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在线全文

琥珀酸脱氢酶缺陷型肾细胞癌11例临床病理分析*

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【摘要】 目的 探讨琥珀酸脱氢酶（succinate dehydrogenase, SDH）缺陷型肾细胞癌的临床病理特征、免疫表型、分子遗传学改变及预后。**方法** 收集四川大学华西医院2016–2023年诊断的11例SDH缺陷型肾细胞癌，总结其形态学、免疫组织化学和DNA测序结果。**结果** 11例患者包括男性5例，女性6例。患者年龄22～71岁，平均39.7岁。其中5例位于右肾，5例位于左肾，1例为双肾肿瘤。镜下肿瘤细胞结构多样，呈片状、巢团状和腺管样分布，少数病例可见乳头状结构。肿瘤胞浆丰富，嗜酸性，呈絮状，部分可见胞浆内空泡。其中7例（63.6%）为低级别〔国际泌尿病理协会（ISUP）/WHO 2016分级1～2级〕，4例（4/11, 36.4%）为高级别（ISUP/WHO 2016分级3级）。低级别患者平均年龄32.1岁，高级别患者平均年龄58.0岁。免疫组织化学染色显示11例肿瘤细胞均SDHB表达缺失，其中1例同时伴SDHA表达缺失，配对盒蛋白8（paired box 8, PAX-8）、延胡索酸水合酶（fumarate hydratase, FH）和上皮细胞膜抗原（epithelial membrane antigen, EMA）阳性，角蛋白7（cytokeratin 7, CK7）阴性，Ki-67阳性指数1%～30%。7例行*SDHB*全部外显子Sanger测序，检出1例移码突变c.236Tdel（p.K80Rfs*），1例错义突变c.725G>A（p.Arg242His）。还有1例通过下一代测序检出*SDHB*大片段缺失（Exon 4-8 del）。10例获得随访资料，随访时间4～138个月，平均随访时间32.8个月，所有患者均存活。其中5例出现肿瘤复发或转移，包括3例高级别患者和2例低级别患者。**结论** SDH缺陷型肾细胞癌少见，总体发病年龄相对较年轻，可出现双侧肿瘤。低级别患者多数较年轻，Ki-67指数通常<5%，个别病例经长期随访可出现复发转移。高级别患者通常年龄较大，Ki-67指数较高，易复发和转移。SDHB免疫组化表达缺失可帮助诊断该肿瘤，但SDHB蛋白表达缺失不一定能检出*SDHB*基因突变。

【关键词】 SDH缺陷型肾细胞癌 基因突变 临床病理特征 预后

Succinate Dehydrogenase-Deficient Renal Cell Carcinoma: Clinicopathological Analysis of 11 Cases

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【Abstract】 Objective To investigate the clinicopathological features, immunophenotypes, molecular genetic alterations, and prognosis of succinate dehydrogenase-deficient renal cell carcinoma (SDH-RCC). **Methods** A total of 11 cases of SDH-RCC diagnosed at West China Hospital, Sichuan University between 2016 and 2023 were selected for clinicopathological, immunohistochemical, and DNA sequencing analyses. **Results** Among the 11 cases of SDH-RCC, there were 5 male patients and 6 female patients. The patients' ages ranged from 12 to 71 years, with an average age of 39.7 years. Among them, 5 patients had tumors located in the right kidney, 5 had tumors located in the left kidney, and 1 patient had bilateral tumors. Microscopic observation showed that the tumor cells of the SDH-RCC patients displayed a wide spectrum of structures, forming sheet-like, nested, and glandular structures. In addition, tumor cells in papillary structures were observed in some cases. The tumor cells had abundant cytoplasm, was eosinophilic, and contained flocculent materials. Intracytoplasmic vacuolations were observed in some of the cells. Among all the patients, 7 (7/11, 63.6%) showed typical low-grade features (grade 1-2 according to the International Society of Urological Pathology [ISUP]/WHO 2016 classification), and 4 (4/11, 36.4%) showed high-grade features (grade 3 according to the ISUP/WHO 2016 classification). The average ages of patients with low-grade and high-grade features were 32.1 years and 58.0 years, respectively. Immunohistochemical staining of all 11 cases demonstrated negative results for SDHB and cytokeratin 7 (CK7), and positive staining results for paired box 8 (PAX-8), fumarate hydratase (FH), and epithelial membrane antigen (EMA). Their Ki-67 index was 1%-30%. In one case, the loss of SDHB expression was also accompanied by a loss of SDHA expression. Sanger sequencing was performed to examine all the exons of *SDHB* in 7 cases. One case showed a frameshift mutation, c.236Tdel (p.K80Rfs*), and another case harbored a missense mutation, c.725G>A (p.Arg242His). In another case, next generation sequencing revealed that large fragments of *SDHB* (Exon 4-8 del) were missing. Follow-up

