

109 例自身免疫性甲状腺疾病中医证型分析

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内容提要 本研究观察了109例不同中医证型的自身免疫性甲状腺疾病患者,不仅甲状腺功能方面有显著差异,而且细胞免疫和体液免疫功能方面也都具有不同的特点。观察结果提示,自身免疫性甲状腺病的阴虚与阳虚病理有其各自的物质基础。

关键词 自身免疫性疾病 甲状腺功能亢进症 甲状腺功能减退症 阴虚证 阳虚证

为了探讨免疫学与内分泌学某些指标在评估自身免疫性甲状腺疾病患者阴虚或阳虚时的作用,我们观察了89例甲状腺功能亢进症(甲亢)和20例因桥本氏病而致甲状腺功能减退症(甲减)的患者,现将患者在免疫功能和甲状腺功能方面的表现及其与中医证型的关系作一分析。

临床资料

一、观察对象:39例伴阴虚证的甲亢病患者中,女性72例,男性17例;年龄19~65岁,平均37.6岁。20例伴阳虚证的甲减患者均为未经过手术、抗甲状腺药物或放射性同位素治疗,并根据Fisher的诊断标准^①临床确诊者,均为女性,年龄30~64岁,平均43.6岁。此外还以82名健康献血者作为对照。

二、诊断依据:甲亢为临床有高代谢表现,血清总甲状腺素(T_4)、三碘甲状腺原氨酸(T_3)含量和甲状腺 ^{131}I 摄取率升高。甲减为临床有低代谢表现,血清促甲状腺素(TSH)升高或/和 T_4 或/和 T_3 含量降低,血清甲状腺球蛋白抗体(TGA)或/和甲状腺微粒体抗体(MCA)结合率明显高于正常值。

三、辨证标准:根据全国郑州会议制定的中医虚证辨证标准^②,阴虚证:主证(1)五心烦热;(2)咽燥口干;(3)舌红或少苔无苔。次证:(1)午后颧红;(2)便结而尿短赤;(3)盗汗;(4)脉细数。符合以上主证两项、次证一项者为阴虚。阳虚证:主证:(1)畏寒肢冷;(2)面目虚浮;(3)舌淡胖苔润。次证:(1)夜尿频多;(2)便溏而尿清长;(3)脉沉

微迟。符合以上主证两项、次证一项者为阳虚。

结 果

一、T淋巴细胞亚群分类:用抗人淋巴细胞的单克隆抗体进行间接荧光免疫法测定,并与健康献血者的标本进行对照,见表1

表1 三组患者T细胞及其亚群比较(%、 $\bar{x} \pm S$)

组 别	OKT ₄ ⁺ (n)	OKT ₈ ⁺ (n)	OKT ₄ ⁺ (n)
甲亢阴虚	53.9±4.2(23)	34.2±2.9(23)	24.8±2.8(23)
甲减阳虚	67.6±5.6(11)	48.6±6.3(11)	20.0±3.8(11)
健康对照	65.2±3.9(50)	41.5±1.7(48)	24.7±2.6(48)

*与健康人相比, $P<0.05$, **与健康人相比, $P<0.001$ 。
()内数据为例数,下同

甲亢阴虚与甲减阳虚证患者OKT₄⁺细胞百分率,前者显著减少,后者明显增多,从而可能导致T细胞内部亚群间比例关系失调。这从甲减阳虚证OKT₄⁺/OKT₈⁺(2.52±0.59)明显高于对照组(1.95±0.34) $P<0.001$ 看得很清楚。至于甲亢阴虚证患者T细胞计数是通过E-花环形成法与单克隆抗体(抗Leu或OKT)间接免疫荧光法同时进行检测的,它们的结果是一致的。

二、自身混合淋巴细胞反应(AMLR)能力与自身花环形成细胞(ARFC)百分率:甲亢阴虚证患者AMLR能力与健康者相比显示严重缺陷($P<0.05$)。该实验的反应细胞是由辅助性T细胞(OKT₄⁺细胞)承担的,联系表1的结果不难看出甲亢患者AMLR能力的缺陷与OKT₄⁺细胞减少密切相关。甲减阳虚证患者外周血淋巴

