

原发性胆汁性肝硬化诊断和治疗的进展

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Recent advances in diagnosis and treatment of primary biliary cirrhosis

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Abstract

Primary biliary cirrhosis (PBC) is a chronic progressive cholestatic autoimmune liver disease characterized by the destruction of small intrahepatic bile ducts and the presence of highly specific serum antimitochondrial antibodies (AMAs). In this article, we will review the clinical, serological and histopathological features of PBC as well as the advances in the diagnosis and differential diagnosis of PBC. In addition, this article systematically describes the advances in the treatment of PBC, and the treatments include ursodeoxycholic acid (UDCA), budesonide, methotrexate (MTX), farnesoid X receptor (FXR) agonists, cyclosporine A, bezafibrate, rituximab, bone marrow-derived mesenchymal stem cell (BM-MSC) transplantation, and liver transplantation. At present, liver transplantation is the only option with known therapeutic benefit for end-stage PBC patients.

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Key Words: Autoimmune liver diseases; Primary biliary cirrhosis; Diagnosis; Therapy

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摘要

原发性胆汁性肝硬化(primary biliary cirrhosis, PBC)是一种慢性进行性胆汁淤积性自身免疫性肝病,以肝内小胆管破坏及血清高特异性抗线粒体抗体(antimitochondrial antibodies)升高为特征。本文详尽阐述了PBC的临床特征、血清学特征、组织病理学特征以及诊断和鉴别诊断的进展。此外,本文还系统地阐述了PBC的治疗进展,包括熊去氧胆酸(ursodeoxycholic acid)、布地奈德(budesonide)、甲氨蝶呤(methotrexate)、法尼酯X受体(farnesoid X receptor)激动剂、环孢素A(cyclosporine A)、苯扎贝特(bezafibrate)、利妥昔单抗(rituximab)、骨髓间充质干细胞(bone marrow-derived mesenchymal stem cells)移植以及肝移植。目前,肝移植仍是治疗终末期PBC患者的唯一有效方法。

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关键词: 自身免疫性肝病; 原发性胆汁性肝硬化; 诊断; 治疗

核心提示: 原发性胆汁性肝硬化(primary biliary cirrhosis, PBC)是免疫介导的慢性胆汁淤积性肝病,血清抗线粒体抗体(antimitochondrial antibodies)升高为其特异性诊断指标,慢性非化脓性破坏性胆管炎为其组织病理学特征,熊去氧胆酸(ursodeoxycholic acid)的早期治疗明显改善了PBC的预后,肝移植仍是治疗终末期PBC的唯一有效方法。

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■背景资料

原发性胆汁性肝硬化(primary biliary cirrhosis, PBC)是一种慢性胆汁淤积性肝病,多见于中年女性,为自身免疫性肝病的一种类型,血清抗线粒体抗体(antimitochondrial antibodies, AMAs),尤其是AMA-M2亚型滴度升高对PBC具有特异性诊断价值。随着对PBC的认识加深以及对AMAs/AMA-M2检查的普遍推广,PBC的发病率呈逐年增加趋势。目前,PBC的基础与临床研究已引起国内外学者关注。

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■ 研发前沿

骨髓间充质干细胞(bone marrow-derived mesenchymal stem cells, BM-MSCs)是一类具有多向分化潜能的多能干细胞。多项动物实验表明, BM-MSC不仅能缓解各种损伤导致的肝纤维化和肝硬化, 而且能明显提高急性肝损伤动物模型的生存率、降低肝损伤程度以及抑制肝细胞凋亡。因此, BM-MSC移植有望成为治疗终末期PBC的治疗方案。