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data were available for 10 patients. The follow-up time ranged from 4 to 138 months, with the average being 32.8 months, and all patients survived. Metastasis and recurrence were reported in 5 cases, with 3 of them showing high-grade features and 2 showing low-grade features. **Conclusion** SDH-RCC is rare and the patients demonstrate a relatively young age of onsets. Patients may present with bilateral tumors. Tumors with low-grade features usually occur in young patients, with their Ki-67 index usually being lower than 5%. Individual cases may experience tumor recurrence and metastasis over a long period of follow-up. Tumors with high-grade features tend to occur in older patients who have a higher Ki-67 index, and who are prone to recurrence and metastasis. Negative immunohistochemical staining results for SDHB can assist in tumor diagnosis, but the loss of SDHB protein expression does not necessarily lead to the detection of SDHB gene mutation.

【Key words】 Succinate dehydrogenase-deficient renal cell carcinoma Gene mutation Clinicopathological characteristics Prognosis

琥珀酸脱氢酶(succinate dehydrogenase, SDH)是由四个亚基A、B、C和D组成的连接三羧酸循环和电子传递链的关键呼吸酶,定位于线粒体内膜,可催化琥珀酸向延胡索酸转化并参与呼吸链中的电子转运[1-3]。SDH四个亚基中任何一个发生突变,都可能导致该酶活性下降或者酶活性丧失,导致肿瘤发生。琥珀酸脱氢酶缺陷型肾细胞癌(succinate dehydrogenase-deficient renal cell carcinoma, SDH-RCC)是一种少见的肾癌亚型,由*SDH*基因突变所致,具有家族遗传性,好发于年轻人,男性略高于女性[4-5]。2016年第四版WHO肾脏肿瘤分类将SDH-RCC列为一种独立的肾细胞癌亚型。2022年第五版WHO肾脏肿瘤分类将SDH-RCC定义为SDHB免疫组化表达缺失的肾细胞癌,归入分子定义的肾细胞癌[6]。

由于SDH-RCC发病率低,目前国内外的报道均较少,病理医生和临床医生对该肿瘤的认知均较欠缺。本研究收集了四川大学华西医院病理科确诊的11例SDH-RCC,总结该肿瘤的临床病理特征、免疫表型和分子检测结果,旨在提高临床及病理医师对此肿瘤的认识。

1 资料与方法

1.1 病例收集

收集四川大学华西医院病理科2016–2023年诊断的SDH-RCC 11例,包括本院手术病例7例,外院会诊4例。以上病例均由2名泌尿病理亚专业医生确诊。收集患者的临床病理资料、分子改变和随访数据。相关研究经我院生物医学伦理审查委员会批准(2022年审271号)。

1.2 免疫组织化学染色

采用Ventata全自动免疫组化染色。SDHB、SDHA、延胡索酸水合酶(fumarate hydratase, FH)、配对盒蛋白8(paired box 8, PAX8)、角蛋白7(cytokeratin 7, CK7)、碳酸酐酶Ⅸ(carbonic anhydrase Ⅸ, CAⅨ)、原癌基因蛋白质类c-kit受体(CD117)、Ki-67,上皮细胞膜抗原(epithelial membrane antigen, EMA)第一抗体购自北京中杉金桥生物有限公司。SDHB、SDHA、FH、EMA、CK7、CAⅨ和CD117阳性信号定位于细胞质,PAX8和Ki-67定位于细胞核。组织内的正常肾小管和血管作为SDHB和FH的阳性内对照。

