看来，重肝时体内的PA倾向正是其体外PA功能降低的一个重要原因。本实验中重肝组病人PAR显著降低，部分病人出现明显的血小板解聚现象，甚至不出现Ⅱ相聚集反应；血小板计数、Fbg与

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PAR一样，随着病情加重逐渐降低。这些变化均可能与其体内血小板活化有关。

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burned area, a"1-3-5" category method for children burn cases is suggested as follows:

1. Mild burns: The affected area is less than 10% TBSA.
2. Moderate burns: The affected area is between 11～30% TBSA.
3. Severe burns: The affected area is between 31～50% TBSA.
4. Extreme severe burns: The affected area is more than 50% TBSA.

(p.33)

The Measurement of Right Ventricle on Left Lateral Chest-films and Its Clinical Application

Dai Shuhua, et al (Department of Diagnostic Radiology, Second Teaching Hospital, Third Military Medical College)

On a left lateral chest radiogram, 3 points are determined: A is the apex of the sternal angle formed by the manubrium and the body of the sternum, B is the highest point of the contact surface between the anterio-superior heart border and the anterior chest wall, and C is the apex of the anterior costophrenic angle. The distances of AC and BC are measured. The ratio of BC:AC is considered as an index of the size of the right ventricle. On the basis of measuring 120 normal subjects, 0.54(0.46±0.04) is employed as the upper limit of normal values.

Left lateral chest radiogram is easy to take. The measuring procedure is simple. The results of this measurement proves to be valuable after the method has been applied clinically. In the evaluation of the size of the right ventricle, this new digital index is helpful in the analysis of serial radiograms. This measurement makes left lateral chest radiogram more useful in detecting cardiac abnormalities.

Key words: Left lateral chset radiogram; Sternal angle (p.35)

Platelet Aggregation in Patients with Severe Viral Hepatitis

Wang Yuming, et al (Department of Infectious Diseases, First Teaching Hospital, Third Military Medical College)

Platelet aggregation ratio (PAR) was assessed in 35 patients with severe viral hepatitis (SVH) with Born's method. The PAR of normal individuals, patients with acute icteric hepatitis, and those with chronic active hepatitis were

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also studied to serve as controls.

It was found that PAR decreased markedly in SVH patients, which was marked in the early stage of SVH, more marked in the intermediate stage, and most marked in the late stage. The changes of PAR were in negative correlation with those of serum total bilirubin, and in positive correlation with those of prothrombin activity. The reduction of PAR in SVH patients might be ascribed to the defect of platelets themselves as revealed by cross-over experiments. The results of this study indicate that PAR may be useful in judging the severity of SVH patients since the degree of PAR reduction parallels closely with the severity of liver damage. Finally the conditions of platelets in vivo and in vitro in SVH were discussed.

Key words: Severe viral hepatitis; Platelet; Platelet aggregation

(p.37)

Remission of Acute Myelofibrosis after Vitamin D_3 Therapy: A Case Report

Wang Kunrong, et al. (Department of Internal medicine, Second Teaching Hospital, Third Military Medical College.)

This article is to report the successful treatment of a case of acute myelofibrosis(AMF) with vitamin D_3. A male, aged 52, was admitted because of severe anemia(hemoglobin 19 g/L) for more than 6 months. He had been treated with various antianemic agents and fetal liver infusion for more than 20 months without any effects. He still had to live on repeated blood transfusions. After 2-month-treatment with vitamin D_3 injections, remarkable remission was obtained and his hemoglobin level steadily rose to 93 g/L without transfusion. In the follow-up period of 9 months, the patient did well. He took care of his own daily life and the hemoglobin level continued to rise to 114 g/L. The findings of the bone marrow improved correspondingly. No side reaction against vitamin D was observed. This is the first case of AMF treated successfully with vitamin D reported in our country.

It is known that vitamin D_3 can be converted in vivo through hydroxylation into $1,25(OH)_2D_3$. This active hormonal metabolite can inhibit the proliferation of abnormal megakaryocytes, decrease the synthesis of platelet-derived growth factor which can promote the genesis of myelofibrosis, and induce the maturation of myeloid cells towards monocytes, macrophages and granulocytes which can release collagenase to decompose collagen in the marrow aod improve myelofibrosis.

Key words: Acute myelofibrosis; Vitamin D_3 (p.40)

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