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泛素连接酶 PC2 在鼻咽癌发生中的作用 *

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摘要 目的：探究泛素连接酶 PC2 在鼻咽癌发生中的作用。**方法：**选择 2017 年 3 月至 2018 年 8 月于我院接受治疗的 68 例鼻咽癌患者为研究组，选择同期于我院接受治疗的 50 例鼻咽良性病变患者为良性对照组，选择同期于我院接受体格检查的 50 例健康个体为对照组，分别检测 3 组个体泛素连接酶 PC2 及其 mRNA 表达水平并实施组间对比，而后将鼻咽癌患者按照病情严重程度分为 I-II 期和 III-IV 期两组，对比两组泛素连接酶 PC2 及其 mRNA 表达水平，最后对鼻咽癌患者实施为期 12 个月的随访，按照其结局区分为死亡组（20 例）和存活组（48 例），对比两组患者泛素连接酶 PC2 及其 mRNA 表达水平。**结果：**（1）研究组泛素连接酶 PC2 蛋白的表达量和 mRNA 表达水平均显著高于良性对照组，且良性对照组的上述指标也显著高于对照组（P<0.05）；（2）II-I-IV 期患者泛素连接酶 PC2 蛋白的表达量及 mRNA 表达水平高于 I-II 期患者（P<0.05）；（3）死亡组泛素连接酶 PC2 蛋白的表达量及 mRNA 表达水平高于存活组（P<0.05）。**结论：**泛素连接酶 PC2 的高表达与鼻咽癌病情具有一定相关性，可以作为鼻咽癌诊断及预后评估指标之一。

关键词：泛素连接酶 PC2；鼻咽癌；发生；作用

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The Role of Ubiquitin Ligase PC2 in the Development of Nasopharyngeal Carcinoma*

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ABSTRACT Objective: To explore the role of ubiquitin ligase PC2 in the development of nasopharyngeal carcinoma. **Methods:** 68 NPC patients who were treated in our hospital from March 2017 to August 2018 were selected as the experimental group, 50 NPC patients who were treated in our hospital at the same time were selected as the benign control group, and 50 healthy individuals who were examined in our hospital at the same time were selected as the control group. The expression levels of ubiquitin ligase PC2 and its mRNA in three groups were detected and compared between groups After that, NPC patients were divided into two groups according to the severity of the disease: I-II and III-IV. the expression level of ubiquitin ligase PC2 and its mRNA were compared between the two groups. Finally, NPC patients were followed up for 12 months. According to the outcome, they were divided into death group (20 cases) and survival group (48 cases). The expression level of ubiquitin ligase PC2 and its mRNA were compared between the two groups. **Results:** (1) The expression level of ubiquitin ligase PC2 protein and mRNA expression level in the study group were significantly higher than those in the benign control group, and the above indicators in the benign control group were significantly higher than those in the control group (P<0.05). (2) The level of ubiquitin ligase PC2 protein and its mRNA expression in the III-IV patients were higher than that in the I-II patients (P<0.05). (3) The expression of ubiquitin ligase PC2 protein and mRNA in the death group was higher than that in the survival group (P<0.05). **Conclusion:** The high expression of ubiquitin ligase PC2 has a certain correlation with the state of NPC, which can be used as one of the indexes for the diagnosis and prognosis of NPC.

Key words: Ubiquitin ligase PC2; Nasopharyngeal carcinoma; Happen; Effect

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前言

鼻咽癌是指发生于鼻咽腔顶部和侧壁的恶性肿瘤，是我国高发恶性肿瘤之一，数据显示，我国及东南亚地区鼻咽癌发病率较高，约为 10/10 万，国内广东、广西、湖南、福建、香港、台湾等地区为高发地[1-3]。鼻咽癌发病具有明显的种族、地区和家族聚集现象，全球约 80 %的鼻咽癌发生于我国，鼻咽癌高发年龄为 30-50 岁，男性发病率约为女性的 2-3 倍[4,5]。目前的研究指