1.3 DNA测序

收集本院手术患者肿瘤的存档石蜡组织,采用FFPE DNA Kit(康为世纪,中国)试剂盒提取石蜡样本总DNA,分光光度计检测DNA的质量和浓度,核酸测定仪测得A_{260}/A_{280}在1.8 ~ 2.0之间。以20 ng DNA为模板,Green Taq Mix(Vazyme,中国)进行PCR反应扩增*SDHB*的全部8个外显子,退火温度为55 ℃。PCR引物序列见表1。以

表 1 *SDHB*基因引物

Table 1 Primers used in *SDHB* mutation analysis

SDHB or globin	Sequence	Product length/bp
E1	5′-GAAGCCGCCTCCCACTTG-3′	250
	5′-GCTTTCCTGACTTTTCCC-3′	
E2	5′-TCTGTTGTGCCAGCAAAATG-3′	287
	5′-GCCTTCCAAGGATGTGAAAA-3′	
E3	5′-ACATCCAGGTGTCTCCGATT-3′	247
	5′-CTATCAGCTTTGGCCAGC-3′	
E4	5′-GTCAGTGCTGCCCCTGAT-3′	284
	5′-TGCAAATAAAAACAAAACCA-3′	
E5	5′-GCTGAGGTGATGATGGAATCT-3′	249
	5′-CCACACTCCTGGCAATCATC-3′	
E6	5′-ATGCACTGACCCCAAAGGTA-3′	271
	5′-CAGCAATCTATTGTCCTCTTG-3′	
E7	5′-CTTTCCTCTGCACTCCCAGA-3′	283
	5′-TTGTGAGCACATGCTACTTC-3′	
E8	5′-GGAAGGAGTTTCACCCAAGA-3′	263
	5′-TGCTGTATTCATGGAAAACCAA-3′	
Globin	5′-GATCTGTCCACTCCTGATGCTG-3′	196
	5′-ATCAAGCGTCCCATAGACTCAC-3′	

Globin为内参照, 无DNA模板的反应体系为空白参照。所有引物均由成都生工生物工程公司合成。使用3730XL DNA测序仪进行DNA双向测序, 结果经ABI公司软件分析。外院会诊的1例患者提供了全外显子检测报告。

2　结果

2.1　临床信息

11例SDH-RCC患者的临床信息详见表2。其中男性5例, 女性6例, 男女比0.83∶1。患者年龄12～71岁, 平均(39±18)岁, 中位年龄41岁。5例肿瘤位于右肾, 5例位于左肾, 1例发生于双侧肾脏。其中3例患者分别因血尿、高血糖和胃痛入院, 5例患者因体检发现肾脏占位, 余3例患者病史不详。患者均行手术切除肿瘤。

2.2　大体检查

本院手术的7例患者肿瘤最大径4.0～14.0 cm, 平均9.3 cm。多数肿瘤界限较清楚, 无明显被膜, 边缘呈推挤性, 局部偶见假包膜; 个别病例呈浸润性生长, 与周围组织分界不清。7例肿瘤切面均呈实性、灰白、灰黄, 其中4例切面呈多彩状, 可见出血坏死区域(图1A, 图2A)。