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0 引言

原发性胆汁性肝硬化(primary biliary cirrhosis, PBC)是一种免疫介导的慢性胆汁淤积性肝病, 为自身免疫性肝病(autoimmune liver diseases, AILDs)的一种类型, 以慢性阻塞性黄疸、血清特异性抗线粒体抗体(antimitochondrial antibodies, AMAs)升高、组织病理学示慢性非化脓性破坏性胆管炎为主要特征^[1]。PBC的发病机制可能涉及遗传易感性、自身免疫、胆管上皮细胞的衰老、自噬、凋亡以及环境因素等^[1]。此外, microRNAs^[2]、外周血单个核细胞的基因表达谱异常^[3,4]、转化生长因子- β 1信号通路^[5]、白介素-12/白介素-23信号通路^[6]、核因子- κ B信号通路^[6]、肿瘤坏死因子信号通路^[6]、磷脂酰肌醇信号通路^[6]以及hedgehog信号通路^[6]等可能也参与其发病机制。PBC患者多数为女性, 主要表现为乏力和皮肤瘙痒, 血清AMAs阳性为PBC的特异性诊断指标^[1]。熊去氧胆酸(ursodeoxycholic acid, UDCA)的治疗明显改善了PBC患者的预后, 但仍有1/3的PBC应用UDCA治疗无效, 肝移植是治疗终末期PBC患者的唯一有效方法^[1]。本文就PBC的诊断和治疗进展概述如下。

1 流行病学

PBC的患病率可能因种族和地域差别而有所不同^[7]。流行病学调查资料显示, 荷兰的PBC时点患病率为13.2/100000^[7], 意大利为1.91/100000-40.2/100000^[8], 爱尔兰为38.3/100000^[9], 而我国则为49.2/100000^[10]。82%的PBC患者为女性, 中位年龄62岁, 平均生存期15年^[9]。46.6%的PBC合并至少一种结缔组织疾病(connective tissue diseases, CTDs)^[11]。其中, 36.2%的PBC合并干燥综合征(sjogren's syndrome, SS), 2.8%合并系统性硬化症(systemic sclerosis, SSc), 3.7%合并系统性红斑狼疮(systemic lupus erythematosus, SLE), 2.8%合并类风湿关节炎(rheumatoid arthritis, RA), 3.1%合并多发性肌炎(polymyositis, PM)^[11]。晚近研究显示, PBC的发病率和患病率呈逐年增加趋势, 但与吸烟、初潮年龄、初孕年龄以及妊娠次数等因素无关^[7]。

2 临床特征

尽管1/3的PBC可能多年无症状, 但多数无症状

者于5年内出现瘙痒和疲倦^[12]。瘙痒是PBC最典型的早期症状, 大约见于20%-70%的患者, 通常先于黄疸数月至数年^[12]。疲倦亦为PBC的早期症状, 发生于约78%的患者^[12]。门静脉高压甚至肝肝硬化前即可出现, 但腹水、食管静脉曲张(esophageal varices, EV)及肝性脑病通常为晚期PBC并发症^[12]。同样, 肝细胞癌(hepatocellular carcinoma, HCC)的发生率在晚期PBC亦逐年增加^[12,13]。Azemoto等^[14]发现, 大约10%的PBC患者以门静脉高压为首发症状。Ikeda等^[15]对256例早期PBC研究显示, 22例于诊断时即有EV, 且血清碱性磷酸酶(alkaline phosphatase, ALP)升高及血小板降低与早期PBC的EV显著相关, 提示这2项指标有助于预测早期PBC的EV。Ali等^[16]证实, 6%的早期PBC存在EV。Tomiyama等^[17]对210例PBC随访发现, 11例(5.2%)并发HCC, 且与PBC的肝纤维化程度显著相关。PBC常并发间质性肺病(interstitial lung disease, ILD)^[18]。Shen等^[19,20]对178例PBC研究发现, 28例(15.7%)并发ILD^[19], 21例(11.8%)并发肺动脉高压(pulmonary hypertension, PH)^[20], 前者多合并雷诺现象和其他CTDs^[19], 后者则与门静脉高压和免疫失调密切相关^[20]。Bektas等^[21]对37例PBC研究显示, 17例(45.9%)存在食管运动功能障碍, 其中非特异性食管运动障碍10例, 食管运动减弱5例, 胡桃夹食管1例, 食管下括约肌高压1例。Wang等^[11]发现, PBC合并SS、SSc、SLE、RA及PM者, 因同时具有相应疾病特征, 使临床表现更为复杂。此外, PBC合并乙型肝炎^[22]、丙型肝炎^[22,23]、自身免疫性胰腺炎^[24]、肝脏假性淋巴瘤^[25]、原发性肝黏膜相关淋巴组织(mucosa-associated lymphoid tissue, MALT)淋巴瘤^[26]以及代谢综合征^[27]的诊断仍面临挑战。

