

宫颈腺样囊性癌6例报道及文献回顾

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【摘要】 宫颈腺样囊性癌(adenoid cystic carcinoma, ACC)是一种罕见且高度侵袭性的宫颈癌亚型,发病率不到所有宫颈癌的1%。该疾病多见于60岁以上的绝经期女性,常以绝经后阴道出血为主要症状,其诊断主要依赖于组织病理学和免疫组化分析。尽管目前尚无标准治疗方案,手术切除结合放疗或同步化疗被认为是ACC较为有效的治疗方式,但疗效有限,尤其是在晚期病例中预后较差。ACC的治疗和预后与肿瘤分期、神经周围侵犯及切缘状态密切相关。本文对复旦大学附属妇产科医院治疗的6例ACC患者的临床资料和随访情况进行总结,并结合文献复习,探讨其临床特点和治疗经验,强调了早期诊断和个体化治疗的重要性。

【关键词】 腺样囊性癌(ACC); 宫颈癌; 宫颈; 治疗

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Adenoid cystic carcinoma of the cervix: 6 cases report and literature review

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【Abstract】 Adenoid cystic carcinoma (ACC) of the cervix is a rare and highly aggressive subtype of cervical cancer, accounting for less than 1% of all cervical cancer cases. ACC predominantly affects postmenopausal women over the age of 60, with postmenopausal vaginal bleeding being the most common symptom. Diagnosis of ACC primarily relies on histopathological examination and immunohistochemical analysis. Although there is currently no standard treatment protocol, surgical resection combined with radiotherapy or concurrent chemoradiotherapy is considered to be an effective approach. However, the effectiveness is limited, particularly in advanced cases, which generally have a poor prognosis. The treatment and prognosis of ACC are closely related to tumor staging, perineural invasion, and margin status. This paper discusses the clinical data and follow-up of six ACC patients treated at our institution, and goes through a literature review, examines its clinical features and treatment outcomes, underscores the critical importance of early diagnosis and individualized treatment.

【Key words】 adenoid cystic carcinoma (ACC); cervical cancer; cervix; treatment

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子宫颈癌是影响女性健康的第四大常见癌症。虽然鳞状细胞癌和腺癌是最常见的病理类型,但腺样囊性癌(adenoid cystic carcinoma, ACC)、腺样基底癌和神经内分泌癌属于罕见散发的类型^[1],且具有很强的侵袭性。因此,由于缺乏经验而造成的误诊可能导致延误治疗。ACC作为一种罕见的宫颈腺癌亚型,通常起源于唾液腺、乳房和头颈部^[2-4],占所有宫颈癌的不到1%^[5-7],其病理类型预后差、死亡率高^[8],具有局部侵袭性强、易发生淋巴管和神经周围空间侵袭的特点,可发生血行转移^[9]。1949年,Paalman和Conseller首次报道了宫颈ACC^[10],迄今也只有少量的文献报道。本文报道复旦大学附属妇产科医院收治的6例宫颈ACC病例并结合文献进行复习,以探讨其临床特点和治疗经验,并强调早期诊断和个体化治疗的重要性。

病例资料 6例宫颈ACC患者的临床特点及治疗见表1。患者确诊时年龄59~74岁,平均年龄(68.2±5.7)岁。所有患者均处于绝经期,既往生产次数为1~5胎不等。绝经后阴道出血是最常见的

症状。所有患者的高危HPV检测结果均呈阳性,其中3例HPV16检测结果呈阳性。共5例患者术前组织病理学诊断为低分化浸润性鳞状细胞癌,病例5经阴道镜引导下活检确认为高级别鳞状上皮内病变。

6例患者均行根治性子宫切除术,术后组织病理学分析证实了ACC的诊断。根据国际妇产科联合会(International Federation of Gynecology and Obstetrics, FIGO) 2018年分期系统,3例患者为IB2期,2例为IB3期,1例为IIA1期。只有1例患者(病例1,65岁),复发后接受辅助放疗和化疗,并在子宫切除术后3年死亡。其余5例患者在随访期间无疾病,随访时间为18~30个月。

5例患者镜检显示宫颈单纯性ACC,1例(病例6)表现为浸润性腺鳞癌、基底细胞鳞癌、腺样囊性癌和腺样基底细胞癌。5例患者肿瘤局限于宫颈,1例患者(病例4)表现为阴道间质受累。免疫组化分析结果显示高度一致性:P16、P63、CD117均为阳性,CgA、Syn均为阴性,淋巴结均为阴性。