2.3　组织学形态

肿瘤大多边界较清, 推挤周围组织形成假被膜, 局部与周围组织交错生长, 可见内陷肾小管。细胞排列结构多样, 呈实性、片状、腺样分布, 个别病例可见乳头状结构; 肿瘤细胞呈圆形或卵圆形, 细胞界限不清楚; 胞浆丰富嗜酸性或呈絮状, 部分细胞浆内可见空泡; 细胞核呈圆形或卵圆形, 界限清楚, 大部分细胞核仁不明显, 染色质均一、细腻。少数病例核增大, 核浆比增加, 异形性明显, 可见凝固性坏死和肉瘤样分化。本组病例中7例(63.6%)呈低级别〔国际泌尿病理协会(ISUP)/WHO 2016分级1～2级〕(图1B～1D)形态, 4例(4/11, 36.4%)呈高级别(ISUP/WHO 2016分级3级)形态, 高级别肿瘤灶区排列呈乳头状和腺样, 细胞异型性明显, 可见脉管内癌栓和淋巴结转移(图2B～2D)。

2.4　免疫组织化学结果

免疫组化染色结果显示11例SDH-RCC中肿瘤细胞SDHB均表达缺失(图1E、图2E), 肿瘤周围正常肾小管和

表 2　11例SDH-RCC患者的临床病理特征及随访情况

Table 2　The clinicopathological features and follow-up data of 11 SDH-RCC cases

Case	Age/yr.	Sex	Location	Size*	Initial symptom	Grade	SDHB (IHC)	SDHA (IHC)	SDHB (Mutation)	Treatment	Progression	Clinical follow-up
1	60	F	R	9.5×8.8×7.2	Hematuresis	3	Loss	Positive	No	Radical nephrectomy	Pulmonary metastasis at 6 months after surgery	9 months, surviving
2	71	F	L	14×13.3×10.5	—	3	Loss	Loss	No	Radical nephrectomy	—	—
3	49	M	L	14×7×4.5	Stomachache	3	Loss	Positive	No	Radical nephrectomy	Lymph node metastasis at primary diagnosis	4 months, surviving
4	52	M	R	—	—	3	Loss	—	—	Radical nephrectomy and everolimus	Retroperitoneal metastasis at 24 months after surgery	28 months, surviving
5	22	F	R and L	—	Identified in physical examination	2	Loss	—	Exon 4-8 del	Radical nephrectomy and partial nephrectomy	Recurrence at 60 months and gastric metastasis at 138 months after surgery	138 months, surviving
6	26	F	R	10×9×4	Identified in physical examination	2	Loss	Positive	c.236Tdel	Radical nephrectomy	Not progression	12 months, surviving
7	46	M	R	4.5×4×4	Hyperglycemia	2	Loss	Positive	c.725G>A	Radical nephrectomy	Not progression	4 months, surviving
8	12	F	L	4×3.8×3	Identified in physical examination	2	Loss	Positive	No	Partial nephrectomy	Not progression	43 months, surviving
9	36	M	L	9×8.5×8	—	1	Loss	Positive	No	—	Not progression	57 months, surviving
10	22	M	L	—	Identified in physical examination	2	Loss	—	—	Radical nephrectomy and camrelizumab injection	Not progression	18 months, surviving
11	41	F	R	—	Identified in physical examination	2	Loss	—	—	—	Bone metastasis at primary diagnosis	15 months, surviving

Grade: ISUP/WHO 2016 grade; F: female; M: male; R: right; L: left; —: not available; IHC: immunohistochemistry staining. * All the numbers are presented in cm.

