

## 论 著

## 鼻腔鼻窦肾透明细胞癌5例报告并文献复习

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**[摘要]** **目的** 分析鼻腔鼻窦肾透明细胞癌的临床特征及治疗方案, 并探讨其治疗策略及预后。**方法** 回顾性分析2005—2020年解放军总医院耳鼻咽喉头颈外科医学部收治的5例鼻腔鼻窦肾透明细胞癌患者的年龄、性别、发病部位、病程时限等临床特征, 探讨其治疗方案及预后, 并对相关文献进行复习与总结。**结果** 5例患者均为男性, 鼻腔鼻窦肿瘤的发病年龄为49~81岁。5例均伴有反复多量鼻出血, 其中1例伴视力下降。发病部位包括上颌窦2例, 筛窦和蝶窦1例, 筛窦和额窦2例。1例以鼻腔肿瘤为首发症状, 全面查体时发现肾癌, 后采用B超引导下腹腔灌注及微波消融进行治疗; 4例鼻腔肿瘤迟发于肾癌, 均在早年进行过肾脏根治性手术。5例患者均行鼻腔鼻窦肿瘤根治性切除, 其中3例曾口服靶向药物治疗, 1例鼻窦局部曾行放疗, 但均无明显效果。截至2020年7月, 1例失联, 2例死亡, 2例带瘤生存。**结论** 鼻腔鼻窦肾透明细胞癌为少见病, 以严重鼻出血和周围临近组织器官侵袭受累为主要临床症状, 放疗、靶向药物治疗、免疫治疗均无明显效果, 鼻腔根治性手术是治疗本病的有效措施, 可以缓解临床症状, 提高生存质量。

**[关键词]** 鼻腔鼻窦; 肾透明细胞癌; 鼻内镜手术; 肿瘤转移

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## Renal clear cell carcinoma in nasal cavity and paranasal sinuses: 5 cases report and literature review

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**[Abstract]** **Objective** To study the clinical features, treatment plan, treatment strategy and prognosis of renal clear cell carcinoma in nasal cavity and paranasal sinuses. **Methods** Five cases of renal clear cell carcinoma in nasal cavity and paranasal sinuses from 2005 to 2020 were retrospectively analyzed. The clinical features, such as age, gender, location of disease, duration of disease and so on, were analyzed. The clinical manifestations, treatment plan and prognosis were fully discussed, and the literature results analyzed comprehensively. **Results** All the 5 patients were male, and the onset age of nasal cavity and paranasal sinuses ranged from 49 to 81 years old. All the 5 patients had recurrent epistaxis, and one of them was accompanied with visual loss. The site of the disease was maxillary sinus in 2 cases, ethmoid sinus and sphenoid sinus in 1 case, ethmoid sinus and frontal sinus in 2 cases. One case with nasal tumor as the first symptom, renal cell carcinoma was found during comprehensive physical examination, and then the renal cell carcinoma was treated with B-ultrasound-guided intraperitoneal perfusion and microwave ablation; four cases with nasal tumor occurred later than renal cell carcinoma, and all had radical operation of kidney in early years. All the 5 patients underwent radical resection of nasal cavity and paranasal sinus tumor. Among them, 3 cases were treated with oral targeted drugs, and 1 case was treated with local radiotherapy, but all of them had no obvious effect. As of July 2020, 1 patient lost contact, 2 patients died and 2 patients survived with tumor. **Conclusions** Renal clear cell carcinoma in nasal cavity and paranasal sinuses is a rare disease. The main clinical symptoms were severe epistaxis and invasion of adjacent tissues and organs. This disease had no obvious effect on radiotherapy, targeted drug therapy and immunotherapy. Radical resection of nasal cavity can relieve the clinical symptoms and improve the quality of life.

**[Key words]** nasal cavity and paranasal sinuses; renal clear cell carcinoma; endoscopic surgery; neoplasm metastasis

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肾透明细胞癌(renal clear cell carcinoma, RCCC)是肾癌中最为常见的类型<sup>[1]</sup>,几乎所有的转移性肾癌病理类型均为肾透明细胞癌<sup>[2]</sup>。25%~30%的肾透明细胞癌患者诊断时已有远处转移,约30%的患者在行肾切除术后发生远处转移,最常见的转移部位为肺、淋巴结、骨、脑、肝脏、肾上腺及对侧肾脏,少见转移至胃、脾脏、胰腺、胆囊、舌、乳腺等脏器<sup>[3-7]</sup>,但鼻腔、鼻窦转移癌非常少见。本研究回顾性分析解放军总医院耳鼻喉头颈外科医学部2005—2020年收治的5例鼻腔鼻窦肾透明细胞癌转移患者的临床资料并进行文献复习,以探讨其治疗策略及预后情况。

