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· 临床研究 ·

腮腺淋巴上皮癌 22 例临床分析

张曙光¹, 尹西腾², 徐文光², 韩伟², 刘喆²

1. 淮安肿瘤医院口腔科, 江苏 淮安(223001); 2. 南京大学医学院附属口腔医院, 南京市口腔医院口腔颌面外科, 江苏 南京(210008)

【摘要】目的 探讨腮腺淋巴上皮癌的诊断方法、治疗方式及预后情况, 为临床提供参考。**方法** 2012年至2019年期间收治的腮腺淋巴上皮癌病例22例, 对患者的临床表现、影像学检查、治疗方式及随访结果进行回顾性分析。**结果** 22例患者中, 男性8例, 女性14例; 年龄26~61岁, 主诉病程3天~18年, 单侧腮腺区多发肿块1例, 其余21例均为腮腺区单侧单发肿块。所有患者均行术前螺旋CT检查, CT所示腮腺组织内软组织肿块影, 其内密度影欠均匀, CT值26~81 HU, 15例表现为类圆形, 界限尚清晰; 7例表现为结节状, 界限稍不清晰或部分不清晰。所有病例诊断最终依据病理学检查, HE染色图像可见肿瘤细胞边界清楚, 上皮细胞生长活跃伴有异型性, 可见核分裂像, 肿瘤间质可见丰富的淋巴细胞浸润。22例患者均接受手术治疗, 其中9例患者未行颈淋巴清扫。20例患者术后接受辅助放疗, 其中10例同时行辅助化疗; 1例患者术后仅行化疗, 1例患者术后未行其他任何辅助治疗。所有病例均得到随访, 21例无瘤生存13个月~8年, 1例患者术后16个月因肝转移死亡。**结论** 腮腺淋巴上皮癌是临床上较为罕见的恶性肿瘤, 病理仍是诊断腮腺淋巴上皮癌的金标准。根治性手术切除肿瘤是首选治疗方法, 根据临床检查及影像学检查及颈部情况进行选择性颈淋巴清扫, 术后辅助放化疗可获得较好的治疗效果。

【关键词】 淋巴上皮癌; 腮腺; 腮腺切除术; 面神经解剖术; 颈淋巴清扫; 放疗; 化疗

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Clinical analysis of 22 cases of lymphoepithelial carcinoma of parotid gland ZHANG Shuguang¹, YIN Xiteng², XU Wenguang², HAN Wei², LIU Zhe². 1. Department of Stomatology, Huaian Tumor Hospital, Huai'an 223001, China; 2. Department of Oral and Maxillofacial Surgery, Nanjing Stomatological Hospital, Medical School of Nanjing University, Nanjing 210008, China

Corresponding author: LIU Zhe, Email: kqliuzhe@163.com, Tel: 86-25-83620346

【Abstract】Objective To investigate the diagnosis, treatment and prognosis of lymphoepithelial carcinoma of the parotid gland. **Methods** Data from 22 patients with parotid lymphoepithelial carcinoma from 2012 to 2019 were collected, and their clinical manifestations, imaging examinations, treatment methods and follow-up results were retrospectively analyzed. **Results** Among the 22 patients, 8 were males and 14 were females. The patients ranged from 26 to 61 years old, with a complaint duration ranging from 3 days to 18 years. One patient had multiple unilateral lumps in the parotid gland, and the other 21 patients had single unilateral lumps in the parotid gland. All patients underwent pre-operative spiral CT examination. CT showed a soft tissue lump in the parotid tissue, the internal density shadow was not uniform, the CT value ranged from 26 to 81 Hu, and 15 patients presented elliptical lesions with clear boundaries. Seven patients presented nodular lesions, and the boundary was not clear. The diagnosis of all cases was ultimately based

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【作者简介】 张曙光, 副主任医师, 硕士, Email: 315725513@qq.com