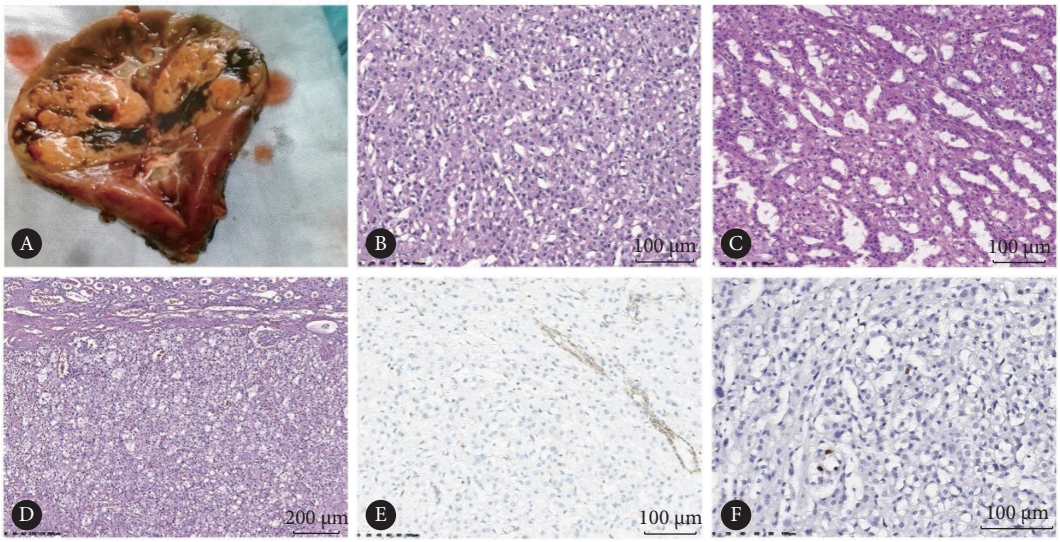

图 1 低级别SDH-RCC

Fig 1 Tumors showing low-grade features of SDH-RCC

A, The gross appearance of the tumor; B, the tumor cells grew in sheet-like structures and had eosinophilic cytoplasm and intracytoplasmic vacuoles, showing low-grade nuclear features; C, the tumor cells grew in glandular structures; D, the tumor boundary was clear, and entrapped renal tubules were observed; E, the tumor tissue showed negative staining results for SDHB, with vascular endothelium as the positive control; F, the proliferation index of Ki-67 of tumor cells was <5%. B-D, HE staining; E-F, immunohistochemistry staining.

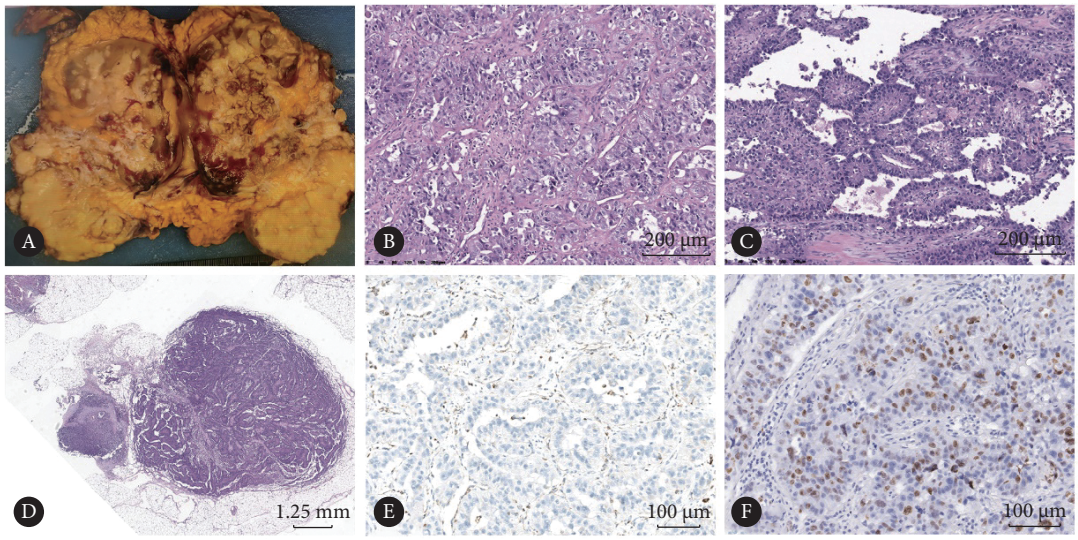

图 2 高级别SDH-RCC

Fig 2 Tumors showing high-grade features of SDH-RCC

A, The gross appearance of the tumor; B, the tumor cells grew in glandular structures and had eosinophilic cytoplasm, large nuclei, and distinct nucleolus; C, the tumor cells grew in a papillary structure and showed distinctive atypia; D, the tumor metastasized to lymph nodes; E, the tumor tissue showed negative staining results for SDHB, with vascular endothelium as the positive control; F, the proliferation index of Ki-67 of tumor cells was about 30%. B-D, HE staining; E-F, immunohistochemistry staining.

