

# World Journal of *Clinical Cases*

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- 1888 Endoscopic transluminal drainage and necrosectomy for infected necrotizing pancreatitis: Progress and challenges  
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- 1903 Functional role of frontal electroencephalogram alpha asymmetry in the resting state in patients with depression: A review  
*Xie YH, Zhang YM, Fan FF, Song XY, Liu L*
- 1918 COVID-19 related liver injuries in pregnancy  
*Sekulovski M, Bogdanova-Petrova S, Peshevska-Sekulovska M, Velikova T, Georgiev T*
- 1930 Examined lymph node count for gastric cancer patients after curative surgery  
*Zeng Y, Chen LC, Ye ZS, Deng JY*
- 1939 Laparoscopic common bile duct exploration to treat choledocholithiasis in situs inversus patients: A technical review  
*Chiu BY, Chuang SH, Chuang SC, Kuo KK*
- 1951 Airway ultrasound for patients anticipated to have a difficult airway: Perspective for personalized medicine  
*Nakazawa H, Uzawa K, Tokumine J, Lefor AK, Motoyasu A, Yorozu T*

**ORIGINAL ARTICLE****Observational Study**

- 1963 Clinicopathological features and expression of regulatory mechanism of the Wnt signaling pathway in colorectal sessile serrated adenomas/polyps with different syndrome types  
*Qiao D, Liu XY, Zheng L, Zhang YL, Que RY, Ge BJ, Cao HY, Dai YC*

**Randomized Controlled Trial**

- 1974 Effects of individual shock wave therapy *vs* celecoxib on hip pain caused by femoral head necrosis  
*Zhu JY, Yan J, Xiao J, Jia HG, Liang HJ, Xing GY*

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- 1985 Very low calorie ketogenic diet and common rheumatic disorders: A case report  
*Rondanelli M, Patelli Z, Gasparri C, Mansueto F, Ferraris C, Nichetti M, Alalwan TA, Sajoux I, Maugeri R, Perna S*
- 1992 Delayed versus immediate intervention of ruptured brain arteriovenous malformations: A case report  
*Bintang AK, Bahar A, Akbar M, Soraya GV, Gunawan A, Hammado N, Rachman ME, Ulhaq ZS*

- 2002** Children with infectious pneumonia caused by *Ralstonia insidiosa*: A case report  
*Lin SZ, Qian MJ, Wang YW, Chen QD, Wang WQ, Li JY, Yang RT, Wang XY, Mu CY, Jiang K*
- 2009** Transient ischemic attack induced by pulmonary arteriovenous fistula in a child: A case report  
*Zheng J, Wu QY, Zeng X, Zhang DF*
- 2015** Motor cortex transcranial magnetic stimulation to reduce intractable postherpetic neuralgia with poor response to other therapies: Report of two cases  
*Wang H, Hu YZ, Che XW, Yu L*
- 2021** Small bowel adenocarcinoma in neoterminal ileum in setting of stricturing Crohn's disease: A case report and review of literature  
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## Pembrolizumab combined with axitinib in the treatment of skin metastasis of renal clear cell carcinoma to nasal ala: A case report

Shuai Dong, Yang-Chun Xu, Yuan-Chen Zhang, Jian-Xin Xia, Yan Mou

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### Abstract

#### BACKGROUND

Renal clear cell carcinoma (RCC) is a malignant tumor of the genitourinary system with a predilection for males. The most common metastatic sites are the lung, liver, lymph nodes, contralateral kidney or adrenal gland, however, skin metastasis has only been seen in 1.0%-3.3% of cases. The most common site of skin metastasis is the scalp, and metastasis to the nasal ala region is rare.

#### CASE SUMMARY

A 55-year-old man with clear cell carcinoma of the left kidney was treated with pembrolizumab and axitinib for half a year after surgery and was found to have a red mass on his right nasal ala for 3 mo. The skin lesion of the patient grew rapidly to the size of 2.0 cm × 2.0 cm × 1.2 cm after discontinuation of targeted drug therapy due to the coronavirus disease 2019 epidemic. The patient was finally diagnosed with skin metastasis of RCC in our hospital. The patient refused to undergo surgical resection and the tumor shrank rapidly after resuming target therapy for 2 wk.