【通信作者】 刘喆, 医师, 硕士, Email: kqliuzhe@163.com, Tel: 86-25-83620346

on pathological examination. Hematoxylin-eosin (HE) staining images showed active epithelial cell growth with atypia, mitotic figures could be seen, and abundant lymphocyte and plasma cell infiltration could be seen in the tumor stroma. All 22 patients received surgical treatment; 9 patients did not undergo cervical lymph node dissection. Twenty patients received adjuvant radiotherapy after surgery, and 10 of them received adjuvant chemotherapy at the same time. One patient only received chemotherapy after surgery, and one patient did not receive any other adjuvant therapy after surgery. All patients received follow-up visits. One patient died of liver metastasis 16 months after the operation, and the remaining patients survived without tumors for periods of 13 months to 8 years until the present. **Conclusion** Parotid lympho-epithelial carcinoma is a rare malignant tumor clinically. Pathology is still the gold standard for the diagnosis of lympho-epithelial carcinoma of the parotid gland. Radical resection of the tumor is the first choice of treatment. Selective neck lymph node dissection and postoperative adjuvant radiotherapy and chemotherapy can obtain better therapeutic effects according to clinical examination, imaging examination and neck conditions.

【Key words】 lymphoepithelial carcinoma; parotid gland; parotidectomy; facial nerve anatomy; neck lymphatic dissection; radiotherapy; chemotherapy

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【Competing interests】 The authors declare no competing interests.

淋巴上皮癌(lymphoepithelial carcinoma, LEC)是临床上一种较为罕见但分化差的恶性肿瘤,以未分化的上皮肿瘤细胞为特征,伴有丰富的淋巴样间质组织;其可以发生在不同的原发部位,如鼻咽、唾液腺、扁桃体、胸腺、肺、乳腺、子宫、胃、尿道、膀胱和皮肤等。涎腺淋巴上皮癌仅占所有涎腺恶性肿瘤的0.4%,其中80%发生在腮腺^[1]。目前临床医生对于腮腺淋巴上皮癌的认识以及治疗尚不统一,因此需要获得更多的临床资料,以期能制定出最佳的治疗策略。本文回顾了南京大学医学院附属口腔医院口腔颌面外科自2012年10月至2019年11月收治的22例腮腺淋巴上皮癌病例,对其临床诊治资料进行总结分析。

1 资料和方法

1.1 病例来源

南京大学医学院附属口腔医院口腔颌面外科2012年10月至2019年11月收治的患者22例,所有病例均经病理学检查,由两名经验丰富的病理科高级职称医师独立诊断,并通过鼻咽纤维镜检查排除鼻咽癌可能。通过查阅病例资料获取所需信息。

纳入标准:①经病理已确诊且为腮腺原发的淋巴上皮癌病例;②按确诊时所有病例已排除鼻咽部和其他部位来源的转移癌;③病变均为单侧;④随访时间为术后至少1年。

1.2 研究方法

对22例腮腺淋巴上皮癌患者的基本临床资料、临床表现、影像学检查、治疗方式及预后情况

进行总结分析。

2 结果

22例腮腺淋巴上皮癌患者临床资料如表1所示。本组病例共22例,其中男性8例,女性14例;年龄26~61岁,平均年龄(44.09±10.26)岁;主诉病程3日至18年不等。

单侧腮腺区多发肿块1例,其余21例均为单侧腮腺区单发肿块;肿块均表现为质地中等偏硬,活动度一般,大部分界清,无明显触压痛。所有病例中仅1例患者术后出现患侧额纹消失的神经损伤症状。

术前检查双侧颌下及颈部均未扪及肿大淋巴结。所有患者均行术前螺旋CT检查,CT所示腮腺组织内软组织肿块影,其内密度影欠均匀,CT值介于26~81 HU,15例表现为类圆形,界限尚清晰(图1a);7例表现为结节状,界限稍不清晰或部分不清晰(图1b)。22例患者颈部CT检查均未见明显肿大淋巴结。