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出,鼻咽癌发病机制尚不清晰,但一般认为遗传因素、环境因素、病毒感染等均对鼻咽癌的发生发展造成了一些影响[6-8]。传统鼻咽癌诊断方式主要为病理切片检测,该检测方式周期长且为有创操作,部分患者难以耐受,且不适用于某些病灶较深患者,因而临床推广受限[9,10]。泛素连接酶是一类能够将泛素分子连接到目的蛋白质的某个赖氨酸上的酶,临床研究证实此类物质广泛参与机体多种生理活动中[11,12]。近些年随着分子生物学的进展,泛素连接酶在癌症鉴别及诊断中的应用逐渐被重视起来,本文作者通过研究发现,泛素连接酶 PC2 的高表达与鼻咽癌病情具有一定相关性,可以作为鼻咽癌诊断及预后评估指标之一。

1 资料与方法

1.1 一般资料

选择 2017 年 3 月至 2018 年 8 月于我院接受治疗的 68 例鼻咽癌患者为研究组，同期于我院接受治疗的 50 例鼻咽良性病变患者为良性对照组，选择同期于我院接受体格检查的 50 例健康个体为对照组,研究组中男性 35 例,女性 33 例,年龄 26-59 岁,平均年龄(43.02± 2.15)岁,良性对照组中男性 27 例,女性 23 例,年龄 23-60 岁,平均年龄(42.98± 2.65)岁,对照组中男性 28 例,女性 22 例,年龄 22-59 岁,平均年龄(43.08± 2.99)岁,三组一般资料对比无统计学意义(P>0.05),具有可比性。

纳入标准:(1) 研究组均经病理学诊断确诊为鼻咽癌且出现相应临床症状;(2)病历资料齐全;(3)能配合实施;(4)经医院伦理学会批准;(5)均签署知情同意书。

排除标准:(1) 合并精神疾者;(2) 并发其他恶性肿瘤者;(3)合并严重肝肾功能障碍者;(4)依从性较差者。

剔除标准:(1)随访期间失访者;(2)主动要求退出调研者。

1.2 方法

分别取病变鼻咽组织(对照组取正常鼻咽组织),使用石蜡包埋后选择上海研生生物有限公司生产的试剂盒采用酶联免疫吸附法对组织内泛素连接酶 PC2 蛋白表达水平进行检测;同时取部分组织实施 RNA 提取并采用荧光定量 PCR 法评测三组患者泛素连接酶 PCA mRNA 表达水平。

1.3 观察指标及评测标准

主要观测指标为三组泛素连接酶 PC2 蛋白及 mRNA 表达水平对比，不同病程鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平对比，同时对鼻咽癌患者实施为期 12 个月的随访,根据其存活结局对比不同结局鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平。

1.4 统计学方法

应用 SPSS19.0,计数资料以率(%)表示,采用卡方检验,计量资料以($\bar{x}\pm s$)表示,采用 t 检验,P<0.05 有统计学意义。

2 结果

2.1 三组泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

研究组泛素连接酶 PC2 蛋白的表达量和 mRNA 表达水平均显著高于良性对照组,且良性对照组的上述指标也显著高于对照组(P<0.05),如表 1。

表 1 三组泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

Table 1 Comparison of ubiquitin ligase PC2 protein and mRNA expression levels in trio groups

Groups	n	Ubiquitin ligase PC2 protein (μg/mL)	mRNA
Experience group	68	1.36± 0.51*#	6.23± 0.21*#
Benign control group	50	0.56± 0.21*	2.65± 0.15*
Control group	50	0.22± 0.06	1.02± 0.06

Note: compared with the control group, *P<0.05, compared with the benign control group, #P<0.05.

2.2 不同病程鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

III-IV 期患者泛素连接酶 PC2 蛋白表达量和 mRNA 表达水平高于 I-II 期患者(P<0.05),如表 2。

表 2 不同病程鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

Table 2 Comparison of ubiquitin ligase PC2 protein and mRNA expression in patients with nasopharyngeal carcinoma of different durations

Groups	Cases	Ubiquitin ligase PC2 protein (μg/mL)	mRNA
Phase I-II	29	1.06± 0.21*	5.01± 0.32*
Phase III-IV	39	1.53± 0.65	7.32± 1.65

Note: compared with the phase III-IV, *P<0.05.