#### CONCLUSION

It is rare for an RCC to metastasize to the skin of the nasal ala region. The tumor size change of this patient before and after treatment with targeted drugs shows the effectiveness of combination therapy for skin metastasis.

**Key Words:** Skin metastasis; Renal clear cell carcinoma; Pembrolizumab; Axitinib; Case report

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**Core Tip:** The skin metastasis of renal cell carcinoma can be diagnosed by pathological biopsy and immunohistochemical staining. The patient's history, laboratory examination and imaging examination can assist in the diagnosis. The occurrence of skin metastasis often indicates a poor prognosis, and surgical treatment may improve the prognosis. Our patient refused surgery and returned to targeted drug therapy, resulting in significant improvement in skin lesions.

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## INTRODUCTION

It is rare for renal clear cell carcinoma (RCC) to metastasize to the facial region, but dermatologists should be alert to the presence of a facial mass in patients with a history of RCC. Here, we report the diagnosis of this patient in detail and provide our experience for the diagnosis of this kind of disease. In addition, this patient also demonstrated the efficacy of pembrolizumab and axitinib for skin metastasis from renal cancer.

## CASE PRESENTATION

### **Chief complaints**

The patient presented to our department due to the tumor on his right nasal ala for three months.

### **History of present illness**

The patient reported that a tumor of 0.3 cm × 0.3 cm × 0.2 cm appeared on his right nasal ala with no significant inducement in January 2022. He felt no pain or itching. There was a small amount of bloody exudation on the surface of the tumor. The diagnosis of granuloma was assigned to the patient and the tumor was treated with CO<sub>2</sub> laser physiotherapy at a local hospital. In March 2022, the tumor recurred and grew up to 2.0 cm × 2.0 cm × 1.2 cm, so the patient presented to our hospital. Since the onset of the tumor, the patient presented no fever, no nausea, no vomiting and no significant loss of body weight.

### **History of past illness**

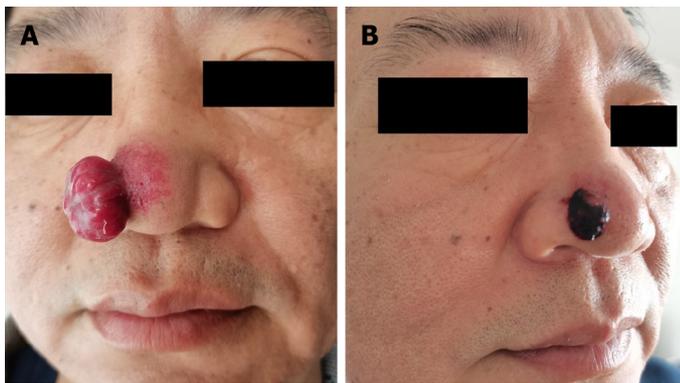
In January 2017, a tumor was identified in the left kidney of the patient by physical examination. The patient underwent a robot-assisted partial nephrectomy at a local hospital. Postoperative pathological examination showed left RCC. No adjuvant therapy was performed. In July 2021, the patient underwent a left renal radical resection in the local hospital. Postoperative pathological examination revealed left RCC. The tumor volume was 3.5 cm × 3 cm × 2.5 cm. Invasion of renal sinus adipose tissue at the maximum diameter of 0.7 cm was observed, vascular cancer infiltration was seen and fat necrosis nodules with fibrosis and calcification occurred in the surrounding renal tissue, pTNM: T3a (2017 AJCC 8<sup>th</sup>). August 2021, the positron emission tomography/computed tomography (CT) results displayed left renal cell carcinoma after surgery, the surgical area showed high metabolism, and metastasis was suspected. It was found that metastasis occurred to the left humerus, 1<sup>st</sup> and 12<sup>th</sup> thoracic vertebrae. In September 2021, posterior thoracic tumor resection and decompression plus radiofrequency ablation, internal fixation plus nerve root exploration were performed in another hospital. Postoperative pathological results showed broken bone and tumor cell infiltration in fibrous soft tissue, cell nest distribution and some empty cytoplasm, which was consistent with renal cell carcinoma metastasis. Pembrolizumab and axitinib were administered regularly after the operation, however, the treatment was discontinued due to the coronavirus disease 2019 epidemic between March and April 2022.