表1 6例ACC患者临床及随访资料

Tab 1 Clinical and follow-up data of six ACC cases

Case No.	Age (y)	Parity	Symptom	HPV-testing	FIGO stage	Treatment	Follow-up
1	65	2	Postmenopausal vaginal bleeding	HPV52(+)	IB3	HBSO-L+R	36 months DWT
2	71	3	Postmenopausal vaginal bleeding	HPV58(+)	IB2	HBSO-L	33 months NED
3	74	1	Postmenopausal vaginal bleeding	HPV58(+)	IB3	HBSO-L	30 months NED
4	67	2	Postmenopausal vaginal bleeding	HPV16(+)	IIA1	HBSO-L	28 months NED
5	59	1	HSIL found by colposcopy-directed biopsy	HPV16(+)	IB2	HBSO-L	22 months NED
6	73	5	Postmenopausal lower abdominal pain for 1 year and vaginal bleeding for 5 months	HPV16,52,58(+)	IB2	HBSO-L	18 months NED

HPV: Human papillomavirus; HSIL: High-grade squamous intraepithelial lesion; FIGO: International Federation of Gynecology and Obstetrics; HBSO-L: Hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy; R: Radiotherapy; DWT: Dead with tumor; NED: No evidence of disease.

讨论 ACC的起源尚不明确,宫颈内的储备细胞被认为是主要来源^[11-12]。据报道,宫颈ACC多见于60岁以上的女性^[13]。临床表现包括阴道出血、阴道分泌物增多、月经量过多等。本研究中,患者诊断时的平均年龄为65岁,最常见的症状是阴道异常出血,尤其是绝经后出血。文献^[5]报道阴道分泌物、子宫肿大和镜检发现不易碎的肿块也很常见。HPV感染在ACC病例中也有很高的发病率,

Grayson等^[14]的研究揭示了整合高危HPV基因组在ACC中的作用,并提出HPV16型与ACC相关。本研究中6例HPV16感染率也较高。研究表明,HPV16是宫颈癌女性中最常见的类型,其患病率随着年龄的增长而下降^[15]。年龄较大的ACC患者的HPV16高感染率表明HPV16对该病的作用显著。

诊断 宫颈ACC的诊断主要依赖于组织病理学检查,其典型组织学特征为肿瘤细胞呈筛状或腺

房样排列,附着于透明基质周围^[16-20]。研究^[20]发现,ACC细胞的排列方式,与乳腺导管癌细胞需要鉴别区分。有研究比较了ACC呈现三维簇状结构,核型不规则且染色质呈粗粒状^[17]。影像学检查如MRI可显示肿块边缘分叶状、内部隔膜样结构和高信号点等特征,有助于诊断。

鉴别诊断 宫颈ACC需与其他类型的宫颈癌相鉴别。一项回顾性研究^[16]显示,ACC和基底细胞癌均表现为肿瘤细胞呈巢状生长,免疫组化存在差异,如CD117在ACC中呈阴性或不确定性,而在基底细胞癌中呈阳性。二者的鉴别诊断很重要,因为形态学特征有重叠,但临床预后完全不同。

治疗方法 由于宫颈ACC罕见,目前尚无标准治疗方案,通常参照宫颈癌相关治疗指南,采用手术切除联合放疗或同步放化疗等综合治疗。对于局部晚期疾病,同步放化疗可能是合理选择。化疗虽被用作复发的辅助治疗,但仍未被公认为标准治疗方法^[9]。

针对唾液腺ACC有一些系统性治疗研究。客观缓解率方面,单药化疗如顺铂、氟尿嘧啶、吉西他滨、米托蒽醌、表柔比星、长春瑞滨和紫杉醇的缓解率约为10%。联合化疗如环磷酰胺-多柔比星-顺铂(CAP)和顺铂-长春瑞滨的缓解率为18%~31%。针对血管内皮生长因子受体的靶向药物仑伐替尼和阿昔替尼的缓解率分别为11%~16%和9%~17%。此外,针对肿瘤干细胞的治疗如MYB、Notch1、p53和表观遗传机制的靶向药物也显示出一定疗效^[21]。