细胞中ARFC百分率明显增高($P<0.001$),表明自身识别能力增强。ARFC是一种不成熟的T细胞,它参与自身混合淋巴细胞反应过程。我们的工作已证明,ARFC增多与 OKT_4^+ 细胞及 OKT_4^+/OKT_8^+ 升高有关($P<0.05, 0.01$)。

AMLR与ARFC是两种反映时淋巴细胞自身反应性的主要体外实验方法,两者所代表的免疫学意义是一致的。从上述结果可以看出,甲亢阴虚与甲减阳虚证患者淋巴细胞自身反应能力呈相反趋势,前者被抑制,后者则过亢。

三、血清自身抗体含量:甲减阳虚患者血清TGA结合率为 $63.55\pm 13.76\%$ (正常值 $<30\%$),MCA结合率为 46.82 ± 12.76 (正常值 $<15\%$);甲亢阴虚患者血清抗TSH受体抗体活性为 $159.47\pm 142.18u/L$ (正常值 $0\sim 10u/L$),均显著高于正常值。

四、血清总 T_4 、 T_3 、TSH含量测定:见表2。

表2 三组患者血清总 T_3 、 T_4 、TSH含量比较($\bar{x}\pm S$)

组别	例数	T_4 (ng/ml)	T_3 (ng/ml)	TSH($\mu U/ml$)
甲亢阴虚	46	$225.28\pm 10.44^{\Delta}$	$4.38\pm 0.25^{\Delta}$	$1.86\pm 0.22^{\Delta}$
甲减阳虚	20	$52.71\pm 42.33^*$	$0.87\pm 0.57^*$	$36.53\pm 28.46^*$
健康对照	35	98.40 ± 4.42	1.48 ± 0.07	8.90 ± 0.63

*同健康人对照组相比, $P<0.001$; Δ 与甲减阳虚组相比, $P<0.001$ 。

甲亢阴虚患者血清总 T_4 、 T_3 含量升高,TSH含量降低,而甲减阳虚患者血清总 T_4 、 T_3 含量降低,TSH含量升高,与健康人相比均有非常显著的差异, $P<0.001$ 。

五、血浆环核苷酸含量测定:见表3。

表3 甲亢阴虚与甲减阳虚证患者血浆环核苷酸含量比较($\bar{x}\pm S$)

组别	cAMP(Pmol/ml)	cGMP(Pmol/ml)	cAMP/cGMP
甲亢阴虚	$32.87\pm 1.60^{\Delta}$ (46)	4.49 ± 0.23 (46)	8.03 ± 0.47 (46)
甲减阳虚	$12.91\pm 7.18^*$ (11)	5.93 ± 4.56 (11)	2.64 ± 1.07 (11)
健康对照	23.30 ± 0.58 (78)	5.95 ± 0.36 (45)	5.20 ± 0.64 (31)

*与健康人相比, $P<0.001$; Δ 与甲减阳虚组相比, $P<0.001$ 。

甲亢阴虚患者血浆cAMP含量明显高于健康人,而甲减阳虚患者血浆cAMP含量低于健康人(P 均 <0.001)。

讨 论

甲亢与甲减两者功能状态相反,阴虚与阳虚在辨证上是相互对立的。本文表明,甲亢阴虚与甲减阳虚证在淋巴细胞自身反应性、T淋巴细胞及其亚群细胞数、血清甲状腺激素水平和血浆环核苷酸含量等方面多呈相对状态,处于两个极端。结合赵伟康等^[3~5]关于甲状腺疾病阴虚阳虚辨证同尿儿茶酚胺、17-羟皮质类固醇排量水平,同血浆环核苷酸含量,血清甲状腺激素水平的关系,说明中医不同证有其不同的病理生理特点,自身免疫性甲状腺疾病的阴虚与阳虚病理有其各自的物质基础的。此外还有研究发现,辨证为阴虚血瘀和气阴虚血瘀型的冠心病心绞痛患者免疫功能呈紊乱状态。本虚与细胞免疫低下尤其是T辅助细胞与T抑制细胞的失衡关系密切,标实与体液免疫亢进有关。这从免疫学方面,以客观的检测资料支持了上述的观点。作者并据此指导治疗,着重扶正固本以增强细胞免疫,恢复T辅助与抑制细胞的协调;祛邪(化瘀)以抑制体液免疫亢进,抑制病理性自身抗体的产生和免疫复合物的形成,在临床上取得良效。