3 血清学特征

绝大多数PBC患者很容易检测到AMAs, 而极少数PBC(<5%)即使应用重组诊断技术, AMAs仍为阴性^[1]。AMAs有9个亚型, 其中AMA-M2、-M4、-M8、-M9与PBC有关, 这4个亚型对PBC的诊断具有相对特异性^[1]。Hu等^[28]研究显示, AMAs对PBC的敏感性和特异性分别为84.5%和97.8%, AMAs是较AMA-M2更好、更全面的PBC诊断标志物^[28], 这似乎颠覆了传统的AMA-M2较AMAs对PBC更为特异的观点。除AMAs外, 应用间接免疫荧光法(indirect immunofluorescence, IIF)可在50%的PBC患者检

测到特异性的抗核抗体(antinuclear antibodies, ANAs),尤其在AMAs阴性的PBC患者更为常见,提示ANAs可作为PBC的辅助血清学标志物^[29]. PBC特异的ANAs包括抗多核点抗体(SP100、PML、NDP52、SP140)、抗核孔抗体(gp210、p62)、抗核膜抗体(核板层蛋白、核板层蛋白B受体)以及抗着丝粒抗体(anti-centromere antibody, ACA)^[1]. Gatselis等^[30]研究发现,4.5%的PBC抗gp210阳性,12.7%的PBC抗SP100阳性,这2种特异性ANAs与PBC的严重程度有关. Valour等^[31]报道1例AMAs阴性者抗gp210阳性对PBC诊断的高度特异性. Mytilinaiou等^[32]证实了SP100、PML阳性对PBC的特异性诊断价值. Liberal等^[33]认为,30%的PBC患者ACA阳性,且与胆管损伤和门静脉高压程度显著相关. Mandai等^[34]对37例PBC研究发现,12例(32%)ACA阳性,且与慢性肾脏疾病(chronic kidney disease, CKD)及估计肾小球滤过率(estimated glomerular filtration rate, eGFR)下降密切相关,提示评估ACA和eGFR对于预防PBC患者的CKD进展十分必要. Shi等^[35]证实,ACA阳性可作为失代偿期PBC的预测因素之一. 此外,血清ALP、 γ -谷氨酰转肽酶(gamma glutamyl transpeptidase, γ -GT)、胆红素以及IgM升高在PBC十分常见^[15]. 但Kawaguchi等^[36]报道1例血清IgA、IgM、IgG均显著降低的PBC病例似乎提示Ig介导机制对PBC的进展并非必要.

4 组织病理学特征

PBC的组织病理学特征为慢性非化脓性破坏性胆管炎^[1],经典的组织病理学分期包括I期(胆管炎期)、II期(胆管增生期)、III期(纤维化期)和IV期(肝硬化期)^[37]. Drebber等^[37]对252例PBC肝活检组织观察发现,>80%的PBC具有典型的组织病理学特征,主要表现为破坏性肉芽肿性小胆管炎及淋巴细胞浸润. Turhan等^[38]研究显示,肉芽肿不仅见于PBC初期,也见于PBC其他3期,55.6%的PBC肉芽肿有3期疾病,除管周肉芽肿外,腺泡内肉芽肿也可见到. You等^[39]发现,经典树突状细胞(dendritic cell, DC)CD11c标志物在PBC肉芽肿呈高度表达,CD11c阳性PBC肉芽肿患者的血清IgM水平显著升高,CD11b(DC的未成熟标志物)使MHC II、IL-23、CCR7和CD83表达下调,使C1q表达上调,PBC肉芽肿周围可见大量B细胞、IgM阳性浆细胞及巨噬细胞浸润,提示DC对肉芽肿的发病机制至关重要,