22例患者首次手术先行腮腺肿物及部分腺叶切除术,术后病理明确诊断后,根据临床分期及结合患者及家属意愿制定进一步治疗方案。手术治疗包括:腮腺肿物及部分腺叶切除+面神经解剖术、腮腺肿物及腮腺全叶切除术、腮腺淋巴上皮癌扩大切除术+腮腺全切术+面神经解剖术+肩胛舌骨上淋巴清扫术、腮腺淋巴上皮癌扩大切除术+腮腺全切术+面神经解剖术+全颈淋巴清扫术(表1)。

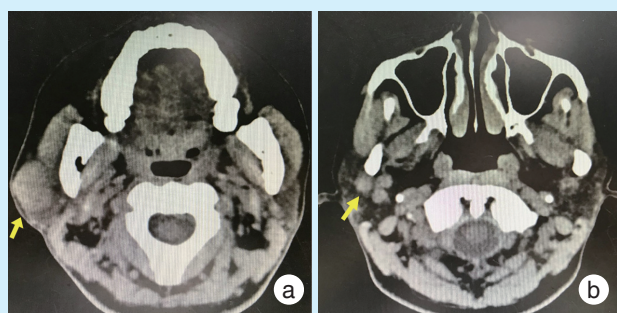
所有病例诊断最终依据病理学检查,镜下可

表1 22例腮腺淋巴上皮癌患者临床资料

Table 1 Clinical data of 22 patients with LEC in the parotid gland

Serial number	Gender	Age	Duration of disease according to patients complaint	Stage	Treatment	Follow-up
1	Male	36 years	18 years	cT1N0M0	S1	Tumor-free survival 8 years
2	Female	34 years	5 years	pT1N0M0	S*+R+C	Tumor-free survival 7 years
3	Female	48 years	7 months	pT3N0M0	S*+R+C	Tumor-free survival 7 years
4	Male	26 years	2 months	pT1N0M0	S*+R+C	Tumor-free survival 7 years
5	Female	56 years	2 years	cT2N0M0	S1+R+C	Tumor-free survival 6 years
6	Female	42 years	1 months	cT2N0M0	S2+R+C	Tumor-free survival 6 years
7	Female	48 years	2 years	cT1N0M0	S1+R+C	Tumor-free survival 6 years
8	Male	60 years	3 days	cT2N0M0	S2+R	Tumor-free survival 5 years
9	Female	28 years	1 week	cT1N0M0	S1+R	Tumor-free survival 5 years
10	Male	54 years	2 weeks	cT3N0M0	S2+R	Tumor-free survival 4 years
11	Female	49 years	4 years	pT2N0M0	S*+R	Tumor-free survival 35 months
12	Male	28 years	2 years	pT2N0M0	S*+R	Tumor-free survival 31 months
13	Female	61 years	10 days	pT2N0M0	S*+R	Tumor-free survival 29 months
14	Female	40 years	3 months	cT2N0M0	S2+R+C	Tumor-free survival 27 months
15	Male	32 years	10 months	cT2N0M0	S1+C	Tumor-free survival 16 months
16	Female	47 years	9 months	pT2N0M0	S*+R+C	Tumor-free survival 26 months
17	Female	41 years	1 year	pT2N0M0	S*+R	Tumor-free survival 25 months
18	Female	47 years	2 months	pT1N0M0	S*+R+C	Tumor-free survival 21 months
19	Female	55 years	7 months	pT2N0M0	S*+R+C	Tumor-free survival 19 months
20	Male	51 years	10 years	pT2N0M0	S*+R	Tumor-free survival 19 months
21	Male	42 years	3 months	pT4aN0M0	S*+R	Tumor-free survival 18 months
22	Female	45 years	2 weeks	pT1N0M0	S*+R	Tumor-free survival 13 months

S1: resection of a lump in the parotid gland and partial parotidectomy + facial nerve anatomy; S2: resection of a lump in the parotid gland and parotidectomy; S*: extended resection of LEC in the parotid gland + parotidectomy + facial nerve anatomy + suprahyoid lymphatic dissection; S⁺: extended resection of LEC in the parotid gland + parotidectomy + facial nerve anatomy + total neck lymphatic dissection; R: radiation therapy; C: chemotherapy; follow-up: the latest follow-up time was 2020-12-29, and the shortest follow-up duration was 13 months; LEC: lymphoepithelial carcinoma



a: the soft tissue lump in the parotid gland tissue is elliptical, with clear boundaries; b: the soft tissue lump in the parotid gland tissue is nodular and the boundary is not clear