血管为阳性内对照。本院手术的7例肿瘤组织中，6例表达SDHA，1例SDHA表达缺失(图3)。4例会诊病例未行SDHA染色(表2)。肿瘤组织均表达PAX8、FH和EMA，不表达CK7、CAIX和CD117。Ki-67为1%～30%，其中低级别肿瘤Ki-67均小于5%(图1F)；高级别肿瘤Ki-67为20%～30%(图2F)。

2.5 DNA测序结果

收集本院手术的7例患者的肿瘤石蜡组织，提取DNA，分别扩增*SDHB*基因的8个外显子区后进行Sanger测序。结果发现，1例检出*SDHB*基因错义突变c.725G>A(Arg242His，精氨酸>组氨酸)；1例检出*SDHB*移码突变c.236Tdel(p.K80Rfs*)(图4)。另1例会诊

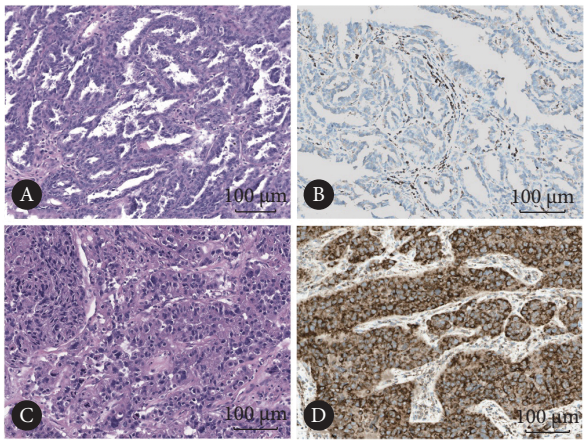

图 3 SDH-RCC肿瘤组织中SDHA蛋白表达情况

Fig 3 The expression of SDHA protein in SDH-RCC tumor tissue

HE staining of case 2 (A) and case 3 (C); immunohistochemistry staining showed SDHA negative results in case 2 (B) and SDHA positive results in case 3 (D).

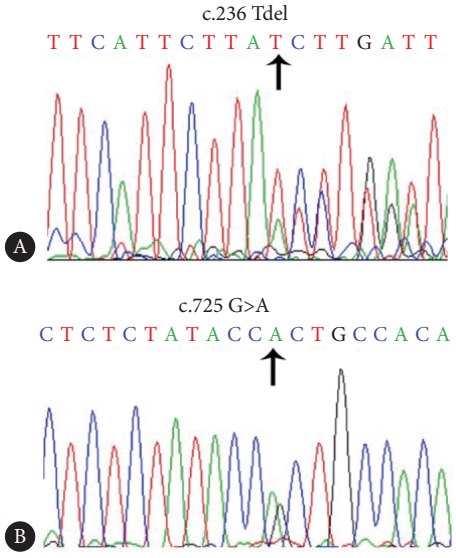

图 4 Sanger测序结果

Fig 4 Results of Sanger sequencing

A, Case 6 showed a frameshift mutation c.236Tdel (p.K80Rfs*) in *SDHB* gene; B, case 7 showed a missense mutation c.725G>A (Arg242His) in *SDHB* gene.

病例通过下一代测序进行了全外显子测序，结果显示*SDHB*外显子4～8大片段缺失（Exon 4-8 del）。余病例未检出*SDHB*基因外显子突变。

2.6 预后情况

10例患者获得随访资料，随访时间4～138个月，平均随访时间32.8个月，中位随访时间16.5个月。其中5例出现肿瘤复发转移，包括3例高级别和2例低级别肿瘤。在发生复发转移的高级别患者中1例患者初诊即发生淋巴结转移，1例患者术后6个月发生肺转移，另1例患者术后24个月出现腹膜后复发。发生复发转移的低级别患者中1例患者初诊即出现骨转移，另1例患者为双肾肿瘤，术后60个月肿瘤出现复发，术后138个月发生胃转移。余患者未见肿瘤转移和复发。2例患者术后进行靶向治疗，余8例患者术后未进行辅助治疗（表2）。所有患者均存活。