### **Personal and family history**

The patient has had a history of hypertension for 5 years and smoked for over 30 years. No member of his family has a similar disease.

### **Physical examination upon admission**

The general condition of the patient was fair, the left kidney was deficient. Physical examination showed bilateral renal tenderness and tapping pain negative, thoracic surgery, spinal tenderness and tapping pain negative. Limbs and lung examination showed no obvious abnormalities.



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**Figure 1** Clinical photograph of the lesion at the initial visit and after resumption of target therapy. A: A 2.0 cm × 2.0 cm × 1.2 cm red mass was seen on the right alar of the nose, with soft texture and clear boundary. A small amount of bloody exudate was seen on the surface. The skin vessels around the mass were hyperplastic and dilated; B: Two weeks after the resumption of combined treatment, the mass was reduced to 0.8 cm × 0.8 cm × 0.5 cm, covered with blood scabs, and the hyperplasia and dilation of skin vessels around the mass decreased.

A tumor of 2.0 cm × 2.0 cm × 1.2 cm was seen on the right nasal ala, there was a small amount of bloody exudation on the surface, and no tenderness (Figure 1A). There was no bleeding in the nasal cavity. The superficial lymph nodes of the whole body were not enlarged.

#### **Imaging examinations**

Lung CT showed nodular high-density shadows in each lobe of both lungs, with a size of about 0.2-1.1 cm, and some edges are lobulated, which indicated lung metastasis. Magnetic resonance results showed once surgery and signal changes at the 1<sup>st</sup> and 2<sup>nd</sup> thoracic vertebrae and their partial attachment area. Based on the disease history of the patient, tumor metastasis to the vertebrae was suspected. There were 2 suspected tumors in the left head of the humerus and shaft of the humerus. No obvious abnormality was found in the blood routine, coagulation routine, liver and kidney function, thyroid function, myocardial enzyme and electrocardiogram.

#### **Laboratory examinations**

There were significant changes in the epidermis, and the tumor cells gathered to form a mass in the dermis, some tumor cells formed a lumen structure. There were a lot of clear cells and abundant blood vessels (Figure 2).

Tumor immune pathology detection: S100-, HMB45-, CK7-, AR-, CK5/6-, CAIX-, Vimentin+, EMA weak+, CD10+, PAX8 weak+, PAX2 weak+ and Ki67 30%+ (Figure 3).

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## **FINAL DIAGNOSIS**

Skin metastasis of RCC.

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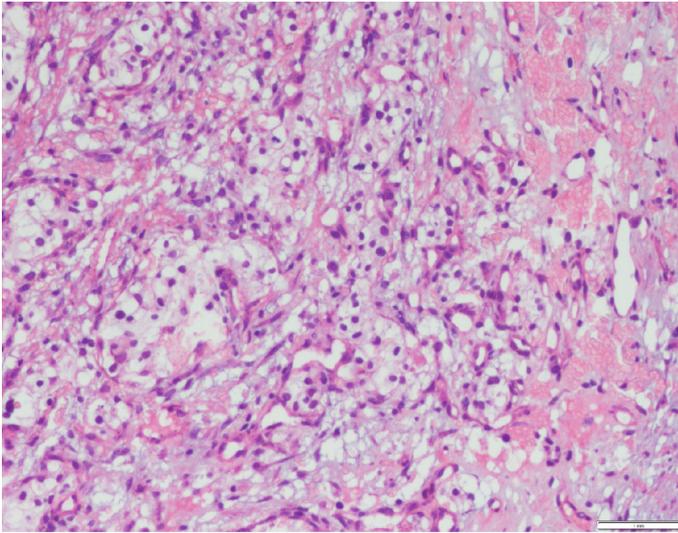
## **TREATMENT**

