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Title: Clinical significance of CSF-DKK1 as a biomarker for diagnosis and therapeutic monitoring of neuroblastoma

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摘要: 目的 定量检测神经母细胞瘤 (neuroblastoma, NB) 患者脑脊液 (cerebrospinal fluid, CSF) 中 Dickkopf 相关蛋白 1 (DKK1), 探讨其作为诊断 NB 及疗效评估标志物的临床价值。 方法 实验组 48 例: NB 患者经 CT、骨髓检查确诊, 年龄 5 个月至 11 岁, 包括男性 25 例, 女性 23 例; Evans 分期: I 期 5 例, II 期 20 例, III 期 15 例, IV 期 8 例。对

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对照组50例：神经系统良性肿瘤25例，年龄5个月至65岁，包括男性13例，女性12例；化脓性脑膜炎10例，年龄5个月至6岁，包括男性4例，女性6例；脑外伤15例，年龄2-45岁，包括男性10例，女性5例。NB患者分别于治疗前、化疗结束后3 d及化疗联合手术治疗后3 d采集CSF样本各1次。ELISA法定量检测CSF中DKK1水平并做ROC曲线分析，对NB患者治疗后（化疗及化疗联合手术治疗）的CSF-DKK1水平进行随访检测。结果 与对照组[(57.0 ± 13.7) pg/mL]相比，NB患者CSF-DKK1水平显著增高[(88.7 ± 22.9) pg/mL, $P < 0.01$]; ROC曲线分析表明，CSF-DKK1诊断NB (Cut-off= 65.0 pg/mL) 的灵敏度为83%，特异性为76%。与治疗前相比，化疗缓解组[$n=35$, (48.5 ± 9.7) pg/mL]及化疗联合手术组[$n=15$, (46.4 ± 7.8) pg/mL]的CSF-DKK1水平均显著下降 ($P < 0.01$)，而化疗无效组的CSF-DKK1水平无明显变化[$n=13$, (89.1 ± 25.7) pg/mL, $P > 0.05$]。结论 NB患者脑脊液中DKK1水平显著升高且与疗效密切相关，可作为NB筛查诊断及疗效评估的标志物。

Abstract: Objective To quantitatively detect the cerebrospinal fluid (CSF)-DKK1 (CSF-DKK1) in patients with neuroblastoma (NB), and to assess the clinical significance of CSF-DKK1 as a biomarker for diagnosis/therapeutic monitoring of NB. Methods The CSF samples were collected from 48 NB patients (experimental group) and 50 patients with other diseases (control group) before and after treatment. In the experimental group, the NB patients were diagnosed by CT scanning and bone marrow examination, including 25 males and 23 females aged from 5 months to 11 years. Evans staging showed that there were 5 patients of phase I, 20 patients of phase II, 15 patients of phase III and 8 patients of phase IV. In the control group, there were 25 patients with benign nervous system tumors (13 males and 12 females, aged from 5 months to 65 years), 10 patients with purulent meningitis (4 males and 6 females, aged from 5 months to 6 years) and 15 patients with brain trauma (10 males and 5 females, aged from 2 to 45 years). ELISA was used to quantify the serum level of CSF-DKK1, and ROC analysis was performed. Results Compared with the control group