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儿童及青少年甲状腺癌特点及颈淋巴结转移风险因素探讨 *

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摘要 目的:探讨儿童及青少年甲状腺癌的临床和病理特征,分析乳头状癌组淋巴结转移的风险因素。**方法:**回顾性分析 2003 年 1 月至 2013 年 12 月间本院收治的儿童及青少年甲状腺癌病例资料,了解临床特征和病理特点及分析乳头状癌亚组淋巴结转移的风险因素。**结果:**共收集 51 例儿童及青少年甲状腺癌资料,49 例甲状腺乳头状癌,2 例甲状腺髓样癌。乳头状癌亚组淋巴结转移率达 77.5 %, 患儿年龄与淋巴结转移相关, Logistic 回归提示年龄是颈部淋巴结转移的独立风险因素 (OR=1.40;95 % CL=1.05, 1.85; P=0.021)。随访中 5 例出现局部复发。**结论:**儿童及青少年甲状腺癌有区别于成人甲状腺癌的特殊性,积极筛查儿童甲状腺疾病、全面彻底的外科手术和制定相应的风险评估标准、积极随访是治疗该病的关键。

关键词:甲状腺癌;儿童及青少年;临床病理特征;颈部淋巴结转移

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Study of Characteristics of Thyroid Cancer and Risk Factors of Cervical Lymph Node Metastasis in Children and Adolescence*

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ABSTRACT Objective: To investigate the clinical and pathological characteristics of thyroid cancer in children and adolescence, analysis the risk factors of cervical lymph node metastasis (CLNM) in papillary thyroid cancer (PTC) group. **Methods:** A retrospective clinical study was performed of children and adolescence with thyroid cancer in Tongji Hospital from January 2003 to December 2013. The clinical and pathological characteristics were noted, and the risk factors of CLNM in PTC were analyzed especially. **Results:** 51 cases were noted in our department, 49 cases were papillary thyroid carcinoma, 2 cases were medullary thyroid carcinoma. In PTC group, the rate of CLNM was 77.5 %, and there was a correlation between age and CLNM, Multivariate Logistic Regression showed that age has an independent effect on CLNM in PTC group (OR=1.40, 95% CL=1.05, 1.85; P=0.021). **Conclusion:** Thyroid cancer in children and adolescence has some special features compared with that in adults. The key to treat this disease is screening thyroid disease in this group, performing comprehensive surgical operation, appropriate post-operative treatment, and formulating a special risk assessment criterion and proper follow-up.

Key words: Thyroid cancer; Children and adolescence; Clinic pathological features; Cervical lymph node metastasis

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前言

儿童及青少年甲状腺癌约占该年龄组肿瘤的 0.5%~3%[1]。相比于成人甲状腺恶性肿瘤,具有性别差异小[2]、淋巴结转移率高[3]、受头颈部照射史影响大[4]等特殊性。其中大多数为分化型癌,其颈淋巴结转移相关因素目前讨论尚少,是否与成人有相同的结论尚无定论[5], 该人群分化型甲状腺癌颈淋巴结转移风险因素评估是临床亟待解决的问题。本研究拟回顾性收集本研究中心收治的儿童及青少年甲状腺癌病例,了解该组人群甲状腺癌临床及病理特点,着重分析甲状腺乳头状癌颈部淋巴结转移可能的风险因素,为临床实践提供参考。

1 资料与方法

1.1 一般资料

回顾性收集 2003 年 1 月至 2013 年 12 月武汉同济医院甲状腺乳腺外科及小儿外科收治的甲状腺癌病例资料,以年龄不超过 18 周岁为纳入标准,共收集甲状腺癌病例 51 例。年龄分布 4-18 岁,平均 14.5± 3.4 岁。男性 16 例(31.3 %),女性 35 例(68.6 %),比例为 1:2.2;首诊病例 45 例,另 6 例于外院切除甲状腺肿块,确诊为甲状腺癌,于我院行进一步手术治疗。病程从 4 天到 8 年不等,22 例(43.1 %)病程在 1 月以上。首诊病例中以体检发现甲状腺肿块就诊 3 例(6.7 %),因颈部明显肿大、双侧不对称就诊 13 例(28.9 %),因 " 声音嘶哑 " 就诊 1 例(2.2 %),余病例以扪及颈部肿块就诊(68.9 %)。

1.2 体检和辅助检查资料

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45 例首诊患者均行一般体检,13 例(28.9 %)患者视诊可见明显颈部肿大,42 例(93.3 %)触诊甲状腺可触及明显结节;36 例病人术前行彩色高频超声检查,其中 25 例(69.4 %)超声提示甲状腺内低回声结节,16 例(44.4 %)提示结节内细小强回声;7 例(19.4 %)提示高回声结节,4 例(11.1 %)未见正常甲状腺组织,弥漫性肿大。20 例(55.6 %)提示双侧颈部淋巴结肿大。

