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原发性子宫内膜鳞癌 1 例并文献复习

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[摘　要] 临床上原发性子宫内膜鳞癌(primary squamous cell carcinoma of the endometrium，PSCCE)极其罕见。江西省妇幼保健院收治1例绝经后阴道不规则出血女性患者，分段诊刮病理提示子宫内膜鳞癌，行腹式全子宫切除+双附件切除+盆腔淋巴结清扫术，术后病理提示：子宫内膜鳞癌IB期；宫颈低级别鳞状上皮内病变(CIN I)，术后辅助放化疗，随访8个月，未见复发。

[关键词] 原发性子宫内膜鳞癌；子宫内膜癌；诊断；治疗

Primary endometrial squamous cell carcinoma: A case report and literature review

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Abstract Primary endometrial squamous cell carcinoma is an extremely rare tumor. We reported a postmenopausal woman with irregular vaginal bleeding, the histopathology of subsection diagnosis suggests endometrial squamous cell carcinoma in Jiangxi Provincial Maternal and Child Health Hospital. The patient underwent abdominal total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node dissection. Postoperative pathological findings were endometrial squamous cell carcinoma phase IB and cervical low-grade squamous intraepithelial lesions (CIN I). With postoperative adjuvant chemoradiotherapy, the patient was followed up for 8 months, and is still survived with tumor-free.

Keywords primary endometrial squamous cell carcinoma; endometrial cancer; diagnosis; treatment

原发性子宫内膜鳞癌(primary squamous cell carcinoma of the endometrium，PSCCE)是一种极为罕见的妇科恶性肿瘤，目前已报导的病例不足100例[1]。其被定义为子宫内膜癌由不同分化程度的鳞状细胞组成[2]。PSCCE发病率、临床病理学表现、治疗及预后目前尚不明确。现报道江西省妇幼保健院收治的1例PSCCE病例，并对相关文献进行复习。

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1 临床资料

患者，女，65岁，因绝经后阴道出血1年于2017年8月28日入院。患者已绝经15年，2016年8月出现阴道不规则少量出血，未予以诊治，2017年2月阴道出血量增多，遂于2017年8月24日来江西省妇幼保健院门诊就诊，行分段诊刮止血，分段诊刮病理提示：(宫腔)片示血块，内见游离异性增生的鳞状上皮，核异形性、深染，考虑鳞癌团块；(颈管)片示少许宫颈组织，上皮增生，核略异性，拟“子宫内膜癌”收入院。患者既往无特殊病史，21岁初产，孕3产2，均足月顺产，流产1次，宫内节育环避孕，已下环10年，无家族性遗传病及癌症病史。

入院后妇科检查：外阴发育正常，已婚经产式；阴道通畅，分泌物少，白色，无异味，黏膜正常；宫颈直径约2.5 cm，光滑，质中，无接触性出血；宫体前位，大小约4 cm×4 cm×3 cm，表面光滑，质地中等，活动度好，无压痛；双侧附件区未及明显异常。经阴道超声检查见子宫肌层回声不均匀，子宫内见液性暗区及光点范围27 mm×10 mm，提示：宫内容物。盆腔MRI示：子宫腔内不规则稍长T1稍长T2信号，与肌层分界不清，考虑子宫内膜病变。血清肿瘤标志物：SCC 6.96 ng/mL(正常值：0~1.5 ng/mL)，CA125，CEA，AFP，HCG，HE4均在正常范围。HPV-DNA扩增定量：2.46 pg/mL(正常值：0~1 pg/mL)。宫颈液基细胞学检查未见上皮内病变细胞或恶性细胞。阴道镜下宫颈活检病理示：宫颈低级别鳞状上皮内病变(LSIL/CIN I)，其余检查结果未见异常。术前诊断：子宫内膜鳞癌(可能)；宫颈低级别鳞状上皮内病变(CIN I)。

排除手术禁忌证，患者于2017年9月5日行腹式全子宫切除+双附件切除+盆腔淋巴结清扫术。术中探查见盆腔腹膜轻度粘连，无腹水，肝、脾、胃、大网膜正常，子宫大小约5 cm×4 cm×3 cm，质中，活动可，双侧附件外观正常，盆腔淋巴结未触及肿大，取腹腔冲洗液送细胞学检查，严格按照手术规范行全子宫切除+双侧附件切除，术中剖视子宫：子宫后壁见大小约3 cm×2 cm菜花状病灶，质脆，宫颈管黏膜未见异常病灶，送术中快速病理检查提示：子宫内膜浸润性鳞状细胞癌(角化型)，浸润深肌层(>1/2)，累及颈管内口黏膜。继续行盆腔淋巴结清扫术，触诊腹主动脉旁淋巴结无肿大，故未活检。