## 1 病例资料

**1.1 一般资料** 2005—2020年解放军总医院耳鼻喉头颈外科收治的鼻腔鼻窦肾透明细胞癌患者5例,均为男性,发现鼻腔鼻窦肾透明细胞癌的年龄

为49~81岁。5例均在我科行鼻部手术治疗,并根据病史、症状、体征,以及辅助检查、临床病理等明确诊断。

**1.2 临床表现及治疗** 4例在诊断肾癌当时即行肾癌根治性手术,鼻腔转移发生在肾癌手术后的4~12年;1例以鼻腔肿瘤为首发症状,全身检查时发现肾癌,故仍考虑鼻腔肿瘤为肾癌的转移灶,该患者采用彩超引导下腹腔穿刺注药,左肾肿瘤穿刺活检,微波消融治疗。5例均以反复发作、大量鼻出血为主诉症状,且有不同程度贫血,血红蛋白含量为80~100 g/L,均低于男性正常值低限(120 g/L)。其中1例因肿瘤侵犯蝶窦,引起视力进行性下降。5例患者术中出血量均超过1000 ml,其中1例侵犯蝶窦和颅底的患者出血量达到3000 ml。有1例因肿瘤较大,曾在术前行血管造影检查,并对肿瘤的主要供血血管颌内动脉进行了栓塞,术中出血明显减少(表1)。

表1 5例鼻腔鼻窦肾透明细胞癌患者的临床资料

Tab.1 Clinical data of 5 patients with renal clear cell carcinoma in nasal cavity and paranasal sinuses

项目	病例1	病例2	病例3	病例4	病例5
肾癌发现时年龄(岁)	43	49	55	55	49
肾癌治疗方式	根治性肾切除	彩超引导下微波消融	根治性肾切除	根治性肾切除	根治性肾切除
发生鼻部转移的年龄(岁)	55	49	59	62	52
主诉症状	鼻出血	鼻出血	鼻出血	鼻出血+视力下降	鼻出血
是否贫血	是	是	是	是	是
受累鼻窦	筛窦、额窦	上颌窦	筛窦、额窦	筛窦、蝶窦	上颌窦
周围邻近组织受累情况	颅底+眼眶	眼眶	眼眶	颅底	无
局部放疗	否	是	否	否	否
靶向药物	是	是	否	是	否
鼻部手术方式	鼻内镜+眉弓鼻外入路	鼻内镜	鼻内镜	鼻内镜	鼻侧切开
肿瘤血管造影栓塞	否	否	是	否	否
肺部等其他全身转移	肺	无	胰腺+肺	肺	肺
目前生存状态	生存	失联	生存	死亡	死亡

**1.3 CT和MRI检查** 可见鼻腔、鼻窦有占位性病变,肿瘤呈浸润性生长,与周围组织界限不清,呈典型的恶性生长表现,如图1所示。

**1.4 术后病理检查** 术后病理检查示透明细胞肿瘤,富于血窦,免疫组化染色示CA9(+),CD10(+),PAX-8(+),Ki-67(+40%),CD117(-),CK7(-)(图2)。

**1.5 随访** 2020年7月对5例患者进行电话随访。5例患者中,病例2失联;病例1生存,行鼻内镜联合眉弓鼻外入路手术2次,目前鼻腔无明显肿瘤复发,但2年前发现了肺转移;病例3生存,鼻腔术后2年,目前鼻部无明显症状,但1年前发现胰腺及肺部转移;病例4死亡,为行鼻侧切开鼻腔鼻窦肿瘤切除术的患者,家属述患者于发现鼻腔转移5年后

死亡,死亡原因为肾透明细胞癌肺转移,导致全身衰竭;病例5死亡,肾癌术后7年发现鼻腔转移,同时发现肺转移,因肿瘤侵犯鞍区及颅底,引起鼻出血和视力下降,行2次鼻内镜下肿瘤切除术,术后鼻出血得到控制,视力未再明显下降,但终因肺转移于发现鼻腔肾透明细胞癌5年后死亡。