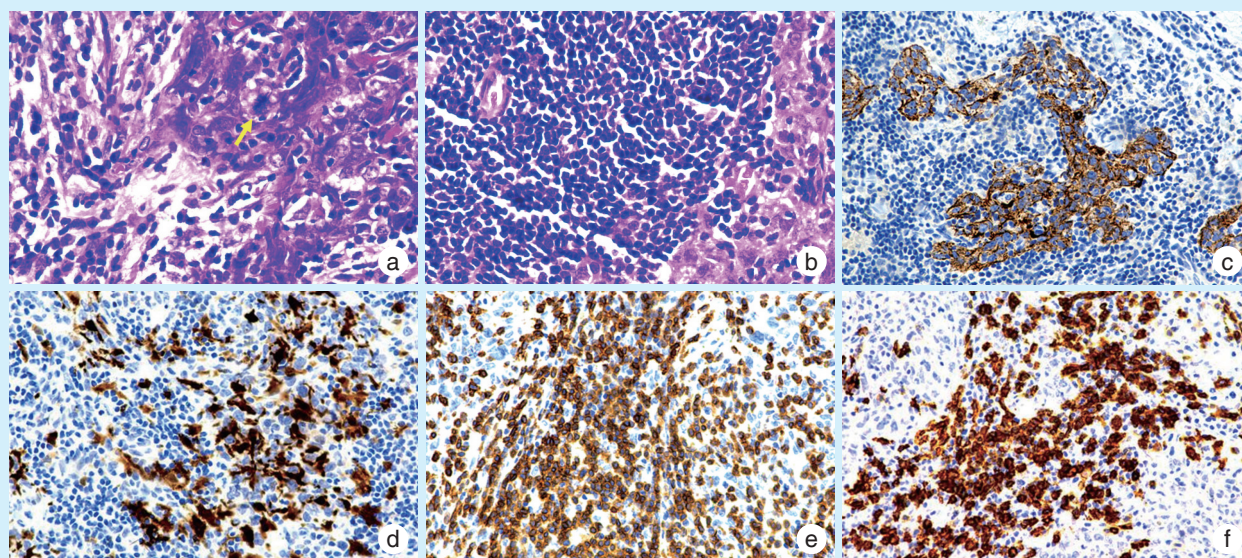
Figure 1 CT axial image of lymphoepithelial carcinoma of the right parotid gland

图1 右侧腮腺淋巴上皮癌CT轴位影像

见肿瘤细胞边界清楚,上皮细胞生长活跃伴有异型性,可见核分裂像,肿瘤间质可见丰富的淋巴细胞浸润;免疫组化检测显示,上皮组织CK8/18(+),CK5/6(+),p63(+),S-100(+),间质淋巴细胞CD3、CD43、CD20均(+)(图2);行颈淋巴清扫的患者有13例,颈淋巴结均未见明显转移癌。

所有患者术后均行鼻咽纤维镜检查提示鼻咽

部未见新生物,排除鼻咽癌可能。22例病例中有13例进行同侧颈淋巴清扫,其中8例患者行肩胛骨上淋巴清扫术,5例患者行全颈淋巴清扫术,全部病例均保留患侧面神经,经治疗后无瘤生存13个月~7年;9例患者未行颈淋巴清扫,其中6例I~II期患者,术中可见肿物包膜完整,与周围组织无明显粘连,术前颈部CT未见明显肿大淋巴



a: HE staining images showed active epithelial cell growth with atypia, and mitotic figures (indicated by the arrow) can be seen ($\times 400$); b: abundant lymphocyte cells infiltration can be seen in the tumor stroma ($\times 400$); c: immunohistochemistry images showed epithelial tissue CK8/18 (+) ($\times 200$); d: immunohistochemistry images showed epithelial tissue S-100 (+) ($\times 200$); e: immunohistochemistry images showed interstitial lymphocytes CD3 (+) ($\times 200$); f: immunohistochemistry images showed interstitial lymphocytes CD20 (+) ($\times 200$)

