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慢性胃炎组织病理特征和 Hp 感染与炎症程度的关系研究

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摘要 目的:探讨慢性胃炎组织病理特征和 Hp 感染与慢性炎症程度的关系。**方法**:抽选我院 2010 年 1 月至 2016 年 2 月行胃镜检查诊断为慢性胃炎的 467 例患儿,作胃窦黏膜病理组织学检查,并检测有无 HP 感染,分析 HP 感染与慢性胃炎病理特征、慢性炎症程度之间的关系。**结果**:在病理检查中,轻度、中度、重度炎症反应患儿 HP 感染率(7.7%、41.2%、51.1%)依次升高,且差异具有统计学意义(P<0.05),有炎症活动度患儿的 HP 阳性率 76.3%明显高于无炎症活动度患儿 23.7%(P<0.05)。随着肠化分级加重、淋巴滤泡形成、萎缩程度分级升高等病理变化,Hp 阳性率明显升高(P<0.05)。轻度、中度、重度炎症三组淋巴滤泡形成、肠化生和胃萎缩发生率明显呈递增趋势,Hp 阳性率明显呈递增趋势,比较差异显著(P<0.05)。**结论**:Hp 是慢性胃炎发病的重要影响因素,与患儿胃窦黏膜炎症程度、活动性、淋巴滤泡形成、肠化分级以及黏膜萎缩萎等病理变化密切相关。

关键词:HP 感染;炎症程度;肠化分级;慢性胃炎

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The Relationship between Characteristic of Pathohistology with Hp Infection and Degree of Inflammation in Chronic Gastritis

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ABSTRACT Objective: To study the relationship between Characteristic of Pathohistology, *Helicobater Pylori* and Degree of inflammation in Chronic Gastritis. **Methods:** 467 cases of chronic gastritis children in our hospital from January 2010 to February 2016 for gastroscopy diagnosis were selected. The histological features of gastric antrum mucosa were examined, and the positive rate of HP was detected, and the relationship between HP infection and pathological features of chronic gastritis and the degree of chronic inflammation was analyzed. **Results:** In the pathological examination, the HP infection rate in children with mild, moderate and severe inflammatory reaction (7.7%, 41.2%,51.1%) was increased, and the difference was statistically significant (P<0.05). The positive rate of HP in children with inflammatory activity of 76.3% was significantly higher than that in children with no inflammatory activity for 23.7% (P<0.05). The positive rate of Hp was significantly increased with the increase of the grade of intestinal metaplasia, the formation of lymphoid follicles and the degree of atrophy. The incidence of lymph follicle formation, intestinal metaplasia and gastric atrophy in three groups of mild, moderate and severe inflammation was significantly increased, Hp positive rate was significantly increased,and the difference was significant (P<0.05). **Conclusion:** HP infection is important factor in the pathogenesis of chronic gastritis,is closely related with gastric mucosal inflammation, activity, lymph follicle formation, intestinal mucosal atrophy atrophy grading and other pathological changes.

Key words: HP infection; Degree of inflammation; Grading of intestinal metaplasia; Chronic gastritis

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幽门螺杆菌(Hp)于上世纪 80 年代被澳大利亚学者 Marshall 和 Warren 首次发现。现代医学发现 Hp 感染是慢性胃炎、胃溃疡、胃淋巴瘤等疾病的重要致病因子,已被国际癌症研究机构(International Agency for Research on Cancer,IARC)列为Ⅰ类或明确的致癌物之一[3]。目前国内外对 Hp 感染与慢性胃炎相关性多集中在 Hp 定性研究方面,对其与胃黏膜局部病理改变、不同程度胃炎关系的研究有限。本研究收集我院 2010 年 1 月至 2016 年 2 月期间行胃镜检测 467 例患儿的临床资料,结合活检病理报告,探讨 Hp 感染与慢性胃炎病理特征、炎症程度的相关性,现报道如下。

1 资料和方法

1.1 临床资料

抽选我院 2010 年 1 月至 2016 年 2 月行胃镜检查诊断为慢性胃炎的 467 例患儿,其中男 212 例,女 255 例,年龄 1-12 岁,平均(8.5± 1.7)岁,病程 4 个月 -2 年,平均(1.2± 0.4)年;连续性行胃镜下黏膜活检,排除内分泌疾病、胃黏膜重度异性增生、胃镜下胃溃疡, 并排除近期使用过抑酸剂、MTL 受体激动剂、胃肠动力药等药物治疗者。本研究中全部内镜及病理诊断均由有经验专职的内镜、病理医师完成。

