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·防治实践·

颌面结缔组织增生性毛发上皮瘤2例报告及文献复习

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【摘要】 目的　探讨结缔组织增生性毛发上皮瘤的诊断和临床治疗方法。**方法**　对2例颌面部结缔组织增生性毛发上皮瘤临床资料进行总结并结合文献分析。**结果**　2例结缔组织增生性毛发上皮瘤患者均为男性，年龄分别为21岁和30岁，临床表现分别为颌面部无痛性浅褐色及浅白色斑块，病变区质韧、界清，中间凹陷无溃疡，病程10～16个月，就医前1～3个月肿物有明显增大病史。手术行沿瘤体外周3 mm切开皮肤、完整切除肿物，邻近皮瓣修复局部组织缺损手术；术后病理报告镜下见病变肿瘤细胞位于真皮层，呈条索状、小梁状或巢状，可见微小囊腔，上皮巢周围可见纤维结缔组织增生，瘤细胞无异型性，核分裂不明显。免疫组化报告bcl-2(-)、CK7(-)、CK19(-)、CD34(+)、P63(+)、CK56(+)、Ki67(±)，病理诊断为结缔组织增生性毛发上皮瘤。患者术后随诊24个月，期内未见肿物复发、手术疤痕不明显、颌面无畸形或功能障碍。**结论**　病理和免疫组化检查是确诊结缔组织增生性毛发上皮瘤的依据，手术切除肿物是有效的治疗方法。

【关键词】 毛发上皮瘤；　增生性；　结缔组织；　颌面；　临床病理；
免疫组化；　治疗分析
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Maxillofacial connective tissue hyperplastic trichoepithelioma: report of two cases and a literature review

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【Abstract】 Objective　To investigate the diagnosis and clinical treatment of maxillofacial connective tissue hyperplastic trichoepithelioma. **Methods**　The clinical data of two cases of maxillofacial connective tissue hyperplastic trichoepithelioma were summarized and analyzed along with the literature. **Results**　Two cases of maxillofacial connective tissue hyperplastic trichoepithelioma were male, aged 21 and 30 years. The clinical manifestations were painless pale brown and pale white plaques in the maxillofacial region. The lesion was tough and clear, with no ulcers in the middle depression. The course was 10-16 months, with 1-3 months before medical treatment, and the tumor had a significant history of enlargement. After surgery, the skin was cut 3 mm along the outer circumference of the tumor, and local tissue defects were repaired by the adjacent flap. The pathological report showed that the tumor cells were located in the dermis, and were striped, trabecular or nested. The tiny sac contained fibrous connective tissue proliferation. The tumor cells were amorphous without obvious nuclear division. Immunohistochemical analysis reported bcl-2(-), CK7(-), CK19(-), CD34(+), P63(+), CK56(+), and Ki67(±). The pathological diagnosis was connective tissue proliferative hair epithelial tumor. The patient was followed up for 24 months. There was no recurrence of the tumor, no obvious scarring, and no

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deformity or dysfunction of the maxillofacial region. **Conclusion**　Pathological and immunohistochemical examination is the basis for the differential diagnosis of maxillofacial connective tissue hyperplastic trichoepithelioma, and surgical removal of tumors is an effective treatment.

【Key words】 hair epithelioma; proliferative; connective tissue; maxillofacial; clinicopathology; immunohistochemistry; therapeutic analysis

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结缔组织增生性毛发上皮瘤(desmoplastic trichoepithelioma, DT)是毛发上皮瘤的一种特殊类型,在1977年由Brownstein首次提出[1];该病发病率较低,仅为0.02%,占皮肤肿瘤不足1%,目前国内外相关报道较少[2-3]。结缔组织增生性毛发上皮瘤与硬斑病样基底细胞癌的组织学鉴别诊断尚无满意的标准[4]。本文报道2例颌面部结缔组织增生性毛发上皮瘤,初步探讨其病理特点、鉴别诊断和治疗。

1　材料和方法

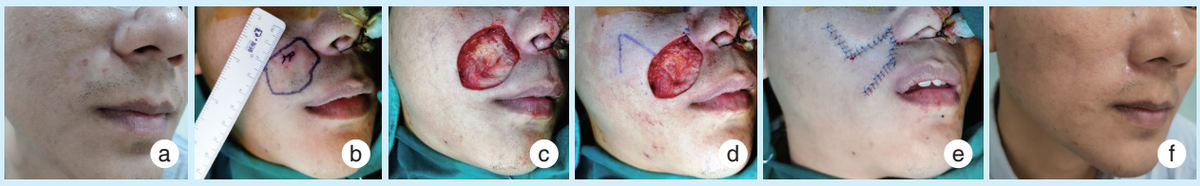
1.1　临床资料

佛山市中医院口腔医疗中心2013年5月~2018年5月收治2例颌面部结缔组织增生性毛发上皮瘤患者,均为男性,年龄分别为21、30岁,临床表现分别为颌面部无痛性浅褐色及浅白色斑块,病变区质韧、界清,中间凹陷无溃疡,病程10~16个月,就医前1~3个月肿物有明显增大史。2例患者均手术治愈,术后组织病理为结缔组织增生性毛发上皮瘤。随访2年,未见复发。