PBC肉芽肿可能由未成熟DC与IgM相互作用所致. 最近,日本学者Bioulac-Sage^[40]结合慢性胆管炎(纤维化、胆汁淤积、胆管缺失)、胆管炎活性(cholangitis activity, CA)、肝炎活性(hepatitis activity, HA)等3种因素,对肝穿刺活检组织采用新的PBC组织学分级系统,分别将PBC分为CA 0-3级和HA 0-3级. Harada等^[41]采用这一新的系统评估发现,CA和HA间互无关联,新系统能正确评估PBC. Kakuda等^[42]和Chan等^[43]研究证实,新系统较经典的PBC分期标准更为有效. Daniels等^[44]研究显示,PBC门管区主要以IgM染色为主,而自身免疫性肝炎则以IgG染色为主. Kikuchi等^[45]发现,PBC过多的IgM来源于其脾脏的淋巴滤泡. 此外,非酒精性脂肪性肝炎(nonalcoholic steatohepatitis, NASH)是以肝细胞丧失、脂肪变性、气球样变、炎性坏死及纤维化形成为特征的病理状态,常见于肥胖患者^[46]. Hindi等^[47]发现,NASH和体质量指数(body mass index, BMI) ≥ 25 kg/m²与PBC的胆管损伤和纤维化程度密切相关,BMI有望成为PBC纤维化进展的有效无创性预测工具.

5 诊断

根据美国肝脏病研究学会(American Association for Study of Liver Diseases, AASLD)PBC诊疗指南^[48]和欧洲肝脏研究学会(European Association for the Study of the Liver, EASL)胆汁淤积性肝病临床实践指南^[49],如果患者血清ALP升高,影像学检查除外胆道梗阻,AMAs高滴度阳性($\geq 1:40$),即可诊断PBC,肝活检主要用于AMAs阴性患者或对PBC的组织病理学分期. Bowlus等^[50]认为,PBC的诊断至少符合3条关键指标中的2条,即持续的血清ALP升高、血清AMAs阳性以及肝组织学示PBC. 此外,特异性ANAs对AMAs阴性的PBC具有诊断价值,且与PBC的进展相关^[50].

6 鉴别诊断

6.1 原发性硬化性胆管炎(primary sclerosing cholangitis, PSC) PSC是一种慢性胆汁淤积性自身免疫性肝病,以肝内胆管和/或肝外胆管的弥漫性炎症、同心性纤维化、局灶性或节段性狭窄为主要特征,最终发展至肝硬化或肝衰竭^[51]. PSC的典型临床表现为慢性胆汁淤积和皮肤瘙痒,常并发炎症性肠病,血清ANAs、SMA、AMAs及p-ANCA等多种自身抗体可以阳性,但以p-ANCA特异性明显^[51].

■ 相关报道

6-乙基鹅去氧胆酸(obeticholic acid, OCA)是鹅去氧胆酸(cchenodeoxycholic acid, CDCA)的一种衍生物,是治疗胆汁淤积性肝病的新药. 初步研究显示,OCA对其受体的兴奋作用是CDCA的100倍. OCA的问世,有望为PBC的治疗开辟新的途径.

■创新盘点

本文详尽阐述了PBC的临床特征、血清学特征及组织病理学特征,重点阐述PBC在诊断和治疗领域的最新进展。

6.2 IgG4相关硬化性胆管炎(immunoglobulin G4-related sclerosing cholangitis, IgG4-SC) IgG4-SC是一种新近认识的以血清IgG4升高、慢性进行性阻塞性黄疸、弥漫性或局限性IgG4阳性浆细胞和淋巴细胞组织浸润、纤维化以及闭塞性静脉炎为特征的慢性炎症性疾病,常并发自身免疫性胰腺炎,其临床、生化及影像学特征与PSC相似,血清 γ -GT、ANAs、AMAs及p-ANCA可升高^[52]。