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Analysis on the TCM Syndromes of the Patients with Autoimmune Thyroid Diseases

—Observation on the Change of Thyroid and Immune Functions in 109 Patients

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Eighty-nine cases of hyperthyroidism and 20 cases of hypothyroidism caused by Hashimoto's thyroiditis were observed in order to analyse the thyroid and immune functions of the patients, and their relationship with the syndromes of TCM. The results showed that, in the patients with Yin(阴) deficiency syndrome, the contents of total T_4 , T_3 were higher than normal and TSH lower than normal, while in Yang(阳) deficient patients, the contents of total T_4 , T_3 were lower than normal and TSH higher than normal. This results suggested that the states of thyroid functions were closely related to the TCM syndromes. It was also found that the percentage of OKT 4⁺ cells and the self-recognizing ability of lymphocytes were lower than normal in patients with hyperthyroidism and Yin deficiency. While in patients with hypothyroidism and Yang deficiency, they were higher than normal. These meant that the abilities of lymphocyte autoreaction in Yin deficient patients were in contrary tendency with those in Yang deficient patients. The former had the manifestation of over-inhibition while the latter, hyperaction. Besides, the contents of auto-antibodies were higher than normal in both the patients with hyperthyroidism and hypothyroidism, which manifested itself as a common character of autoimmune thyroid diseases. The results indicated that there were common characters as well as individual characters of thyroid and immune functions between hyperthyroid patients and hypothyroid patients, and these characters might well be the material bases of various syndromes in TCM.

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Investigation on Blood Stasis Syndrome of Patients with Gastric Malignant Tumor

Pre-, Post-Operation and Before Death

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In the past three years, the authors observed substance of tongue and 5 indexes of blood coagulation (AT-III, Fn, Fa, VIII R:Ag and β TG) for a long time in 140 patients of gastric malignant tumor pre-operation, one month post-operation and 3 months before death. All patients were verified as gastric carcinoma by pathological section. The results showed that the positive rate of substance of tongue in patients pre-operation was as high as 58% (51/88), 5 indexes of blood coagulation in patients had obvious difference ($P < 0.001$) comparing to that of healthy persons. This implied it existed relationship between gastric malignant tumor and blood stasis in TCM, and accorded with diagnosis of blood stasis syndrome. With the resection of tumor focus, the states of blood stasis in patients had been improved to a certain extent. But the positive rate of substance of tongue post-operation was still as high as 51.1% (45/88) comparing to that pre-operation ($P > 0.05$). 5 indexes of blood coagulation in patients post-operation had no obvious improvement comparing to those pre-operation. This showed that the simple resection did not basically improve blood stasis in patients. The another important result was that the substance of tongue and 5 indexes of blood coagulation of 23 patients in last 3 months before death had more obvious blood stasis comparing to those post-operation even those pre-operation. This explained that blood stasis is one of the main characters of gastric malignant tumor before death. In conclusion, the extent of blood stasis syndrome can be used as an objective index to judge seriousness and prognosis of gastric malignant tumor patients' condition.

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Effects of *Ligusticum wallichii* on the Plasma Levels of β -TG, PF₄, TXB₂ and 6-keto-PGF_{1 α} in Rabbits under Acute Experimental Cerebral Ischemia

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By occluding the bilateral carotid arteries of rabbits to produce bilateral partial cerebral ischemia, and by using RIA and ELISA to measure the levels of Beta-thromboglobulin (β -TG),