1.2　典型病例

患者男,30岁,因右面部无明显诱因出现无痛性浅白色斑块10个月就诊。患者起病时无明显不适症状,未予诊治,近1个月斑块逐渐扩大、偶有瘙痒感觉,影响美观,遂来佛山市中医院就诊。既往体健,否认家族中类似疾病患者,无药物过敏史。专科检查见右侧面部皮肤直径35 mm的浅白色不规则斑块,边缘轻度隆起,中央轻度凹陷萎缩,斑块表面光滑,无毛发生长,边界清楚,质韧,无明显压痛。门诊诊断:右侧面部肿物性质待查。

患者入院后完善相关检查,排除手术禁忌,在手术室经鼻孔气管内插管全麻下沿瘤体外周3 mm切开皮肤,行右侧颌面肿物切除+邻近组织瓣转移修复术,术后抗炎治疗,术后7 d拆线、伤口愈合良好(图1)。术后组织病理报告:病变肿瘤细胞位于真皮层,呈条索状、小梁状或巢状,可见微小囊腔,上皮巢周围可见纤维结缔组织增生,瘤组织无异型性,核分裂不明显(图2)。

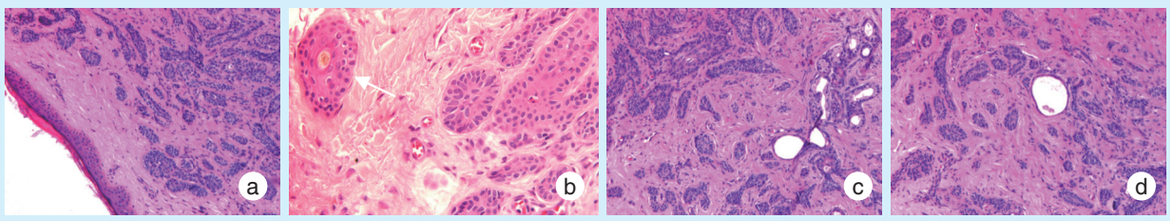


a: a white irregular patch on the right cheek, with a diameter of approximately 35 mm; b & c: the tumor was completely removed in the operating room; d & e: adjacent flap was transferred to repair the tissue defect; f: one year after the operation, no obvious scar or dysfunction was found

Figure 1　Preoperative, intraoperative and postoperative illustrations of patients with maxillofacial connective tissue hyperplastic trichoepithelioma

图1　颌面结缔组织增生性毛发上皮瘤患者术前、术中、术后图像

免疫组化检查报告:bcl-2(-)提示肿瘤为良性肿物;CK7(-)、CK19(-)提示为非汗腺来源肿物;CD34(+),肿瘤间质细胞表达,提示肿物为毛发源性肿瘤;P63(+)、CK56(+)提示肿瘤组织为鳞状上皮细胞;Ki67(±),核增殖指数不高提示为良性肿物。病理诊断为结缔组织增生性毛发上皮瘤。出院后2年内随诊,未见肿物复发、右颌面未见明显手术疤痕,无颌面畸形或功能障碍,疗效满意。



a: the tumor cells were located in the dermis; b: arrows identify hair follicles and hairs in the tumors; c & d: tumor cells are embedded in the dermis with tiny sacs in the form of cords, trabeculae, or nests. Connective tissue proliferation can be observed around the epithelial nests with no heteromorphism or nuclear fission (H&E, × 200)

Figure 2　Histopathological images of tumors in patients with maxillofacial connective tissue hyperplastic trichoepithelioma