6.3 自身免疫性肝炎(autoimmune hepatitis, AIH) AIH是一种免疫介导的肝实质损害,多发于女性,以血清转氨酶和IgG升高、自身抗体阳性、组织学示界面性肝炎以及对免疫抑制剂应答为特征^[53]。AIH主要表现为疲劳、食欲不振、黄疸、肝脾肿大及皮肤瘙痒等症状,部分患者可进展至肝硬化或肝衰竭,血清ANAs、SMA、抗LKM-1、抗SLA以及抗LP等自身抗体可阳性^[53]。

6.4 AIH-PBC重叠综合征 AIH-PBC重叠综合征是指患者在同一时间段或病程中同时具备AIH和PBC两种疾病的临床、血清学、生物化学以及组织学特征的一种疾病状态,常表现为厌食、黄疸、乏力等症状,血清ANAs、AMAs阳性,ALP、 γ -GT及IgG显著升高^[54]。

6.5 AIH-PSC重叠综合征 AIH-PSC重叠综合征是指患者在同一时间段或病程中同时具备AIH和PSC两种疾病的临床、血清学、组织学或影像学特征的一种疾病状态,主要表现为疲劳、厌食、皮肤瘙痒等症状,血清ALP、 γ -GT升高,血清ANAs、SMA、LKM-1及p-ANCA可阳性^[54]。

6.6 PBC-PSC重叠综合征 PBC-PSC重叠综合征是指患者同时具备PBC和PSC两种疾病的临床、组织学及影像学特征的一种疾病状态,目前仅有个别病例报告^[54]。

6.7 PBC-IgG4-SC重叠综合征 PBC-IgG4-SC重叠综合征是指患者同时具备PBC和IgG4-SC两种疾病的临床、血清学、组织学及影像学特征的一种疾病状态,目前仅见1例病例报告^[54]。

7 自然史和预后

PBC的自然史模式在过去20年发生了巨大变化^[55]。目前,越来越多的组织学早期PBC在无症状时即被诊断并接受治疗,预后远好于从前,但这些数据主要来源于发达国家,发展中国家的结果却大相径庭,多数患者是在有症状和肝硬化时被诊断为PBC^[55]。PBC的自然史包括临床前期、无症状期、症状期及肝功能不全期4个阶段^[55]。有

症状PBC的平均生存期为5-8年,约25%于10年内并发肝衰竭,一旦黄疸进行性加重,即进入终末期,血清胆红素达100 μ mol/L,伴有或不伴有消化系出血、腹水或肝性脑病,终末期可持续2年^[55]。Baldursdottir等^[9]对168例PBC研究发现,82%为女性,I期、II期PBC的总发病率分别为2.0/100000和2.5/100000,28%PBC的III期、IV期肝纤维化在20年内并无显著变化,PBC的平均生存期为15年,5例接受了肝移植治疗。

8 治疗

8.1 熊去氧胆酸(ursodeoxycholic acid, UDCA) UDCA是目前唯一被美国肝脏病研究学会(AASLD)推荐并被美国食品和药品管理局(Food and Drug Administration, FDA)批准用于治疗PBC的药物^[48]。UDCA是一种亲水性天然胆汁酸,具有扩张亲水性胆汁酸池、直接促进胆汁酸分泌、抗炎以及抑制肝细胞凋亡等功能^[55],其机制还可能涉及趋化因子CXCR3轴对PBC的介导作用^[56]。UDCA的最佳使用剂量为13-15 mg/(kg \cdot d),分次或一次顿服^[55]。UDCA不仅可显著改善PBC的肝功能指标,同时也可以改善肝脏的组织学特征,从而阻止肝纤维化及肝硬化的进展,提高生存质量,延长生存期^[57]。Zhang等^[57]的一项Meta分析显示,UDCA可部分缓解PBC的皮肤瘙痒和黄疸,有效降低血清ALT、ALP、IgG及IgM水平,延缓组织学进展,减少死亡率和肝移植手术。Boberg等^[58]证实,UDCA不仅降低PBC死亡率,还可节省治疗费用。UDCA对PBC的生化反应可强力预测其远期疗效,以便及时确认是否应采取其他治疗方法,多数以UDCA治疗1年的生化反应为预测标准^[59]。Zhang等^[59]发现,对UDCA有生化反应者于治疗头3 mo最为显著,而后则维持相对稳定数月之久。因此,UDCA治疗第6个月的生化反应可替代治疗1年的生化反应,这有助于尽快确认是否应采取新的治疗措施^[59]。Lammert等^[60]研究显示,76%的PBC对UDCA治疗有生化反应,24%则无反应,前者不良事件的发生率显著低于后者。Carbone等^[61]发现,UDCA对PBC的治疗反应与性别和年龄密切相关,男性PBC对UDCA的反应率显著低于女性(72% vs 80%, $P<0.05$),70岁以上PBC对UDCA的反应率显著高于30岁以下者(90% vs 50%, $P<0.0001$)。