2.3 不同结局鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

68 例鼻咽癌患者治疗后 12 个月存活 48 例，死亡 20 例,死亡组泛素连接酶 PC2 蛋白表达量及 mRNA 表达水平高于存活组(P<0.05),如表 3。

3 讨论

鼻咽癌是一种高发于我国南部地区的恶性肿瘤,该病的临床表现较为复杂,包括鼻出血、头痛、视力障碍、听力下降等,部分患者还会出现脑神经损害,严重降低其生活质量[13,14]。目前鼻

表 3 不同结局鼻咽癌患者泛素连接酶 PC2 蛋白及 mRNA 表达水平对比

Table 3 Comparison of ubiquitin ligase PC2 protein and mRNA expression in patients with nasopharyngeal carcinoma with different outcomes

Groups	Cases	Ubiquitin ligase PC2 protein (μg/mL)	mRNA
Survival group	48	0.98± 0.12*	4.26± 0.66*
Death group	20	1.79± 0.21	9.56± 0.51

Note: compared with the death group, *P<0.05.

咽癌的首选治疗手段仍为放射治疗,但临床实践发现,部分患者仍会出现局部复发或远处转移[15,16]。及早准确的诊断是提高鼻咽癌患者生存率的基础,目前鼻咽癌常用的复诊手段仍主要为影像学检查,但鼻咽癌患者接受治疗后会出现局部水肿、组织结构紊乱、纤维化、粘膜炎或疤痕,明显改变鼻咽癌患者的 CT 或 MRI 征象,影响临床医师对鼻咽癌病程的判断[17,18];此外还有研究指出,CT、MRI 等影像学检查对远处转移病灶诊断特异性较低,难以早期实施评估[19]。病理学检测仍是鼻咽癌复发及转移诊断的金标准,但一方面采集复发灶或转移灶标本采集难度较大,尤其是部分粘膜下复发或鼻咽深部复发灶,另一方面病理学检测为侵入性操作,可能会对预后产生一定的不良影响,因而实施便捷性较低[20,21]。

随着近些年分子生物学的发展,各类生物学指标在鼻咽癌发生发展以及诊断中的应用价值逐渐被重视起来,泛素化在细胞生命活动中的许多进程中都发挥着至关重要的作用[22,23]。有学者的研究指出,泛素连接酶在细胞基本进程(凋亡、细胞周期调控等)、抗原传递、炎症反应等一系列通路中都扮演着重要角色[24],也有学者的研究指出,泛素连接酶的表达异常与许多疾病诸如恶性肿瘤、神经退行性病变等关系密切,因而近些年泛素连接酶被广泛应用于临床疾病的诊断中[25,26]。学者 Chen C[27] 通过动物实验发现,肺癌大鼠病变组织中泛素连接酶呈现明显的高表达态,较癌旁组织及正常大鼠明显升高,学者 Li B[28]等的研究则指出,泛素连接酶与卵巢癌患者病情呈现明显的相关性,病情越重,患者泛素连接酶表达水平越高。

本研究显示,研究组泛素连接酶 PC2 蛋白的表达量和 mRNA 表达水平均显著高于良性对照组,且良性对照组的上述指标也显著高于对照组,III-IV 期患者泛素连接酶 PC2 蛋白表达量和 mRNA 表达水平高于 I-II 期患者,说明于健康对照组及良性对照组相比,鼻咽癌患者病变组织中泛素连接酶 PC2 呈现明显的高表达态,进一步分析显示泛素连接酶 PC2 蛋白和 mRNA 也明显高于其他两组,这与学者 Tang M[29]的研究结果相一致,该学者的研究指出,泛素连接酶能够参与集体 80 %以上蛋白质的降解过程,对机体细胞的增值、分化和存活会产生明显影响,说明癌变患者机体内泛酸连接酶呈现明显的高表达态,同时与鼻咽癌患者的分化程度、淋巴结转移、肿瘤浸润深度等指标相关。最后本研究还就泛酸连接酶 PC2 与鼻咽癌患者预后的相关性进行了分析,结果显示,死亡组泛素连接酶 PC2 蛋白表达量及 mRNA 表达水平高于存活组,这与学者 Wu J X[30] 等的研究结果相一致,提示泛酸连接酶高表达的乳腺癌患者无进展生存期要明显降低,其原因与泛酸连接酶能够直接影响蛋白质的降解、合成进而影响了癌细胞的迁移进程有关。本研究也存在一定的不足,研究的样本量少,结果可能存在一定的偏倚,由于时间问题,且没有深入的研究泛素连接酶 PC2 与鼻咽癌发病的机制,在后续会采用细胞实验进一步深入探究机制,为鼻咽癌的治疗提供新的思路和靶点。

总而言之,泛素连接酶 PC2 的高表达与鼻咽癌病情具有一定相关性,可以作为鼻咽癌诊断及预后评估指标之一。

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