The proposal for surgical resection of the tumors on the nasal ala was rejected by the patient and the patient also refused to have his suspected bone metastasis or lung metastasis biopsied and treated. The patient resumed his treatment with pembrolizumab and axitinib for 2 wk, and the tumor on his nasal ala shrank to 0.8 cm × 0.8 cm × 0.5 cm (Figure 1B).

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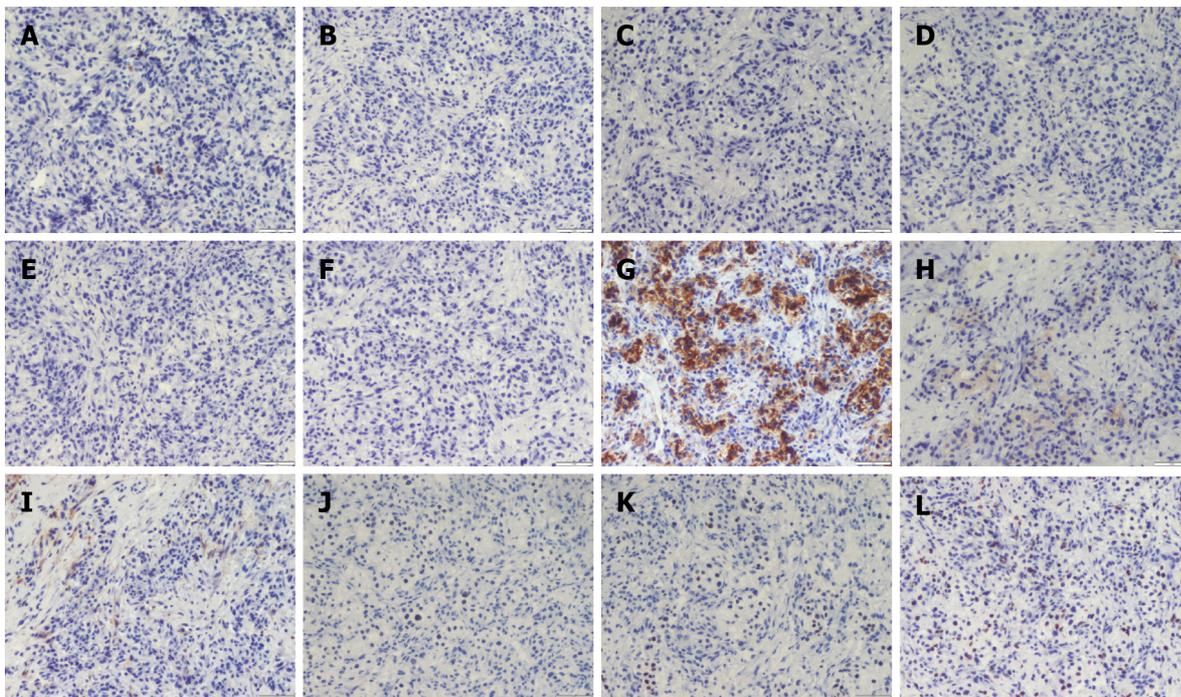
## **OUTCOME AND FOLLOW-UP**

200 mg pembrolizumab was administered to the patient through intravenous infusion once every 3 wk combined with axitinib 5 mg twice a day orally. After 8 wk of treatment, the skin lesion was 0.6 cm × 0.6 cm × 0.4 cm. Upon subsequent follow-up, his lesion remained 0.6 cm × 0.6 cm × 0.4 cm and there were no new lesions. Unfortunately, he died of multiple organ failure in December 2022.