图2　颌面结缔组织增生性毛发上皮瘤患者肿物组织病理图片

2　讨　论

2.1　临床表现

毛发上皮瘤来自毛囊和毛基质的外壁，起源于原发性上皮胚芽或多能胚胎细胞，可分3种临床类型：孤立型、多样型和罕见的巨大孤立型[5]，常见于面部或头皮[6]。结缔组织增生性毛发上皮瘤为单发性毛发上皮瘤，因其具有独特的临床和组织学特征，临床特点为早期呈单发性皮损，常位于面部，明显硬化，多数边缘高起呈环状，中央凹陷不破溃，多见于青少年女性，是毛发上皮瘤的一种特殊类型。颌面结缔组织增生性毛发上皮瘤病例罕见。本组2例颌面结缔组织增生性毛发上皮瘤病例均为男性，年龄21、30岁，病程10～16个月；肿瘤生长缓慢、病程长、无自觉症状、长期无明显变化，但在就诊前短期内突然增大明显、有瘙痒不适。结缔组织增生性毛发上皮瘤的早期临床确诊存在一定的困难，结缔增生性毛发上皮瘤是一种比较罕见的良性皮肤附属器肿瘤，其发生的原因至今未明[7]；肿瘤持续发展可造成组织破坏，影响器官功能或者美观，发生于面部的损害，可导致容貌损毁。

2.2　鉴别诊断

结缔组织增生性毛发上皮瘤可能是起源于多潜能的基底细胞，向毛发结构分化的良性肿瘤；其与一般的毛发上皮瘤不同，主要由3种成分组成：狭窄的瘤细胞束、角质囊肿和结缔组织基质[8]；一般无神经周围浸润；肿瘤细胞不表达bcl-2，Ki67增殖指数低[9]；肿瘤损害周围的成纤维细胞无基质溶解素3的表达；周围基质中有$CD34^+$细胞。与一般的毛发上皮瘤相比，结缔组织增生性毛发上皮瘤在镜下可以看到更多的树突状细小血管穿通于高度纤维性的间质中[10]。

2.2.1　硬斑病样基底细胞癌　结缔组织增生性毛发上皮瘤最易与硬皮病样基底细胞癌相混淆[11]，硬斑病样基底细胞癌多见于青年人，常单发，好发于面、额部，皮损为扁平或轻度凹陷的黄白色蜡样硬化性浸润斑块，呈不规则或匍行状，无珍珠状边缘或溃疡、结痂，边界不清，发展缓慢。结缔组织增生性毛发上皮瘤缺乏外周细胞栏栅状排列、坏死、有丝分裂，鲜有溃疡发生，而硬皮病样基底细胞癌通常无角质囊肿形成[12-13]，且过碘酸雪夫染色（PAS）阴性[7]。但结缔组织增生性毛发上皮瘤与硬斑病样基底细胞癌的组织学鉴别到目前为止尚无满意的标准。

2.2.2　汗管瘤、微囊肿性附属器癌　结缔组织增生性毛发上皮瘤可能会被误诊为汗管瘤、微囊肿性附属器癌或小汗腺上皮瘤。汗管瘤是向小汗腺末端导管分化的错构瘤，多见于女性，与内分泌、妊娠、月经及家族遗传等因素有关，也有研究显示日晒会显著促进其发生[14]。其皮损通常为多发的、皮色为淡黄色的小丘疹，无自觉症状；多数病例皮损局限于下眼睑及额部皮肤，稍高出皮肤表面。

2.2.3　扁平疣　结缔组织增生性毛发上皮瘤还应与扁平疣相鉴别，扁平疣皮损多发于面部、手背，表现为大小不等的扁平丘疹，轻度隆起，呈圆形、椭圆形或多角形，境界清楚，无明显的自觉症状，病程慢，好发于青少年的病毒感染性疾病，主要依据临床表现和实验室常规检查诊断。

2.3　临床治疗

颌面巨大的结缔组织增生性毛发上皮瘤是毛发上皮瘤中较为难治的一种，本病治疗上首选手术切除。本组2例颌面部的结缔组织增生性毛发

上皮瘤患者行肿物手术切除+邻近组织瓣修复组织缺损，术后7～9 d拆线，伤口愈合良好，颌面无明显手术疤痕，随访2年未见肿瘤复发。对于儿童或者不愿采取手术切除治疗的患者，有报道口服异维A酸20 mg/d[15]、外用维胺酯及5%咪喹莫特[16]等保守治疗也可明显好转。激光、冷冻、高频电离子等方法容易造成面部皮肤损伤留下疤痕[17]，影响美容和功能，不适宜治疗颌面部的巨大结缔组织增生性毛发上皮瘤。

综上所述，组织病理、免疫组化检查是结缔组织增生性毛发上皮瘤的确诊依据，手术切除+皮瓣修复是治疗颌面结缔组织增生性毛发上皮瘤首选的有效方法。颌面结缔组织增生性毛发上皮瘤的临床特征、病程进展以及疾病转归有待收集更多的病例分析，远期治疗效果有待进一步观察。

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参考文献

[1] Brownstein MH, Shapiro L. Desmoplastic trichoepithelioma[J]. Cancer, 1977, 40(6): 2979-2986. doi: 10.1002/1097-0142(197712)40:6<2979: aid-cncr2820400633>3.0.