8.2 布地奈德(budesonide) 布地奈德是一种糖皮质激素受体/孕烷X受体(pregnane X receptor, PXR)激动剂,涉及胆汁酸(bile acids, BAs)的合

成、代谢及转运,对于早期PBC患者,布地奈德与UDCA短期联合治疗效果显著^[62]。2009年欧洲肝脏研究学会胆汁淤积性肝病临床实践指南^[49]建议,对于无肝硬化(组织学分期 I -III期)的PBC患者给予UDCA联合布地奈德6-9 mg/d治疗。Rabahi等^[63]对UDCA单独治疗无反应的PBC采用UDCA(13-15 mg/d)、布地奈德(6 mg/d)及霉酚酸酯(1.5 g/d)联合治疗发现,三联疗法对于无肝硬化的重症PBC患者疗效显著。

8.3 甲氨蝶呤(methotrexate, MTX) MTX作为免疫抑制剂,具有抑制淋巴细胞增生、抑制中性粒细胞产生粒细胞和单核细胞趋化因子以及抑制白介素6活性等作用,对于UDCA治疗无反应者,联合MTX治疗不仅能改善PBC症状,也显著改善其肝功能指标^[64]。Leung等^[65]对PBC采用UDCA联合MTX治疗10年后发现,二联疗法可持续缓解PBC的临床症状。此外, Kaplan等^[66]研究显示,对UDCA反应不佳者,应用秋水仙碱和MTX联合治疗可显著改善PBC的肝脏酶学指标及组织学特征。

8.4 法尼酯X受体(farnesoid X receptor, FXR)激动剂 6- α -乙基鹅去氧胆酸(obeticholic acid, OCA)是一种FXR激动剂,在BAs的肝肠循环中起重要作用^[62]。OCA是半合成的鹅去氧胆酸(chenodeoxycholic acid, CDCA)的衍生物,可激活FXR,具有抗淤胆、抗纤维化作用^[62]。Le Blanc等^[67]研究发现,FXR激活可改善胆汁淤积动物模型的肝损伤,减少胆汁BAs的输出,促进富含HCO₃⁻的胆汁分泌。初步研究证实, OCA单独或联合UDCA治疗可显著改善PBC的生化指标^[62,64]。

8.5 环孢素A(cyclosporine A) 环孢素A可抑制机体的某些免疫反应而被用于PBC的辅助治疗,环孢素A不仅可改善瘙痒症状,还可以降低肝功酶学指标^[68]。Shiba等^[68]发现,环孢素A可有效预防PBC的肝移植术后复发。此外,有研究显示,亲环素(cyclophilin)是环孢素A的细胞内受体,介导环孢素A的免疫抑制作用,同时参与信号传导和免疫调节,亲环素抑制剂在PBC的治疗中也发挥作用^[69]。

8.6 苯扎贝特(bezafibrate) 苯扎贝特为常用的降血脂药物,是一类人工合成的过氧化物增殖体激活受体 α (peroxisome proliferator-activated receptor α , PPAR α)的配体。Lens等^[70]研究显示,苯扎贝特联合UDCA治疗不仅明显缓解PBC的瘙痒症状,而且也显著降低其血清ALP、 γ -GT及