1.3 手术方式

51 例患者均行手术治疗。19 例行甲状腺腺体全切 +" 中央区 " 淋巴结清扫 + 患侧侧方组淋巴结清扫;5 例行甲状腺腺体全切 +" 中央区 " 淋巴结清扫 + 双侧侧方组淋巴结清扫;13 例行甲状腺腺体全切 +" 中央区 " 淋巴结清扫;7 例行甲状腺腺体全切 + 双侧颈部淋巴结清扫(未分 " 中央区 " 和颈侧区);二次手术病例行残余甲状腺切除 +" 中央区 " 淋巴结清扫 + 患侧颈侧方淋巴结清扫; 其中 2 例行残余甲状腺切除 +" 中央区 " 淋巴结清扫。

1.4 统计学分析乳头状癌组淋巴结转移的危险因素

在乳头状癌病例中,将最终病理诊断确诊淋巴结转移(" 中央区 " 和 / 或颈侧方组)划为颈淋巴结阳性组,病理诊断淋巴结阴性且清扫淋巴结在 5-6 枚以上划为淋巴结阴性组。研究两组在临床病理特点上可能存在的差异。采用 Empower Stats (易侕统计)和 R 软件进行统计分析,计量资料用均数± 标准差表示,计数资料用百分数表示。分类变量两组间比较采用 Pearson 卡方检验或 Fisher 确切概率法。分析年龄、性别、肿瘤最大直径、肿瘤多中心性、及是否合并桥本甲状腺炎与颈淋巴结转移的相关性,多因素 logistic 回归分析年龄与淋巴结转移的风险,以 P 值小于 0.05 认为差异具有统计学意义。

2 结果

2.1 病理结果

51 例甲状腺癌病例中,甲状腺乳头状癌 49 例,占 96%,髓样癌 2 例,无滤泡状癌及未分化癌。49 例乳头状癌中,有 2 例甲状腺微小乳头状癌,肿瘤最大径在 9 mm-60 mm 不等,平均 26.7± 12.5 mm。其中 18 例(36.7%)为双侧甲状腺乳头状癌;乳头状癌组淋巴结转移 38 例 (77.5 %),1 例单纯 " 中央区 " 淋巴结转移。14 例(27.4%)乳头状癌患者合并桥本氏甲状腺炎。

表 1 51 例临床及病理特征

Table 1 The clinical and pathological characteristic of 51 cases of thyroid cancer in children and adolescence

Clinical characteristic			Pathological characteristic		
Age		14.5± 3.4	Diameter		26.7± 12.5mm
Gender	Boy	16(31.3 %)	Pathological type	PTC	48(96 %)
	Girl	35(68.6 %)		MTC	2 (4 %)
Complaint	Physical examination	3 (6.7 %)	Multicentricity	Unilateral	33(63.3 %)
	Cervical asymmetry	13(28.9 %)		Bilateral	18(36.7 %)
	hoarseness	1 (2.2 %)	CLNM[1]	Yes	35/41(85.3 %)
	Palpable mass	34(68.9 %)		No	6/41(14.7 %)
Duration	＜1mouth	39(56.9 %)	Combined with HT[2]	Yes	14(27.4 %)
	≥ 1mouth	22(43.1 %)		No	37(72.6%)

Note: [1]CLNM cervical lymph node metastasis, [2] HT Hashimoto's Thyroiditis.

2.2 乳头状癌亚组淋巴结转移的风险因素

颈部淋巴结转移与性别、肿瘤最大直径、多中心性及是否合并桥本甲状腺炎并无明显差异,但与年龄有相关性(P=0.036,表 2)。Logistic 回归分析得出,该组乳头状癌患儿,随着年龄的升高,颈部淋巴结转移风险也随之升高(OR=1.36;95 % CL=1.09,1.69;P=0.007),在调整了性别、肿瘤最大直径、多中心性及是否合并桥本等临床及病理因素后, 结果无明显改变(OR=1.40;95 % CL=1.05,1.85; P=0.021) (表 3)。

3 讨论

儿童及青少年人群中,甲状腺结节较成人少见,但是恶性比例较高。美国 1975 年的一项研究显示,约 1.79 %的儿童有明显的甲状腺结节[6,7],随着超声诊断的广泛应用[8],发病率升高到 0.2-5.1%[9,10]。其中约 25 %为恶性,而成人约 5 %[3,9]。SEER[1,8]统计数据显示,在 1975-2006 年间,儿童甲状腺癌总发病率为十万分之一(5-9 岁),十万分之五(10-14 岁),十万分之十八(15-19 岁)。这与本研究纳入病例的年龄分布基本一致。该组人群甲状腺癌性别差异较成人较小[11],但仍以女性患者较多[2]。