[2] Carter JJ, Kaur MR, Hargitai B, et al. Congenital desmoplastic trichoepithelioma[J]. Clin Exp Dermatol, 2007, 32(5): 522-524. doi: 10.1111/j.1365-2230.2007.02431.x.

[3] Samaila MO. Adnexal skin tumors in Zaria, Nigeria[J]. Ann Afr Med, 2008, 7(1): 6-10. doi: 10.4103/1596-3519.55691.

[4] Wang Q, Ghimire D, Wang J, et al. Desmoplastic trichoepithelioma: a clinicopathological study of three cases and a review of the literature[J]. Oncol Lett, 2015, 10(4): 2468-2476. doi: 10.3892/ol.2015.3517.

[5] Lovgren ML, Rajan N, Joss S, et al. Inherited desmoplastic trichoepitheliomas[J]. Clin Exp Dermatol, 2019, 44(7): e238-e239. doi: 10.1111/ced.13876.

[6] Mathur M, Kedia SK. Multiple familial trichoepithelioma: a case report[J]. J College Medical Sciences-Nepal. 2012, 6(4). doi: 10.3126/jcmsn.v6i4.6731.

[7] Gulseren D, Kwock JM, Patterson JW. A case of combined desmoplastic trichoepithelioma and compound melanocytic nevus[J]. J Cutan Pathol, 2017, 44(7): 657-659. doi: 10.1111/cup.12948.

[8] Macdonald DM, Jones EW, Marks R. Sclerosing epithelial hamartoma[J]. Clin Exp Dermatol, 1977, 2(2): 153-160. doi: 10.1111/j.1365-2230.1977.tb01559.x.

[9] Smith KJ, Williams J, Corbett D, et al. Microcystic adnexal carcinoma: an immunohistochemical study including markers of proliferation and apoptosis[J]. Am J Surg Pathol, 2001, 25(4): 464-471. doi: 10.1097/00000478-200104000-00005.

[10] Huet P, Jegou MH, Bourlond F, et al. Anatomoclinical and dermatoscopic study of trichoadenoma[J]. Ann Dermatol Venereol, 2020, 147(5): 334-339. doi: 10.1016/j.annder.2020.01.014.

[11] Kunz M, Kerl K, Braun RP. Basal cell carcinoma mimicking desmoplastic trichoepithelioma: a case with correlation of dermoscopy and histology[J]. Case Rep Dermatol, 2018, 10(2): 133-137. doi: 10.1159/000489164.

[12] Takei Y, Fukushiro S, Ackerman AB. Criteria for histologic differentiation of desmoplastic trichoepithelioma (sclerosing epithelial hamartoma) from morphea-like basal-cell carcinoma[J]. Am J Dermatopathol, 1985, 7(3): 207-221. doi: 10.1097/00000372-198506000-00002.

[13] Gordon S, Fischer C, Martin A, et al. Microcystic adnexal carcinoma: a review of the literature[J]. Dermatol Surg, 2017, 43(8): 1012-1016. doi: 10.1097/DSS.0000000000001142.

[14] Lee JH, Jy C, Lee KH. Syringoma: a clinicopathologic and immunohistologic study and results of treatment[J]. Yonsei Med J, 2007, 48(1): 35-40. doi: 10.3349/ymj.2007.48.1.35.

[15] 罗育武, 黄振明, 刘玉梅, 等. 结缔组织增生性毛发上皮瘤误诊一例[J]. 中华皮肤科杂志, 2005 (10): 657. doi: 10.3760/j.issn:0412-4030.2005.10.028.
Luo YW, Huang ZM, Liu YM. A misdiagnosed case of connective tissue hyperplastic trichoepitheliom [J]. Chin J Dermatology, 2005, (10): 657. doi: 10.3760/j.issn:0412-4030.2005.10.028.

[16] Seo SH, Kim GW, Sung HW. Imiquimod as an adjuvant treatment measure for desmoplastic trichoepithelioma[J]. Ann Dermatol, 2011, 23(2): 229-231. doi: 10.5021/ad.2011.23.2.229.

[17] 林鑫, 林博杰, 陆思锭, 等. 额面部皮肤软组织扩张术治疗多发性毛发上皮瘤一例[J]. 中华整形外科杂志, 2017, 33(3): 230-232. doi: 10.3760/cma.j.issn.1009-4598.2017.03.018.
Lin X, Lin BJ, Lu SD, et al. A case of multiple trichoepithelioma treated by frontal skin soft tissue dilatation[J]. Zhonghua Zheng Xing Wai Ke Za Zhi, 2017, 33(3): 230-232. doi: 10.3760/cma.j.issn.1009-4598.2017.03.018.

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