Figure 2 Pathological manifestations of lymphoepithelial carcinoma

图2 淋巴上皮癌的病理表现

结,则未予以同期颈淋巴清扫,余下3例与患者及家属交代治疗方案无法接受颈淋巴清扫术,未行颈淋巴清扫的病例无瘤生存16个月~8年。

20例患者术后接受辅助放疗,其中10例同时行辅助化疗;1例患者术后仅行化疗,1例患者术后未行其他任何辅助治疗。术后辅助放疗剂量66~70 Gy,放疗范围包括原发病灶区加同侧颈部淋巴引流区域;术后辅助化疗,化疗药物为5-氟尿嘧啶加顺铂。

3 讨论

淋巴上皮癌又称为淋巴上皮瘤样癌、恶性淋巴上皮病变、伴有淋巴样间质的未分化癌等^[2]。1962年,Hilderma及同事首次报道1例40岁男性患者的腮腺淋巴上皮癌。该病具有明显的人种和区域差异,好发于北极地区的爱斯基摩人、日本人及中国南方人^[3]。一般女性发病率高于男性。

腮腺淋巴上皮癌临床表现为质地中等偏硬的无痛性肿块,生长缓慢,界限尚清,活动度一般,常与腮腺多形性腺瘤和腺淋巴瘤较难区分。当病程较长时可出现与周围组织粘连,累及面神经出现面瘫症状,颈部出现肿大淋巴结等。术前行CT或

MRI检查可以评估肿物的位置及与周围组织的关系,仍然是术前检查重要的辅助工具。对于唾液腺淋巴上皮癌是否存在特征性影像学表现,Ban等^[4]通过回顾性分析28例涎腺淋巴上皮癌的CT及MRI影像学表现,根据边缘及形态将病变分为三类:边界清晰的类圆形、部分或界限不清的分叶状或斑块状及浸润生长界限模糊的不规则形状,并且病变内未见囊性病变及钙化,病变中心未见坏死,这可与唾液腺常见的恶性肿瘤如粘液表皮样癌、腺样囊性癌相区分。本组病例影像学检查结果显示腮腺肿物CT表现为2种情况,其中68.2%(19/22)病例的影像学表现为肿块形态规则、界限清晰,与涎腺良性肿瘤特征相似,31.8%(7/22)病例表现为界限不清的结节状。淋巴上皮癌在临床表现和影像学上均缺乏特征,鉴别较为困难。而本组病例术前均未出现颈部淋巴结转移,这与术前影像学提示颈部未见明显肿大淋巴结基本一致。因此,术前行影像学检查对于制定手术方式及术后放疗方案具有参考价值。