由于ACC的免疫原性低和缺乏PD-L1表达,其对免疫检查点抑制剂治疗存在耐药性^[22],导致ACC发生和预后的危险因素也不明确^[23],相关的癌症疫苗治疗正在进行临床试验。针对其他部位的ACC的治疗对宫颈ACC的治疗可能有借鉴作用。头颈部ACC临床上表现为长期侵袭性的生物学行为,因此彻底的肿瘤切除仍是治疗的“金标准”;粒子放疗和系统性分子生物学方法也提供了新的治疗选择。

预后 宫颈ACC晚期患者预后较差,但是患者的总生存期(overall survival, OS)和复发(regional recurrence, RR)情况仍不清楚。一项回顾性研究^[24]显示,在84例宫颈腺样囊性癌和82例宫颈腺样基底细胞癌患者中,腺样囊性癌的10年总生存率较

差。以往研究^[25-26]的5年生存率为37%,10年生存率为40%。研究人群的扩大和随访时间的相对不足可能解释了结果的差异。与鳞状癌和腺癌一样,宫颈ACC患者的预后与肿瘤分期高度相关。既往研究^[5]报道,RR与ACC的肿瘤类型相关,RR范围为59%~100%。

在晚期疾病中,腺样囊性癌预后很差,且易局部复发和远处转移^[5,9]。一项病例报告^[27]也显示,1例腺样囊性癌IB1期患者在术后12个月出现了阴道顶复发。综合文献报道,影响预后的主要因素包括年龄、分期、神经周围侵犯、切缘状态等^[5,9]。

综上所述,宫颈ACC是一种罕见且具有高度侵袭性的宫颈癌亚型,其发病多见于老年女性,常以绝经后阴道出血为主要症状,主要依赖于组织病理学和免疫组化分析进行诊断,由于其与其他宫颈癌类型的相似性,鉴别诊断至关重要。虽然目前尚无标准治疗方案,但手术切除结合放疗或同步放化疗被认为是较为有效的治疗方式。尽管部分研究尝试了化疗和靶向治疗,但疗效有限。此外,ACC患者的预后较差,尤其是在晚期阶段,预后与肿瘤分期、神经周围侵犯及切缘状态等因素密切相关。因此,早期诊断和个体化治疗对于改善ACC患者的预后至关重要。宫颈ACC的诊断和治疗仍需更多研究,以改善患者预后。

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参 考 文 献

- [1] CIBULA D, POTTER R, PLANCHAMP F, *et al.* The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer[J]. *Radiother Oncol*, 2018, 127(3): 404-416.
- [2] HO AS, KANNAN K, ROY DM, *et al.* The mutational landscape of adenoid cystic carcinoma[J]. *Nat Genet*, 2013, 45(7): 791-798.
- [3] GHABACH B, ANDERSON WF, CURTIS RE, *et al.*