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**Figure 2** The histopathology of the mass (hematoxylin & eosin staining). Lumplike infiltration of tumor cells was observed in the dermis, some of which formed lumenlike structures with a large number of clear cells and abundant blood vessels.



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**Figure 3** Immunopathology of the mass. A: S100(-); B: HMB45(-); C: CK7(-); D: AR(-); E: CK5/6(-); F: CAIX(-); G: Vimentin(+); H: EMA(+); I: CD10(+); J: PAX8(+); K: PAX2(+); L: Ki67(+).

## DISCUSSION

RCC is a kind of malignant tumor of the genitourinary system, which usually occurs in males. The most common metastatic sites are the lung, liver, lymph node, contralateral kidney or adrenal gland. Skin metastasis is rare, only in 1.0%-3.3% of RCC cases[1]. Skin metastasis from renal carcinoma mostly occurs in the scalp, rarely in the nasal ala[2]. Balawender *et al*[3] reported cases of cutaneous metastasis of renal cell carcinoma from 2000 to 2019, with only two cases of nasal cutaneous metastasis.

A cutaneous metastatic lesion from renal cell carcinoma is often present as painless nodules, plaques or pulsatile masses of normal to purplish-red skin and grow rapidly[4]. Vascular-rich metastases are hard to distinguish from hemangiomas, pyogenic granulomas or Kaposi's sarcoma[5]. The histopathology of this case showed a mass-like infiltration of tumor cells in the dermis with clear

cytoplasm and nuclei in the center, which should be differentiated from sebaceous adenocarcinoma, melanoma and clear cell squamous cell carcinoma. PAX8 and PAX2 are nuclear transcription factors that are expressed in approximately 90% of renal cell tumors and can be used as markers for the diagnosis of distant metastatic tumors originating from the kidney; CD10 can be used as a marker for the recognition of tumors originating from the renal tubules and CD10 is positive in clear cell renal tumor; EMA and Vimentin are frequently expressed in clear cell renal cell carcinoma, which is uncommon in other clear cell tumors[6]. Immunohistochemical staining of this case showed that melanoma could be excluded because S100 and HMB45 were negative, sebaceous adenocarcinoma could be excluded because CK7 and AR were negative, clear cell squamous cell carcinoma could be excluded because CK5/6 and CAIX were negative[7]. Vimentin positive, EMA weakly positive, CD10 positive, PAX8 weakly positive, PAX2 weakly positive and Ki67 30% positive can be diagnosed as skin metastasis of RCC.

Metastatic RCC is insensitive to both radiotherapy and chemotherapy[8]. Surgical resection of isolated skin metastases has the potential to improve survival[9]. Axitinib is a class of oral small-molecule tyrosine kinase inhibitors that inhibit receptors such as VEGFR and PDGFR-B, thereby inhibiting tumor angiogenesis and preventing tumor growth and metastasis[10]. Pembrolizumab, a humanized monoclonal antibody that binds to the PD-1 receptor, blocking the interaction of PD-1 with PD-L1 and PD-L2, relieving the suppression of the immune response mediated by the PD-1 pathway, enhances the body's immune system for the killing of tumor cells. Pembrolizumab and axitinib are used as first-line therapy for advanced renal cancer, the skin lesion of this patient developed rapidly after discontinuation of this regimen, and the tumor shrank significantly after treatment was resumed, which demonstrated the effectiveness of this treatment for skin metastases.

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## CONCLUSION

It is very rare for RCC to metastasize to the skin of the nasal ala region. It is easily misdiagnosed as hemangioma, pyogenic granuloma or Kaposi's sarcoma. Learning the detailed medical history and histopathology examination can help to avoid misdiagnosis. RCC patients with skin metastases often have a poor prognosis, and surgical removal of the metastases can be an option to improve the prognosis, but further systemic examination and comprehensive treatment are necessary. In this patient, pembrolizumab in combination with axitinib significantly reduced the size of the lesion, demonstrating the efficacy of the targeted drug for skin metastases.

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## FOOTNOTES

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