唾液腺淋巴上皮癌的治疗方式包括手术切除、放疗和化疗,而规范治疗存在一定的争议,目前,手术切除加术后辅助放疗被认为是唾液腺原

发性淋巴上皮癌的首选治疗方法^[5]。由于淋巴上皮癌局部侵袭性强,在考虑功能和解剖情况下应尽可能扩大范围切除,保证足够的安全边界。淋巴上皮癌具有区域淋巴结转移倾向,文献中唾液腺淋巴上皮癌的颈部淋巴结转移率大不相同,一般为20%~67%,20%出现局部复发和继发淋巴结转移,20%在3年内出现远处转移,累及部位包括肺、肝、骨、脑等^[6]。对于是否同期行颈淋巴清扫,主要争议存在于临床检查及影像学未见可疑淋巴结转移的患者是否需行预防性颈淋巴清扫,大多学者认为应该重视淋巴上皮癌的早期转移,选择性颈淋巴清扫有一定的必要性,颈清的范围包括Ib、II区;利伟军等^[7]对25例唾液腺淋巴上皮癌的研究指出,预防性颈淋巴清扫,可使1/5(5/25)患者免于带瘤离院,减少复发;Yin等^[8]报道,对于腮腺淋巴上皮癌的淋巴转移分布,T1-2和T3-4肿瘤的淋巴受累发生率差异无统计学意义,这表明颈部切除范围或预防性颈部放疗剂量不应取决于原发灶大小。而本组病例中,13例患者进行颈淋巴清扫,9例患者未行颈淋巴清扫,术后随访中1例未行颈淋巴清扫且术后未行放疗的患者死亡,其余患者均未发生复发或转移;基于本次研究,对于不同临床分期的患者,预防性颈淋巴清扫与不做颈淋巴清扫的患者相比,并没有显著提高患者生存率及降低肿瘤复发率,但考虑本研究病例数量有限,该结论需更多病例验证。同样有文献报道,对于临床及影像学检查均未发现颈淋巴结转移的早期唾液腺淋巴上皮癌,预防性颈淋巴清扫对生存率无明显改善,建议仅行原发灶切除及所在腺体摘除即可,不必行颈淋巴清扫,但同时应保证严密随访。而对于临床上颈部有可疑小淋巴结转移时应应对同侧颈部淋巴结进行清扫^[9]。

尽管面神经在临床上80%都是完整的,但是腮腺淋巴上皮癌经常侵犯神经,Whelan等^[10]认为保留面神经会影响肿瘤安全性,主张同期切除累及神经以降低术后复发率。本研究中,所有患者术前均未累及面神经出现相应面瘫症状,术中视面神经与肿物的关系均予以面神经解剖,保留面神经,术后仅1例患者出现患侧额纹消失,其余均无面神经损伤症状。从本次研究中可见,对于术前无面瘫症状,术中肿物与面神经无明显粘连者可保留面神经,可提高患者术后生存质量,且对术后生存率无明显影响。

与其他的唾液腺癌相比,淋巴上皮癌具有未

分化癌的特性,比其他未分化唾液腺癌有更好的预后,部分原因是由于对放射治疗极为敏感。术后放疗适应于所有淋巴上皮癌患者,并且放疗靶区包括瘤床及同侧颈部淋巴引流区^[11]。研究显示,放疗对淋巴上皮癌的局部控制率超过90%^[12]。本次研究中,91%(20/22)患者术后均予以放疗,治疗后没有出现局部复发及远处转移,说明手术联合放疗可取得较好的效果。

淋巴上皮癌的预后存在差异,5年生存率大概在50%~87%^[13],局部复发率高达28.9%,约20%患者3年内发生远处转移。唾液腺淋巴上皮癌的5年、10年和15年生存率分别为90%、75%和54%^[14]。也有研究报道生存率相对较低,1年、3年和5年分别为86.15%、48.46%、24.23%^[15]。预后的多样性可能反映了早期研究对疾病的认知欠缺及治疗方式差异相关。

腮腺淋巴上皮癌是临床上较罕见的恶性肿瘤,临床诊断和治疗还存在一定争议。腮腺淋巴上皮癌的诊断需排除鼻咽癌转移后才可确定腮腺原发,其治疗仍需进一步研究制定规范诊疗流程。本文通过22例腮腺淋巴上皮癌回顾分析认为彻底切除肿瘤仍是主要治疗方式,根据临床检查及影像学检查颈部情况进行选择性颈淋巴清扫,术后辅助放疗;对于病变范围较大,存在淋巴结转移的患者增加辅助化疗,以提高术后生存率,考虑到本次研究患者数量有限,随访时间较短,这一结论需要更多的病例研究来证明。

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《口腔疾病防治》入选中国医药卫生核心期刊

2021年1月,中华出版促进会医学出版专业委员会、中国医师协会科研出版工作委员会按照《中国医药卫生核心期刊标准专家共识(第一版)》、《医务人员职称论文类型专家共识(第一版)》及核心期刊一票否决的情况要求,确定并发布了2020年中国医药卫生核心期刊目录。由广东省卫生健康委员会主管,南方医科大学口腔医院、广东省牙病防治指导中心主办的《口腔疾病防治》入选其中。

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