1.2 方法

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1.2.1 **病理变化诊断及炎症分级、活动度判断** 病理诊断按2000版WHO标准[4],对所取胃黏膜组织予以固定、脱水、包埋、切片、染色等一系列处理,制成病理切片,由2名经验丰富的专职病理医生在显微镜下共同明确其慢性胃炎的组织类型、炎症分级及活动度、固有层淋巴滤泡形成、肠化等病理变化。(1)肠化分级:在400倍光镜下整个视野或者选择3-5个视野,观察肠化腺管占腺管总数1/3者为轻度;2/3者为中度, 全层腺管肠化者为重度。(2)萎缩性胃炎分级:直视下胃窦大弯侧、小弯侧、胃角、胃体大小弯侧、贲门下及胃底各取一块黏膜组织,典型部位另取,每部位分开装瓶,常规石蜡制片,行HE及Giemsa染色。萎缩分度以固有腺体萎缩进行分度。减少1/3以内为轻度;1/3 -2/3之间为中度;减少超过2/3为重度。(3)根据炎症细胞密集程度以及浸润深度进行分级。轻度:炎症细胞较少,并仅在黏膜浅层局部可见,范围不超过其1/3;中度:可见密集的炎症细胞,范围超过黏膜层1/3,达2/3;重度:可见密集的炎症细胞,覆盖了黏膜全层。如固有层见中性粒细胞浸润,则判定为活动性炎症。(4)病理采用HE染色观察胃黏膜淋巴滤泡增生情况。

1.2.2 **Hp检测** 在胃镜下采用活检钳钳取胃窦组织标本作快速尿素酶试验,同时做14C尿素呼气试验,两者检测结果同时为阳性诊断为Hp阳性,结果同时为阴性者诊断为Hp阴性,其他情况排除出实验。

1.3 统计学方法

采用SPSS18.0软件统计分析,计量资料以($\bar{x}\pm s$)表示,组间采用t值检验;计数资料以n%表示,采用x^2检验,等级资料采用秩和检验,P<0.05为差异有统计学意义。

2 结果

2.1 HP感染与慢性炎症程度及活动度的关系

467例慢性胃炎患儿中,检出Hp感染274例(58.7%)。在病理检查中,轻度、中度、重度炎症反应患儿HP感染率分别为7.7%、41.2%、51.1%, 呈依次升高趋势, 且差异有统计学意义(P<0.05),有炎症活动度患儿的HP阳性率为76.3%,明显高于无炎症活动度患儿的23.7%,差异有统计学意义(P<0.05),见表1。

表1 HP感染与慢性炎症程度及活动度的关系

Table 1 The relationship between HP infection and the degree of chronic inflammation and activity

HP infection	Cases	Degree of inflammation			Degree of activity	
		Mild	Moderate	Severe	No	Yes
+	274	21(7.7)	113(41.2)	140(51.1)	209(76.3)	65(23.7)
−	193	136(70.5)	55(28.5)	2(1.0)	10(5.18)	183(94.8)
X^2/Z		42.088		27.518		
P		0.000		0.000		

2.2 慢性胃炎组织病理特征与Hp感染的关系

随着肠化分级加重、淋巴滤泡形成、萎缩程度分级升高等病理变化,Hp阳性率明显升高(P<0.05),详见表2。

2.3 慢性胃炎组织病理特征与慢性炎症程度的关系

轻度、中度、重度炎症三组淋巴滤泡形成、肠化生和胃萎缩发生率明显呈递增趋势,Hp阳性率明显呈递增趋势,差异有统计学意义(P<0.05),详见表3。

表2 慢性胃炎组织病理特征与Hp感染的关系

Table 2 The relationship between histopathological characteristics of chronic gastritis and Hp infection

Pathologic features		Hp infection		χ^2/Z	P
		+	−		
Intrinsic layer lymph follicles	Yes	100(97.1)	3(2.9)	78.403	0.000
	No	174(47.8)	190(52.2)		
Intestinal metaplasia grade	Without intestinal metaplasia	140(51.9)	130(48.1)	14.587	0.002
	Mild intestinal metaplasia	73(64.6)	40(35.4)		
	Moderate intestinal metaplasia	41(67.2)	20(32.8)		
	Severe intestinal metaplasia	20(87.0)	3(13.0)		
Degree of atrophy	No atrophy	72(50.3)	71(49.7)	8.080	0.044
	Mild atrophy	138(60.8)	89(39.2)		
	Moderate atrophy	52(63.4)	30(36.6)		
	Severe atrophy	12(80.0)	3(20.0)		

表 3 慢性胃炎组织病理特征与慢性炎症程度的关系

Table 3 The relationship between histopathological characteristics of chronic gastritis and degree of Inflammation

