肿瘤防治研究 » 2012, Vol. 39 » Issue (6): 687-690 DOI: 10.3971/j.issn.1000-8578.2012.06.018

TEL/AML1、BCR/ABL、E2A/PBX1、MLL/AF4阳性儿童急性淋巴细胞白血病的临床特点及预后

王颖超[1]，殷楚云[1]，李涛[2]，冯磊[1]，王春美[1]，盛光耀[1]

1.450052 郑州，郑州大学第一附属医院儿科，2.血液病研究所

Clinical Features and Prognosis in Childhood Acute Plymphoblastic Leukemia with TEL/AML1,BCR/ABL,E2A/PBX1 and MLL/AF4 Positive

Wang Yingchao[1],Yin Chuyun[1],Li Tao[2],Feng Lei[1],Wang Chunmei[1],Sheng Guangyao[1]

1.Department of Pediatrics，The First Affiliated Hospital of Zhengzhou University,Zhengzhou 450052，China，2.Department of Hematology

摘要

目的

探讨儿童急性淋巴细胞白血病（ALL）TEL/AML1、BCR/ABL、E2A/PBX1、MLL/AF4四种融合基因的表达及其临床诊治意义。方法用实时荧光定量PCR(RQ-PCR)方法检测TEL/AML1、BCR/ABL（p190和p210两种亚型）、E2A/PBX1、MLL/AF4四种融合基因在312例ALL患儿中的表达情况，并总结融合基因阳性患儿的临床和生物学特点、治疗反应及预后情况。结果（1）融合基因阳性共120例，TEL/AML1阳性组72例(23.1%)，BCR/ABL阳性组22例(7.1%)，p190 16例（5.1%）、p210 6例（1.9%），E2A/PBX1阳性组18例(5.8%)，MLL/AF4阳性组8例(2.6%)。（2）TEL/AML1阳性组诊断时WBC平均值为(18.02±6.45)×109/L，诱导化疗结束完全缓解率(CR)100%，随访期间无复发；BCR/ABL阳性组发病时年龄(9.40±3.55)岁，诱导化疗结束CR 81.8%，强化治疗末仍有6例融合基因未转阴，随访中有8例（36.3%）复发，8例死亡；E2A/PBX1阳性组全部按高危标准给予化疗，诱导化疗结束CR 88.9%，强化治疗期末仍有3例基因微量表达，随访中2例复发；MLL/AF4阳性组发病时WBC(38.41±9.30)×109/L，强化治疗期末仍有2例基因呈阳性，随访中均复发死亡。结论融合基因可作为ALL危险度分层、监测微小残留病、判断预后的重要指标之一。

关键词： 急性白血病 儿童 融合基因 TEL/AML1 BCR/ABL E2A/PBX1 MLL/AF4

Abstract：

Objective

To explore the expression and clinical significance of TEL/AML1,BCR/ABL，E2A/PBX1 and MLL/AF4 fusion gene in childhood acute lymphoblastic leukemia(ALL).MethodsBone marrow samples were collected from 312 children with newly diagnosed ALL，and E2A/PBX1，BCR/ABLp190(e1a2)and p210(b2a3,b3a2) isoforms，TEL/AML1 and MLL/AF4 fusion gene were detected by RQ-PCR.Meanwhile，Clinico-biological characteristic，therapeutic response and outcome were retrospectively analyzed.Results（1） The fusion genes were positive in 120 ALL children.72 cases(23.1%) expressed TEL/AML1，22 cases(7.1%) expressed BCR-ABL(including 16 cases(5.1%)p190 and 6 cases(1.9%) p210，18 cases(5.8%) expressed E2A/PBX1 and 8 cases(2.6%) expressed MLL/AF4).（2） In TEL/AML1 positive children，the leukocyte count was(18.02±6.45)×109/L with a 100% complete remission(CR) rate and none relapsed during follow-up.In BCR/ABL positive children，the mean age was(9.40±3.55) years old with 81.8% CR rate.6 cases still expressed the fusion gene at the end of intensive treatment.8 children relapsed and 8 children died during follow-up.In E2A/PBX1 positive children，all of them were given chemotherapy according to high risk standard.The CR rate was 88.9%.Three cases expressed micro-content fusion gene at the end of intensive treatment.2 cases relapsed during follow-up.In MLL/AF4 positive children，the leukocyte count was(41.53±9.46)×109/L.2 cases still expressed the fusion gene at the

end of intensive treatment，and both of them relapsed and died.Conclusion
Fusion genes are important indexes for risk stratification,MRD monitoring and prognosis estimation in children with ALL.