3 讨论

SDH又称琥珀酰辅酶Q还原酶或线粒体复合物Ⅱ。该酶是一种高度保守的异源四聚体跨膜蛋白，由A、B、C、D四个亚单位组成。编码SDH复合物的四个亚基*SDHA*（5p15.33）、*SDHB*（1p36.13）、*SDHC*（1q23.3）和*SDHD*（11q23.1）的基因分别位于不同的染色体上。SDH任何一个亚基发生基因突变都会导致该复合物不稳定，导致线粒体复合物Ⅱ功能缺陷而诱导肿瘤发生。

2004年，在肾细胞癌中发现*SDH*基因突变[7]。SDH-RCC中最常见是*SDHB*突变，其次为*SDHC*和*SDHA*突变，*SDHD*基因突变相对少见[5, 8-9]。*SDHB*基因突变人群罹患肾细胞癌的风险为10%～15%[10]。此外，*SDH*基因胚系突变的患者还易发生副节瘤、嗜铬细胞瘤和胃肠道间质瘤[11]。但在本组收集的11例SDH-RCC病例中，所有患者均未发现其他部位肿瘤。

SDH-RCC发病率极低，约占肾癌的0.05%～0.2%，好发于中青年，平均年龄约40岁[4-5, 12]。SDH-RCC多为单侧肿瘤，部分患者表现为多灶或双侧肾脏肿瘤[5, 12]。多数患者无临床症状，因体检发现肿瘤。目前，关于SDH-RCC的大宗病例报道较少[4-5, 12]。本组11例中5例男性，6例女性，未见明显性别差异。患者平均发病年龄39.7岁，与文献报道一致[5]，本组病例肿瘤多发生于单侧肾脏，仅1例患者为双侧肾脏发病。

早期研究报道SDH-RCC具有独特的形态学特征，典型病例肿瘤细胞排列呈片状、巢状、腺管状，肿瘤周边可见内陷的肾小管结构。细胞核形态较规则，染色质细腻，核仁不明显，少见核分裂像及坏死。胞浆嗜酸性，可见絮状包涵体样结构，电镜下提示其为增大的线粒体，常见特征性的胞质内空泡[5, 13-14]。后续研究逐渐报道一些病例可出现一些高级别特征，如核异形性增加、凝固性坏死或肉瘤样形态等[4-5, 12, 15]。SDH-RCC的诊断依赖于免疫组化，编码SDH复合物的四个亚基A、B、C和D中任何一个亚基突变，SDHB免疫组化检测均可表达缺失，这也是诊断SDH-RCC的必要条件。在判读为SDHB免疫组化阴性结果时，一定需要阳性内对照（如周围正常组织或血管内皮细胞）的存在。

研究显示，多数SDH-RCC为低级别形态，生物学行

为惰性,预后较好,长期随访结果显示其转移率为11%[5, 12],然而当肿瘤出现高级别形态,如肿瘤凝固性坏死或肉瘤样转化时,转移风险高达70%[5]。在本组病例中,7例低级别患者的平均年龄为32.1岁。其中,2例患者分别于初诊时及术后60个月出现肿瘤复发和转移。另外4例高级别患者平均年龄58.0岁,其中3例患者分别于初诊时、术后6个月和术后24个月发生转移和复发。以上结果提示,低级别SDH-RCC总体预后较好,长时间可能出现转移和复发,需进行长期观察随访;与低级别SDH-RCC相比,高级别SDH-RCC常发生于中老年患者,具有较高的转移和复发风险,预后较差,可能需要采取更积极的治疗手段。另外,本研究还发现,低级别SDH-RCC肿瘤增殖指数较低,通常小于5%,而高级别肿瘤增殖指数较高,可常规用于临床提示肿瘤预后。