儿童甲状腺癌几乎均是分化癌。在我们的病例资料中,甲状腺乳头状癌占 96 %(49/51),髓样癌占 3.9 %(2/51),没有滤泡状癌和未分化癌等。但儿童比成人更易出现淋巴结转移[3,14],有研究示发生率达 78.9%[15,16],该组甲状腺乳头状癌病例中,淋巴结转移率达 77.5 %,与文献报道的淋巴结转移发生率接近。针对本研究中的乳头状癌患儿,我们进一步分析了该组颈淋巴结转移的风险因素,统计学分析得出,年龄是该组颈淋巴结转移的独立风险因素 (OR=1.40;95 % CL=1.05,1.85; P=0.021), 而性别、肿瘤多中心性、肿瘤最大直径及是否合并桥本甲状腺炎等临床病理因素对淋巴结转移影响并不显著。这可能与本研究病例的年龄分布有关,结论尚需进一步研究证实。但也有文献报道,年龄是儿童及青少年甲状腺癌预后的相关因素[17,18]。成人

表 2 乳头状癌组淋巴结转移与临床病理特点的关系

Table 2 The relationship between CLNM and clinipathological characteristics in PTC group

		None-CLNM[1]	CLNM	P value
Age		11.64± 4.99	15.29± 2.30	0.036
Gender	Female	8 (72.7%)	27 (71.1%)	0.914
	Male	3 (27.3%)	11 (28.9%)	
Diameter(max)		29.73± 13.84	27.13± 11.79	0.631
Multicentricity	Unilateral	10(90.9%)	26(68.4%)	0.246
	Bilateral	1(9.1%)	12(31.6%)	
Combined with HT[2]	No	6(54.5%)	28(73.7%)	0.275
	Yes	5(45.5%)	10(26.3%)	
Total		11	38	

Note: [1]CLNM cervical lymph node metastasis, [2] HT Hashimoto's Thyroiditis.

表 3 年龄与颈部淋巴结转移的 Logistic 回归分析

Table 3 The Multivariate Logistic Regression of age and CLNM in PTC group

	Model 1			Model 2		
	OR	95% CL	P value	OR	95% CL	P value
Age	1.36	(1.09, 1.69)	0.007	1.40	(1.05, 1.85)	0.021

Note: Model 1, non-adjusted variable; model 2: An adjusted analysis of gender, multicentricity, diameter-Max, HT.

甲状腺乳头状癌淋巴结转移风险评估可能对该组人群并不适用[5]。因此,对于该组人群,也需要制定相应的风险评估标准。

外科手术是治疗儿童及青少年甲状腺癌的首要治疗方法[19,20],合适的手术方案是影响预后的重要因素。目前尚无统一的手术范围,有学者建议行甲状腺全切以最大限度的切除多发的肿瘤病灶,并能更准确地进行术后随访[21]。但也有研究者认为,儿童甲状腺癌整体预后较好,腺体全切对整体预后和生存率无太大影响,仅需行腺体次全切除即可[22],传统的甲状腺癌预后因素并不影响患儿的 PFS[12]。对于该年龄组甲状腺癌患者,彻底的手术方式会是良好预后和进行准确风险评估的先决条件[23]。

虽然甲状腺肿瘤大多进展缓慢[12],但由于延误治疗出现肿瘤直径变大, 远处转移和甲状腺滤泡上皮较高的非典型性增生,可能导致预后变差和死亡率增高[9], 且儿童及青少年时有出现生理性甲状腺肿的情况,恶性结节往往会被误诊为甲状腺肿或甲亢[13]。因此提倡早期诊断和治疗。本组研究中,患儿一般以颈部明显肿大就诊,占 28.9%,而通过体检发现的不足 7 %。整体从发现到就诊的时间较长,43.1 %的患儿病程在一月以上。积极进行甲状腺的系统体检和筛查,对及早发现该人群甲状腺疾患具有重要意义。

与成人相比,该人群甲状腺癌具有男女发病率差异较成人低、淋巴结转移率高、与头颈部射线接触史关系较大[4,24-26]、有合并遗传综合征等疾病的特点[27]。全面彻底的临床手术并根据病理结果制定适合的术后辅助治疗方案及相关的风险评估标准,积极进行筛查和监测,对提高该组人群甲状腺癌的整体预后水平具有重要意义。

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