## 2 文献检索及复习

在PubMed以clear cell carcinoma of the kidney in nasal cavity为检索词进行检索,获得全文25篇<sup>[8-32]</sup>,其中英文21篇,中文3篇,西班牙文1篇。时间跨度为2002—2020年。上述文献共报告43例患者,男34例,女9例,平均60.4(30~80)岁,分别来自9个国家,其中法国8例(1项研究),韩国2例(2项研究),

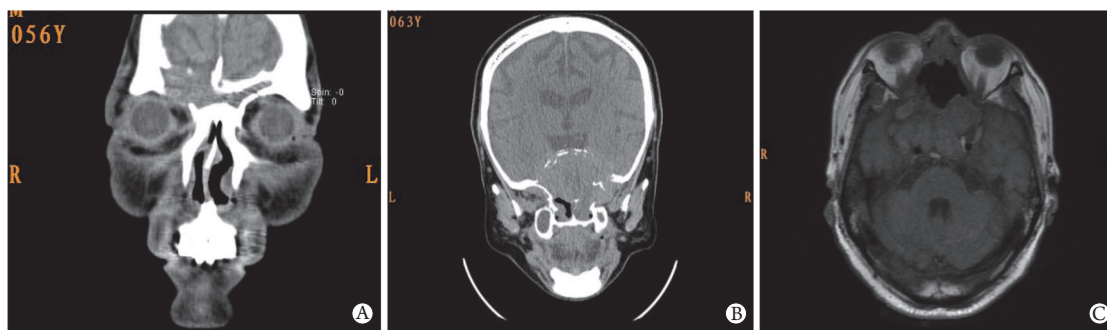


图1 鼻腔鼻窦肾透明细胞癌患者鼻窦影像学检查示例(病例4)

Fig.1 Imaging examination of nasal sinuses in patients with renal clear cell carcinoma in nasal cavity and paranasal sinuses (case 4)

A. 鼻窦冠状位CT, 右侧额窦及筛窦区可见占位性病变, 软组织密度灶伴多发骨质破坏, 侵犯颅底; B. 鼻窦冠状位CT, 蝶窦区域可见肿瘤性病变膨胀性生长, 局部正常结构消失, 骨质破坏, 颅底及蝶鞍受压, 蝶骨显示不清; C. 鼻窦轴位MRI影像, 蝶窦区域可见占位性病变, 与周围组织界限不清, 团块状混杂信号, 肿瘤呈分叶状

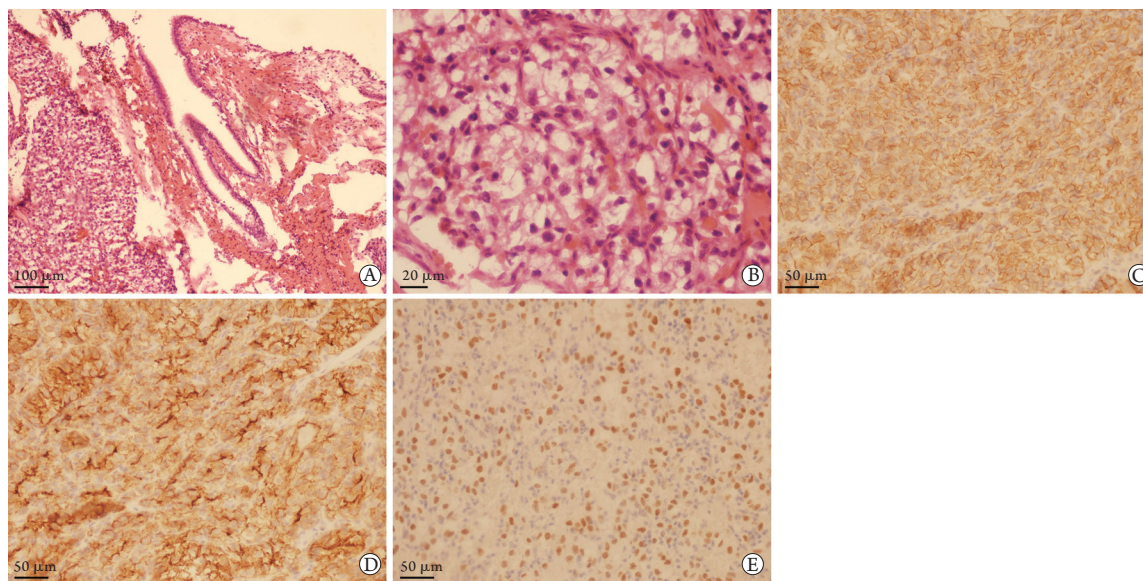


图2 鼻腔鼻窦肾透明细胞癌病理切片示例(病例4)