SDH-RCC需与多种肾脏肿瘤进行鉴别。①嗜酸细胞瘤[16]:该肿瘤为良性。肿瘤细胞排列呈实性巢团状、腺泡状、小管状或微囊结构,肿瘤细胞呈多角形或圆形,胞质中含有丰富的嗜酸性颗粒,核分裂像罕见,肿瘤胞质内无透明空泡或包涵体样结构,间质可见疏松水肿或瘢痕样结构。免疫组化染色通常表达CD117,无SDHB表达缺失[17]。②透明细胞肾细胞癌:为最常见的肾癌类型。肿瘤细胞主要由透明细胞组成,也可出现嗜酸性细胞,肿瘤多排列呈巢团状结构,细胞间可见丰富的毛细血管网,免疫组化染色通常表达CAⅨ[18],无SDHB表达缺失。③嫌色细胞癌[19-20]:肿瘤细胞可呈实体、腺泡状及梁索状排列。典型的嫌色细胞癌由体积较大的胞浆空亮细胞和体积较小的嗜酸性细胞构成,细胞呈多边形或卵圆形,胞膜清楚似植物细胞壁。细胞核形态不规则,可见双核、核膜皱褶、核沟、核内包涵体及明显的核周空晕。免疫组化染色通常表达CK7和CD117[21],无SDHB表达缺失。④延胡索酸水合酶缺陷型肾细胞癌[22-23]:为*FH*基因突变胚系或体系突变所导致的肿瘤。肿瘤细胞多排列呈乳头状结构,也可表现为管囊状、筛状、实性片状等多种结构混合存在。典型形态为细胞胞质丰富、嗜酸性,核大,核仁明显并可见核仁周空晕。免疫组化染色上通常FH表达缺失、2-琥珀酸半胱氨酸阳性[24-25],无SDHB表达缺失。

SDH复合物中任何亚基双等位基因突变或SDH亚基启动子CpG岛的高甲基化修饰均可导致其编码的蛋白结构不稳定而降解,免疫组化染色表现为SDHB表达缺失[8, 26]。*SDHA*基因突变时[27],可表现为SDHA和SDHB蛋白同时表达缺失;但*SDHB*、*SDHC*和*SDHD*基因突变时,SDHA免疫组化染色为阳性[4, 28-29]。有研究显示免疫组化标记SDHB蛋白表达缺失对SDH家族基因突变的特异性可达100%,而敏感性为84.6%[30]。个别SDH亚基发生基因突变时SDHB免疫组化染色可呈弱阳性表达[30-31]。也有研究发现SDHB蛋白缺失的肾癌中未检出SDH复合物的任何一个亚基突变[32],在卡尼氏三联征发现是由于表观遗传异常影响SDH家族成员的蛋白表达导致[33]。因此,SDHB免疫组化染色结果与*SDHB*基因突变并不完全吻合。本组病例对7例SDH-RCC肿瘤组织的8个外显子进行DNA测序,仅2例患者检出*SDHB*基因突变,可能是由于*SDHB*基因发生了非点突变的其他基因改变或表观遗传调控紊乱,也可能是由非SDHB的其他SDH亚基突变所致,需进一步研究证实。因此,当肿瘤组织SDHB表达缺失时可以确定其存在SDH复合物缺陷;而当SDHB弱阳性或局灶阳性表达时,不能完全排除患者为SDH缺陷型肿瘤;当SDHB表达缺失而未发现*SDH*基因点突变时,需进一步完善基因检测或SDH复合物亚基CpG岛修饰水平的检测[34]。

综上,SDH-RCC是*SDH*基因失活导致SDHB蛋白表达缺失的罕见肾癌类型。目前,SDH-RCC的治疗首选手术切除。低级别SDH-RCC相对预后较好,但需要长期随访,高级别SDH-RCC患者易复发转移。SDH-RCC肿瘤具有复杂的形态学,SDHB免疫组化有助于诊断,必要时行基因检测进一步确诊,并建议患者家庭成员进行相关临床咨询和筛查。

* * *

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本 刊 征 稿 启 事

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