Degree of Inflammation	Cases	Pathologic diagnosis			Hp positive(%)
		lymphoid follicle	Intestinal metaplasia	Atrophy	
Mild	249	0(0.0)	39(15.7)	150(60.2)	113(45.4)
Moderate	195	90(46.2)	138(70.8)	155(79.1)	140(71.8)
Severe	23	13(56.5)	20(87.0)	19(82.6)	21(91.3)
Totals	467	103(22.1)	197(42.2)	324(69.4)	274(58.7)

3 讨论

世界范围内约有半数人感染 Hp，我国 Hp 感染率为 40%～90%。Hp 是一种微需氧、革兰阴性菌，与消化溃疡、急慢性胃炎、消化不良、胃癌等许多消化道疾病都有关系，是临床感染率最高的细菌之一[5,6]。HP 是非侵入性细菌，其外膜成分脂多糖可刺激血管内皮细胞、单核 / 巨噬细胞、上皮细胞、巨噬细胞释放大量炎症趋化因子，促进炎症的发生[7-9]。HP 的鞭毛蛋白也具有协同诱导细胞因子分泌的作用。造成胃黏膜巨噬、淋巴及中性粒细胞浸润，引发胃黏膜炎症反应，这是 Hp 引发黏膜损伤的重要发病机制。

目前对于 Hp 与慢性胃炎相关性的临床研究较多。有研究[10,11]发现 Hp 持续根除组第 1、4 年，随访其慢性活动性胃炎患者比例明显下降，而 Hp 持续未根除组第 4 年活动性炎症患者比例明显增多。国外也有研究[12,13]发现，根除 Hp 感染能显著改善慢性胃炎病人胃黏膜内的炎症反应程度。本研究发现，在病理检查中，轻度、中度、重度炎症反应程度，无活动性炎症、有活动性炎症患儿的 HP 阳性率依次升高(P<0.05)。说明 HP 感染可加重慢性胃炎患儿的炎症反应，与上述研究报道一致。Hp 一部分根植于上皮细胞表面，一部分经上皮细胞进入到固有层，如果患儿持续感染 Hp，则可引发机体固有层淋巴滤泡形成[14,15]。目前国内外临床对成年人 Hp 感染与固有层淋巴滤泡形成相关性的研究报道较少，本研究结果显示，Hp 感染率与固有层淋巴滤泡形成也有重要关系。

肠上皮化生是患儿持续感染 HP 的结果，胃上皮出现类似肠上皮改变时即为肠化，是临床常见的一种胃粘膜病理改变，并临床研究认为其是胃癌的“癌前病变”[16]。Hp 感染与肠化生的相关性的临床各家报道不一致[17]。本研究结果显示，在无肠化和轻度、中度、重度肠化病理改变的样本中 Hp 感染率慢性升高，比较差异具有统计学意义，因此认为 Hp 感染与慢性胃炎患儿的肠化进程存在相关性。Chacaltana Mendoza A 等[18]研究认为 Hp 感染与胃黏膜肠化呈正相关，与本研究结果一致。

有研究发现，Hp 感染会加重机体胃黏膜炎性反应，进而导致萎缩性胃炎发生，这可能与 Hp 定植、感染、产生酶与毒素激发免疫应激反应，胃黏膜发生炎性反应，可破坏胃固有腺体而发生萎缩。本研究结果显示，随着萎缩程度分级升高，重度萎缩性胃炎患儿的 Hp 阳性率明显高于中度和轻度患儿(P<0.05)。这表明 Hp 感染可促进胃粘膜萎缩。有研究[19]认为，早期根除 Hp 可延缓萎缩性胃炎发病进程。据国外报道[20]，因 Hp 毒性产物分泌增多、胃酸减少等因素影响，每年大约有 1-3%Hp 感染者会发生萎缩性胃炎，亦充分论证了 Hp 感染与萎缩性胃炎密切相关。

本研究结果还显示，轻度、中度、重度炎症三组淋巴滤泡形成、肠化生和胃萎缩发生率明显呈递增趋势，Hp 阳性率明显呈递增趋势，比较差异显著(P<0.05)，可见淋巴滤泡存在、肠化生、胃萎缩等病理变化与胃炎的严重程度呈正相关。既往研究发现，Hp 存在于胃腔黏液内，释放出毒素，可刺激血管内皮细胞、巨噬细胞等释放一系列炎症因子，首先引起胃炎，长期感染，继而逐渐导致胃黏膜萎缩、肠上皮化生、淋巴细胞形成等一系列病理恶化。临床上有必要对长期 Hp 感染、炎症程度加重的病人进行 Hp 根除治疗，定期进行病理筛查。

综上所述，Hp 是慢性胃炎发病的重要影响因素，与患儿胃窦黏膜炎症程度、活动性、淋巴滤泡形成、肠化分级以及黏膜萎缩萎等病理变化密切相关，提示当存在上述病理变化时，应及时检测 HP 指标，高度警惕 HP 感染。

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