Fig.2 Pathological section of renal clear cell carcinoma in nasal cavity and paranasal sinuses (case 4)

A. 鼻腔肿瘤组织, 呼吸道黏膜上皮见肾透明细胞癌浸润( $\times 100$ ); B. 肾透明细胞癌组织( $\times 400$ ); C. 免疫组化 CA9 胞膜阳性( $\times 200$ ); D. 免疫组化 CD10 胞膜阳性( $\times 200$ ); E. 免疫组化 PAX-8 胞膜阳性( $\times 200$ )

美国8例(6项研究), 日本3例(3项研究), 土耳其3例(3项研究), 西班牙1例(1项研究), 伊朗1例(1项研究), 印度1例(1项研究), 中国16例(7项研究)。上述病例的共同临床特点是以鼻腔阻塞和严重出血为主要表现, CT和MRI检查可见鼻腔鼻窦占位性病变, 周围骨质破坏, 并向周围组织浸润, 鼻内镜检查发现鼻腔有暗红色富含血供新生物, 经手术后病理明确为肾透明细胞癌转移。

肾透明细胞癌鼻腔转移目前国内发现较少, 检索国内报道, 2001—2020年共14篇文献<sup>[33-46]</sup>, 均为1或2个病例的个案报道, 其中18例患者为男性。本研究5例也均为男性, 故考虑本病发病具有明显的性别差异, 但因整体病例数有限, 具体比例仍需大数据予以支持。国内14篇文献中, 发现鼻腔转移

时患者平均56岁, 5例肾癌发病年龄为43~55岁, 平均50岁; 鼻腔转移发生在发现肾癌后4~12年, 平均5.4年, 即发现鼻腔转移时, 平均年龄为55.4岁, 与国内病例报告的平均年龄相符。

### 3 讨 论

鼻腔鼻窦的转移癌非常少见, 其中肾透明细胞癌转移比例最高<sup>[47]</sup>。肾细胞癌大多转移部位为肺、骨、肝及脑, 而发生鼻腔或鼻窦转移者仅占全部转移部位的1%<sup>[4,48]</sup>。肾细胞癌多通过血液转移, 主要有两种途径: 一是腹腔压力增大, 使肿瘤细胞进入椎静脉丛, 越过肺静脉丛到达面部翼丛<sup>[49]</sup>; 二是肿瘤侵犯肾静脉, 瘤细胞通过上腔静脉而进入血液循环, 在全身各部位形成转移灶。孤立的鼻腔转移灶

的发生机制可能更倾向于第一种。

鼻腔鼻窦的肾透明细胞转移癌非常少见,我科15年间仅收治5例患者,以严重鼻出血和周围邻近组织器官的侵袭受累为主要临床症状,文献回顾分析结果与我科的治疗经验一致,本病对放疗、靶向药物治疗、免疫治疗均不敏感,治疗方案以手术为主,以减轻局部症状,提高生存质量。

本组5例患者中,2例肿瘤位于上颌窦,其中1例侵犯眼眶;2例位于筛窦、额窦,其中1例侵犯眼眶,另外1例侵犯颅底及眼眶;1例位于筛窦、蝶窦,肿瘤侵犯颅底。肿瘤转移部位没有明显的特异性,引起的症状与肿瘤部位相关。视力下降者,是因为其肿瘤位于蝶窦,侵犯蝶鞍、颅底,压迫视神经所致;2例肿瘤侵犯眼眶者,因未侵犯视神经,视力无明显改变。

本病为肾癌转移至鼻腔所致,患者既往有肾癌病史,或者全面查体时发现肾脏病灶,如有反复发作的鼻出血症状,鼻腔检查发现形似血管瘤的病变<sup>[46]</sup>,结合影像学表现,应首先考虑本病的可能。

本研究回顾性收集了15年来我院收治的5例肾透明细胞癌转移至鼻腔鼻窦的患者,数量上超过了绝大部分国内外的临床病例报道,在手术方式、术前准备、患者预后方面积累了难得的经验。本病对放疗、化疗、靶向药物等现有的治疗措施都不敏感,手术切除、对症处理是目前主要的治疗手段。随着等离子消融手术的推广应用,术中出血可得到很好的控制,但目前对于控制肿瘤复发仍缺乏有效的措施。相信随着手术器械的开发,生物信息学、基因测序等手段的完善,会有更加有效、安全的治疗措施出现,来帮助我们共同攻克这一临床难题。

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