- Adenoid cystic carcinoma of the breast in the United States (1977 to 2006): a population-based cohort study[J]. *Breast Cancer Res*, 2010, 12(4):R54.
- [4] COCA-PELAZ A, RODRIGO JP, BRADLEY PJ, *et al.* Adenoid cystic carcinoma of the head and neck--An update [J]. *Oral Oncol*, 2015, 51(7):652-661.
- [5] BENHAYOUNE K, FATEMI HEL, BANNANI A, *et al.* Adenoid cystic carcinoma of cervix: two cases report and review of the literature[J]. *Pan Afr Med J*, 2015, 20:77-84.
- [6] NISHIDA M, NASU K, TAKAI N, *et al.* Adenoid cystic carcinoma of the uterine cervix[J]. *Int J Clin Oncol*, 2005, 10(3):198-200.
- [7] SINAA M, OUKABLI M, ALBOUZIDI A. Adenoid cystic carcinoma of cervix in younger women: report of two new cases[J]. *Pan Afr Med J*, 2014, 19:99-103.
- [8] Du F, ZHOU CX, GAO Y. Myoepithelial differentiation in cribriform, tubular and solid pattern of adenoid cystic carcinoma: A potential involvement in histological grading and prognosis[J]. *Ann Diagn Pathol*, 2016, 22:12-17.
- [9] KAUR P, KHURANA A, CHAUHAN AK, *et al.* Adenoid cystic carcinoma of cervix: treatment strategy[J]. *J Clin Diagn Res*, 2013, 7(11):2596-2597.
- [10] PAALMAN RJ, COUNSELLER VS. Clyindroma of the cervix with procidentia[J]. *Am J Obstet Gynecol*, 1949, 58(1):184-187.
- [11] KING LA, TALLEDO OE, GALLUP DG, *et al.* Adenoid cystic carcinoma of the cervix in women under age 40[J]. *Gynecol Oncol*, 1989, 32(1):26-30.
- [12] VUONG PN, GUETTIER C, BALATON A, *et al.* Adenoid cystic carcinoma (cylindroma) of the uterine cervix. Histology, immunohistochemistry, ultrastructure in a case, with review of the medical literature [J]. *Arch Anat Cytol Pathol*, 1994, 42(3-4):154-162.
- [13] FERRY JA, SCULLY RE. "Adenoid cystic" carcinoma and adenoid basal carcinoma of the uterine cervix. A study of 28 cases[J]. *Am J Surg Pathol*, 1988, 12(2):134-144.
- [14] GRAYSON W, TAYLOR L, COOPER K. Detection of integrated high risk human papillomavirus in adenoid cystic carcinoma of the uterine cervix[J]. *J Clin Pathol*, 1996, 49(10):805-809.
- [15] HAMMER A, ROSITCH A, QEADAN F, *et al.* Age-specific prevalence of HPV16/18 genotypes in cervical cancer: A systematic review and meta-analysis [J]. *Int J Cancer*, 2016, 138(12):2795-2803.
- [16] 王利群,王昀,晋薇,等. 子宫颈腺样基底细胞癌与腺样囊性癌的临床病理特点比较[J]. *中华病理学杂志*, 2020, 49(8):800-805.
- [17] JEONG J, HA SY, CHO HY, *et al.* Comparison of cytologic characteristics between adenoid cystic carcinoma and adenoid basal carcinoma in the uterine cervix [J]. *J Pathol Transl Med*, 2015, 49(5):396-402.
- [18] SETH A, AGARWAL A. Adenoid cystic carcinoma of uterine cervix in a young patient[J]. *Indian J Pathol Micr*, 2009, 52(4):543-545.
- [19] RAIS M, KHARMOUM J, ECH-CHARIF S, *et al.* Adenoid cystic carcinoma of the uterine cervix: a report of 2 cases[J]. *Case Rep Pathol*, 2017, 2017:8401741.
- [20] CHEN TD, CHUANG HC, LEE LY. Adenoid basal carcinoma of the uterine cervix: clinicopathologic features of 12 cases with reference to CD117 expression [J]. *Int J Gynecol Pathol*, 2012, 31(1):25-32.
- [21] SAHARA S, HERZOG AE, NOR JE. Systemic therapies for salivary gland adenoid cystic carcinoma [J]. *Am J Cancer Res*, 2021, 11(9):4092-4110.
- [22] NIGHTINGALE J, LUM B, LADWA R, *et al.* Adenoid cystic carcinoma: a review of clinical features, treatment targets and advances in improving the immune response to monoclonal antibody therapy [J]. *Bba-Rev Cancer*, 2021, 1875(2):188523.
- [23] DEWENTER I, OTTO S, KAKOSCHKE TK, *et al.* Recent advances, systemic therapy, and molecular targets in adenoid cystic carcinoma of the head and neck[J]. *J Clin Med*, 2023, 12(4):1463-1475.
- [24] LIU K, SHI Y, QIAO L, *et al.* The prognostic value of chemotherapy or/and radiotherapy in adenoid cystic carcinoma and adenoid basal carcinoma of the uterine cervix [J]. *Ann Transl Med*, 2022, 10(10):554-569.
- [25] VAN DINH T, WOODRUFF JD. Adenoid cystic and adenoid basal carcinomas of the cervix[J]. *Obstet Gynecol*, 1985, 65(5):705-709.
- [26] ELHASSANI LK, MRABTI H, ISMAILI N, *et al.* Advanced adenoid cystic carcinoma of the cervix: a case report and review of the literature [J]. *Cases J*, 2009, 2:6634.
- [27] DAPONTE A, GRAYSON W, MOISUC D, *et al.* Adenoid cystic carcinoma stage Ib1 treated with radical surgery displaying human papilloma virus 33 (HPV 33): immunoelectron microscopy and review [J]. *Gynecol Oncol*, 2003, 90(3):673-676.

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