ALT水平。Honda等^[71]认为,对UDCA应答不佳的早期PBC而言,苯扎贝特是抑制胆汁淤积的强力PPAR α /PXR双重激动剂。

8.7 利妥昔单抗(rituximab) 利妥昔单抗是一种选择性消耗B细胞的抗CD20单克隆抗体,其与B淋巴细胞上的CD20结合,进而引发B细胞溶解的自身免疫反应^[72]。B细胞参与PBC发病机制中免疫机制的非化脓性胆管炎和胆管破坏的炎性改变^[72]。Myers等^[72]研究显示,利妥昔单抗选择性地消耗B细胞安全可行,并与PBC的自身抗体生成下降显著相关,但对UDCA反应不佳者的血生化指标却作用有限。Lazrak等^[73]研究证实,尽管B细胞在PBC的发病机制中至关重要,但利妥昔单抗不能有效改善PBC的肝功能指标。

8.8 骨髓间充质干细胞(bone marrow-derived mesenchymal stem cells, BM-MSC)移植 BM-MSC是有多向分化潜能的多能干细胞,具有调节免疫、阻止炎性介质释放以及修复病损组织的功能,为治疗PBC提供了新的途径^[64]。动物实验表明, BM-MSC对各种损伤引起的肝纤维化和肝硬化均有明显的改善作用^[64]。Wang等^[74]发现, BM-MSC移植可调节全身免疫反应,促进PBC小鼠模型的肝脏炎症恢复,提示同种异体BM-MSC的临床应用有望用于治疗早期PBC患者。此外, Roderfeld等^[75]研究证实, BM-MSC移植可明显缓解PBC小鼠模型的肝纤维化。

8.9 肝移植 PBC的早期诊断及UDCA的临床应用明显改善了PBC的预后,但仍有1/3的PBC应用UDCA治疗无效,肝移植仍是终末期PBC患者的唯一有效治疗方法^[1]。肝移植术后的5年生存率接近80%,但术后复发问题仍十分普遍,少数肝移植术后患者的供肝失活以及排斥反应问题也较严重^[76]。

9 结论

PBC是一种慢性胆汁淤积性肝病,对于早期PBC及时采用UDCA治疗不仅能缓解症状、降低肝脏酶学指标,也能有效延缓PBC的进展,对于UDCA反应不佳者,应及时联合其他免疫抑制剂治疗。BM-MSC为治疗PBC提供了新的思路和途径,但仍有待于更广泛的临床验证。肝移植仍是终末期PBC患者的唯一有效治疗措施,但术后复发问题仍有待解决。

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■应用要点

本文结合大量国内外文献,详尽阐述PBC在诊断和治疗领域的最新进展,对临床工作有重要指导意义。

■同行评价

本文结合大量国内外文献, 详尽阐述了PBC在流行病学、临床特征、血清学特征、组织病理学特征和治疗领域的最新进展, 对临床诊治工作具有重要的指导意义。

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• 消息 •

《世界华人消化杂志》再次入选《中文核心期刊要目总览》 (2011年版)

本刊讯 依据文献计量学的原理和方法,经研究人员对相关文献的检索、计算和分析,以及学科专家评审,《世界华人消化杂志》再次入选《中文核心期刊要目总览》2011年版(即第六版)核心期刊。

对于核心期刊的评价仍采用定量评价和定性评审相结合的方法。定量评价指标体系采用了被引量、被引量、他引量、被摘率、影响因子、被国内外重要检索工具收录、基金论文比、Web下载量等9个评价指标,选作评价指标统计源的数据库及文摘刊物达到60余种,统计到的文献数量共计221177余万篇次,涉及期刊14400余种。参加核心期刊评审的学科专家达8200多位。经过定量筛选和专家定性评审,从我国正在出版的中文期刊中评选出1982种核心期刊。

《世界华人消化杂志》在编委、作者和读者的支持下,期刊学术水平稳步提升,编校质量稳定,再次被北京大学图书馆《中文核心期刊要目总览》(2011年版)收录。在此,向关心、支持《世界华人消化杂志》的编委、作者和读者,表示衷心的感谢!(《世界华人消化杂志》编辑部)。