对离体组织进行多点活检，显微镜下见：整个子宫内膜由大且多边形，胞质丰富，嗜酸性的高分化鳞状细胞构成(图1)，可见细胞间桥或角化珠(图2)，癌灶侵及深肌层，累及颈管内口黏膜层，反复取材未见腺癌成分，宫颈黏膜组织大部分表面坏死剥脱，可见局灶性低级别鳞状上皮内病变(图3)，双侧卵巢及输卵管未见癌，(左、右漏斗韧带)片示纤维血管脂肪充血伴淋巴结慢性炎，盆腔摘除12组淋巴结均显慢性炎(0/13)。免疫组织化学染色：ER(−)，PR(−)，P53(+)，P16斑块状(+)，P63(+)(图4)，P40(++)(图5)，Ki-67约50%(+)(图6)，CK(+)，CK10/13(+)，CK8/18(−)，CK(−)，VEGF(−)，EGFR(−)。腹腔冲洗液未见异倍体细胞。术后诊断：子宫内膜鳞癌IB期；宫颈低级别鳞状上皮内病变(CIN I)。

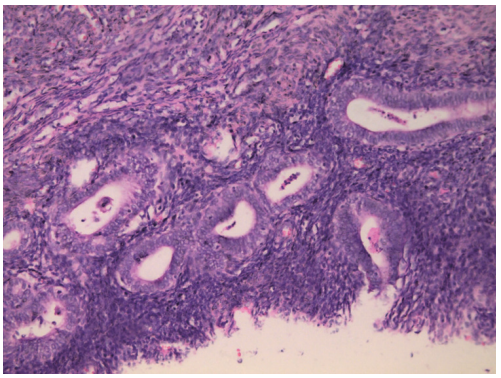

图1 子宫内膜由大且多边形，胞质丰富，嗜酸性的高分化鳞状细胞构成(HE，×100)

Figure 1 Endometrium is composed of large polygonal, cytoplasmic, eosinophilic and highly differentiated squamous cells (HE, ×100)

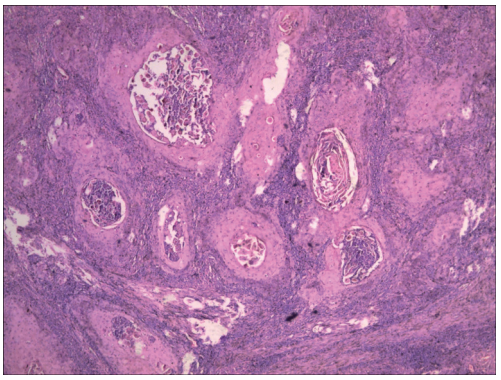

图2 鳞癌细胞中可见角化珠(HE，×100)

Figure 2 Keratin pearl is seen in squamous cell carcinoma (HE, ×100)

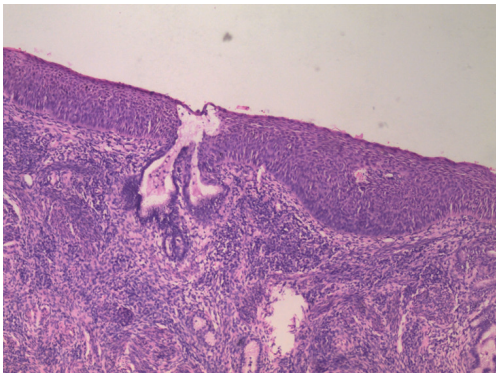

图3 宫颈组织标本取全，仅见宫颈组织呈局灶低级别鳞状上皮内病变(HE，×100)

Figure 3 Only low grade squamous intraepithelial lesion is found in complete cervical tissue (HE, × 100)