Key words： Acute Leukemia Children Fusion gene TEL/AML1 BCR/ABL E2A/PBX1 MLL/AF4

收稿日期: 2011-08-01;

作者简介: 王颖超（1970-），男，硕士，副教授，主要从事儿童血液或肿瘤疾病的研究

引用本文:

王颖超,殷楚云,李涛等. TEL/AML1、BCR/ABL、E2A/PBX1、MLL/AF4阳性儿童急性淋巴细胞白血病的临床特点及预后[J]. 肿瘤防治研究, 2012, 39(6): 687-690.

Wang Yingchao,Yin Chuyun,Li Tao et al. Clinical Features and Prognosis in Childhood Acute Plymphoblastic Leukemia with TEL/AML1,BCR/ABL,E2A/PBX1 and MLL/AF4 Positive[J]. Cancer Research on Prevention and Treatment, 2012, 39(6): 687-690.

[1]

[1] TThe Subspecialty Group of Hematology Diseases.The society of pediatrics,Chinese Medical

[2]

Association.The Editorial Board.Chinese Journal of Pediatrics.Suggestion of diagnosis and treatment

[3]

of acute lymphoblastic leukemia in childhood(The 3rd revised version)［J］.Zhonghua Er Ke Za

[4]

Zhi,2006,44(5):392-5.

[5]

［中华医学会儿科学分会血液学组.儿童急性淋巴细胞白血病诊疗建议(第三次修订草案)［J］.中华儿科杂

[6]

志,2006,44(5):392-5.］

[7]

[2] SSzczepański T，Orf o A，van der Velden VH，et al.Minimal residual disease in leukaemia

[8]

patients［J］.Lancet Oncol，2001,2(7):409-17.

[9]

[3] JJiménez-Morales S，Miranda-Peralta E，Salda a-Alvarez Y,et al.BCR-ABL，ETV6-RUNX1 and E2A-

[10]

PBX1:prevalence of the most common acute lymphoblastic leukemia fusion genes in Mexican patients［J

[11] ］.LeLeuk Res，2008,32(10):1518-22.

[12]

[4] CChowdhury T，Brady HJ.Insights from clinical studies into the role of the MLL gene in infant

[13]

and childhood leukemia［J］.Blood Cells Mol Dis,2008,40(2):192-9.

[14]

[5] BBalgobind BV，Raimondi SC，Harbott J，et al.Novel prognostic subgroups in childhood 11q23/MLL

[15]

rearranged acute myeloid leukemia:results of an international retrospective study

[16]

[J].Blood,2009,114(12):2489-96.

[17]

[6] BBardini M, Galbiati M, Lettieri A,et al.Implementation of array based whole-genome high-
[18]
resolution technologies confirms the absence of secondary copy-number alterations in MLL-AF4-
[19]
positive infant ALL patients [J] .Leukemia, 2011,25(1):175-8.
[20]
[7] NNa IK, Kreuzer KA, Lupberger J, et al.Quantitative RT-PCR of Wilms tumor gene transcripts (WT1)
[21]
for the molecular monitoring of patients with accelerated phase bcr/abl+CML [J] .Leuk Res,2005,29
[22]
[3] ::343-5.
[23]
[8] PPui CH,Relling MV,Downing JR.Acute lymphoblastic leukemia [J] .N Engl J Med,2004,350 (15):1535-
[24] 48.
[25]
[9] BBartley PA, Ross DM, Latham S,et al.Sensitive detection and quantification of minimal residual
[26]
disease in chronic myeloid leukaemia using nested quantitative PCR for BCR-ABL DNA [J] .Int J Lab
[27]
Hematol,2010,32(6 Pt 1):e222-8.
[28]
[10] Lin D,Liu SH,Zhu XF,et al.Study of the childhood acute lymphoblastic leukemia with t(12;21) [J
[29]] .ZhZhonghua Xue Ye Xue Za Zhi,2004,25(1):17-21.
[30]
[林冬，刘世和，竺晓凡，等.t(12；21）儿童急性淋巴细胞白血病的研究 [J] .中华血液学杂志，2004,25
[31]
[1] ::17-21.]
[32]
[11] Loh ML, Goldwasser MA, Silverman LB, et al.Prospective analysis of TEL/AML1-positive patients
[33]
treated on Dana-Farber Cancer Institute Consortium Protocol 95-01 [J] .Blood,2006,107 (11):4508-13.
[34]
[12] Foa R,Vitale A,Mancini M,et al.E2A-PBXI fusion in adult acute lymphoblastic
[35]
leukemia:biological and clinical features [J] .Br J Hematol,2003, 120(3):484-7.
[36]
[13] Pui CH, Sandlund JT, Pei D, et al.Results of therapy for acute lymphoblastic leukemia in black
[37]
and white children [J] .JAMA,2003,290(15):2001-7.
[38]