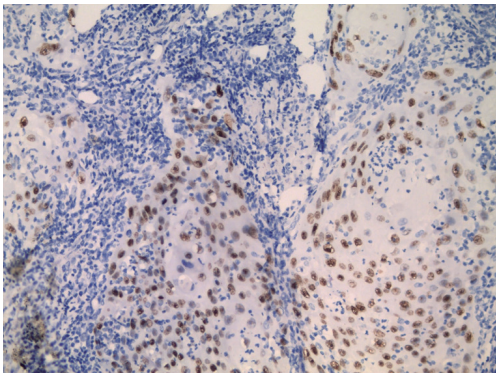

图4 免疫组织化学示肿瘤细胞P63(+)(EnVision，×200)

Figure 4 Immunohistochemistry show the strong expression of P63 in tumor cells (EnVision, × 200)

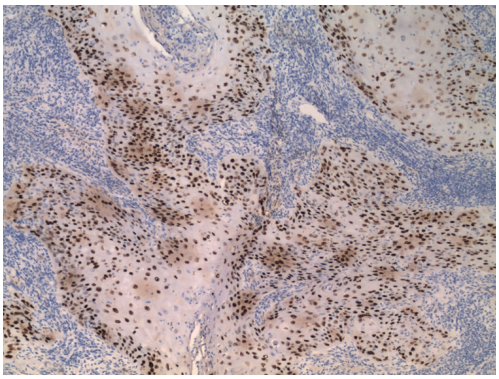

图5 免疫组织化学示肿瘤细胞P40(++)(EnVision，×100)

Figure 5 Immunohistochemistry shows the strong expression of P40 in tumor cells (EnVision, × 100)

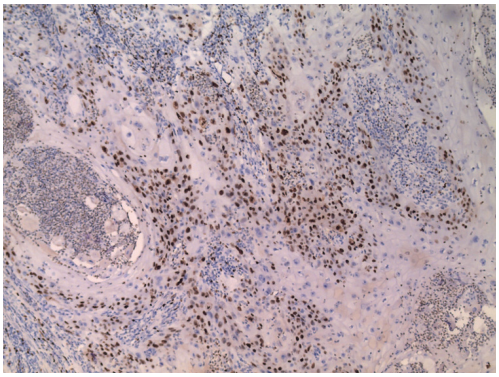

图6 免疫组织化学示肿瘤细胞中Ki-67阳性区50%(EnVision，×100)

Figure 6 Immunohistochemistry shows 50% of Ki-67 positive areas in tumor cells (EnVision, × 100)

2017年9月14日予以多西他赛110 mg+卡铂450 mg静脉化疗。2017年10月10日再次入院行适形调强放疗，放疗剂量：盆腔淋巴引流区(髂总、髂内、髂外、骶前、宫旁及闭孔淋巴引流区)，瘤床区，阴道残端，阴道旁(上界：腹主动脉分叉处，下界：闭孔下缘)45 Gy/25 fx/1.8 Gy；放疗期间予以每周化疗4次，多西他赛60/40 mg+卡铂100 mg静脉化疗。随访8个月未见复发。

2 讨论

PSCCE多发生于绝经后女性，平均发病年龄为67岁[3]，仅有3例育龄期女性PSCCE的报道[4-6]。Lee等[7]认为子宫内膜鳞癌的细胞起源于：1)腺基底膜和子宫内膜柱状细胞层之间的储备细胞或干细胞；2)正常子宫内膜的鳞状上皮化生；3)异位宫颈组织。子宫积脓[8-9]、子宫脱垂[10]、宫内器械[11]、子宫鱼鳞病[12]、宫腔慢性炎症[13]、低雌激素状态[7]等均可诱发具有双向分化能力的子宫内膜前体细胞异常分化为鳞状细胞，继而发展为鳞癌。关于人乳头瘤病毒(human papilloma virus，HPV)感染在PSCCE中的作用仍有争议，Kataoka等[14]在PSCCE标本中检测到HPV31的感染，但其他学者[6-7,15-19]通过HPV-DNA扩增技术或原位杂交技术等对PSCCE标本进行检测并未发现HPV感染的迹象。基因突变可能也是导致肿瘤发生发展的原因之一，Giordano等[17]和Terada等[20]均发现子宫内膜鳞癌与p53基因

的突变有关。本例患者65岁，发病年龄近似于平均值，长期使用宫内节育器持续刺激子宫内膜可能是PSCCE诱发因素之一，宫颈HPV-DNA扩增定量稍高于正常水平，且伴宫颈低级别鳞状上皮病变，考虑患者存在宫颈HPV感染，但术后内膜病变病理标本未进行HPV检测，故HPV是否参与了子宫内膜鳞状上皮的癌变仍不明确。免疫组织化学提示：ER(−)，PR(−)，P53(+)，提示p53抑癌基因突变参与了PESCC的发生发展，且细胞癌变使子宫内膜细胞已丧失正常生物学功能。

Goodman等[21]报道PSCCE从症状出现到确诊的中位时间为11.5个月。本例患者绝经后阴道出血1年后来江西省妇幼保健院就诊而明确诊断，与文献报道[21]时间相符。阴道不规则出血为最常见的就诊原因，妇科检查多无特异性，合并宫腔积脓时患者可自觉腹胀、阴道排液甚至排尿不畅，妇科检查可触及宫体不同程度的增大[6,8-9]。鳞状上皮细胞癌抗原(squamous cell carcinoma antigen，SCC)主要在恶性病变的上皮细胞和不同器官鳞状上皮细胞癌患者的血清中表达增加[22]。癌抗原125(Cancer antigen 125，CA125)是一种与体腔上皮组织有关的表面糖蛋白，在体腔上皮衍生物的肿瘤中可异常表达。子宫内膜腺癌多表现为血清CA125升高，对于子宫内膜鳞癌，癌变的子宫内膜表达鳞状细胞抗原使血清SCC升高。本例患者阴道超声及MRI提示宫内容物，SCC高于正常水平，CA125水平在正常范围内，考虑为患者期别较早，癌灶主要局限于子宫体内，暂未刺激盆腔腹膜。Wu等[6]报道了1例IV期PSCCE病例，血清CA125升高至80.09 U/mL，表明患者已发生盆腹腔转移，转移癌灶刺激盆腔腹膜而致血清CA125高于正常水平。术前影像学结合血清学检查，可对患者期别早晚进行初步评估，以此指导后续治疗。

1928年Fluhmann[23]提出了诊断PSCCE的3个标准：1)无子宫内膜腺癌同时存在；2)内膜鳞癌与宫颈鳞状上皮无联系；3)无原发子宫颈鳞癌存在。1975年，世界卫生组织(WHO)[24]增加了PESCC的另外2个标准：细胞间桥和角化珠的存在。本例患者子宫内膜癌巢由大多边形，胞质丰富，嗜酸性的高分化鳞状细胞构成，细胞内可见角化珠形成，反复取材未见腺癌成分，宫颈有低级别鳞状上皮内病变但未见癌变，宫颈和宫体交界处未见明显异常，子宫内膜免疫组织化学染色p63，P40阳性证实细胞鳞变，符合PSCCE的诊断。对于PSCCE患者，最重要的是排除宫颈鳞癌向子宫内膜的延伸和子宫内膜样腺癌的鳞状分化，故病理制片时需要广泛取样，判断宫颈病变情况及子宫内膜组织中是否有腺癌成分。也有上皮样滋养叶细胞肿瘤误诊为子宫内膜鳞癌的报道[25]，但上皮样滋养叶细胞肿瘤中存在大片的透明样物质与地图样坏死[26]，且透明样物质与坏死交替分布，但鳞状细胞癌无此种表现。

据研究[20]报道：PSCCE比子宫内膜样癌预后差，但由于其发病率低，5年生存率难以评估。Jetley等[9]对1例病变局限于黏膜层的患者仅行全子宫切除+双附件切除，随访7个月健在；Varras等[27]对1例IB期患者仅行全子宫切除+双附件切除，随访5年健在；Terada等[20]报道了1例FIGO分期IC期患者，行根治性全子宫切除+双附件切除+淋巴结清扫+放疗和辅助化疗，术后随访15个月未见复发转移；Wu等[6]对1例IV期患者行广泛性全子宫切除+双附件切除+淋巴结清扫+术后放化疗，随访近半年预后尚可。考虑到子宫内膜鳞癌多伴Ki-67高表达[20]，目前认为PSCCE应进行根治性手术和辅助放射治疗[28]。本例患者术后诊断为IB期，Ki-67阳性区约50%，行全子宫切除+双附件切除+盆腔淋巴结清扫，术后辅助放化疗，随访8个月未见肿瘤复发，但随访时间较短，具体预后情况需要更长时间的随访。

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