[14] Stams WA, Beverloo HB, den Boer ML, et al.Incidence of additional genetic changes in the TEL

[39]

and AML1 genes in DCOG and COALL-treated t(12;21) positive pediatric ALL, and their relation with

[40]

drug sensitivity and clinical outcome [J].Leukemia,2006, 20(3):410-6.

[41]

[15] Dong M, Blobe GC.Role of transforming growth factor-β in hematologic malignancies [J].Blood

[42]

, 2006, 107(12):4589-96.

[1] 江亚军，李秀梅，韩秀华. 改良Hyper-CVAD/MA方案治疗儿童淋巴母细胞性淋巴瘤的疗效观察[J]. 肿瘤防治研究, 2012, 39(6): 716-718.

[2] 李建厂;贾秀红;唐慎华;韩琳. Livin 基因在儿童急性白血病中的表达及其意义[J]. 肿瘤防治研究, 2012, 39(1): 41-43.

[3] 孙少勤;范金章;崔惠卿;成志勇. 参麦注射液对急性白血病化疗患者T淋巴细胞亚群和NK细胞水平的影响[J]. 肿瘤防治研究, 2011, 38(2): 216-217.

[4] 毕慧;刘琳;张利娟;汤宏宇;何勤. 急性白血病PTEN的表达及甲基化状态[J]. 肿瘤防治研究, 2011, 38(10): 1187-1189.

[5] 廖艺玮;袁贤瑞;彭泽峰;蒋星军;简志宏. 13例儿童垂体腺瘤的诊断和治疗[J]. 肿瘤防治研究, 2009, 36(6): 515-517.

[6] 徐双年;陈洁平. 急性白血病的表观遗传学治疗进展[J]. 肿瘤防治研究, 2009, 36(11): 976-979.

[7] 叶中绿;陈铭珍;陈日玲;黄秀兰;庞伟君;陈水文;. 白细胞介素15及其受体在儿童急性白血病中的表达和作用探讨[J]. 肿瘤防治研究, 2008, 35(08): 579-582.

[8] 张文彬;张海红;孔维;查晓;陈廷清;邓碧芳;任原;黄建鸣. 转染融合基因的DC抗肿瘤免疫效应[J]. 肿瘤防治研究, 2007, 34(9): 647-650.

[9] 万楚成;章正华;夏云金;龙志国;胡明均;张霞;郭仁慈;. ETIOP方案治疗成人急性淋巴细胞白血病疗效观察[J]. 肿瘤防治研究, 2006, 31(2): 121-121.

[10] 邵剑波;胡道予;夏黎明;王承缘. 小儿恶性肝肿瘤的**CT**与**MRI**诊断—附**45** 例分析[J]. 肿瘤防治研究, 2005, 32(12): 777-781.

[11] 张英;朱强;顾江英;朱平;. 白血病和淋巴瘤常见染色体融合基因的检测分析[J]. 肿瘤防治研究, 2004, 31(6): 341-344.

[12] 王俊祥;王金铠;孟建波;吕鸿雁;. 血清IL-12、IFN-γ、VEGF在急性白血病中的表达及其意义[J]. 肿瘤防治研究, 2004, 31(3): 156-157.

[13] 邵剑波;王明甫;. 小儿肾脏恶性肿瘤的CT诊断(附52例分析)[J]. 肿瘤防治研究, 2004, 31(10): 619-622.

[14] 杨志祥;糜漫天;杨剑;郎海滨;韦娜;. 视黄酸依赖Fas/RARα融合基因转染MCF-7细胞启动的凋亡效应研究[J]. 肿瘤防治研究, 2003, 30(5): 346-348.

[15] 林友平;. 儿童头颈部横纹肌肉瘤[J]. 肿瘤防治研究, 2002, 29(5): 390-390.