A Case of Cutaneous Metastasis from a Clear Cell Renal Cell Carcinoma with an Eosinophilic Cell Component to the Submandibular Region

Yusuke Amano 1, Sumie Ohni 1, Toshiyuki Ishige 1, Taku Homma 1, Tsutomu Yamada 1, Nobuyuki Nishimori 2 and Norimichi Nemoto 1

1 Department of Pathology, Nihon University School of Medicine
2 Department of Dermatology, Nihon University School of Medicine

Herein, we present a case report of the metastasis of a clear cell renal cell carcinoma (ccRCC) with an eosinophilic cell component to the skin of the submandibular region. An eosinophilic component has not been reported previously in the histological findings of ccRCC. The patient was a 74-year-old man who had a painless papula in the right submandibular region. Six years earlier, he had undergone nephrectomy and had been diagnosed with stage 1 ccRCC (pT1a, N0, M0). At the current presentation, the dermis in the resected specimen was composed of a clear cell neoplasm with glycogen deposits. Upon immunohistochemical analysis, the clear cells were found to be positive for CD10 and vimentin. As these findings were similar to those from the nephrectomy specimen, the cutaneous lesion on the skin of the submandibular region was confirmed to be a lesion of the metastatic ccRCC. Even when a low-stage ccRCC with an eosinophilic cell component is diagnosed, critical pathological and clinical examinations are needed because distant metastases may occur to the head and neck region, as in this case. Furthermore, when a skin tumor is found in the head and neck region, metastatic RCC must be considered in the differential diagnosis.

Key words: renal cell carcinoma, eosinophilic cell component, skin, head and neck, metastasis


Introduction

Renal cell carcinoma (RCC) accounts for >90% of all renal malignancies 1 and 2–3% of all malignancies in adults 2. Similar to other malignancies, approximately one-third of RCC patients (27.4–38.1%) present with distant metastases to the lungs 2, liver 2, bone 2, brain 2, adrenal glands 2, and skin 3–5. However, cutaneous metastasis from RCC to the skin of the submandibular region is rare, with an incidence of approximately 3.4–6% 3–5. Moreover, while Koga et al. reported cutaneous metastasis of RCC to the trunk, scalp, extremities, and face in 47.6%, 30.1%, 12.6%, and 9.5% of cases, respectively, they did not find RCC metastasis to the skin of the submandibular region 6. Lookingbill et al. reported that the skin of the scalp was the most predominantly affected by metastatic RCC and found only one case of cutaneous RCC metastasis to the neck 7. In the present report, we describe a rare case of cutaneous metastasis from RCC to the submandibular region. Histopathological examination of the primary site showed clear cell RCC (ccRCC) with an eosinophilic cell component; this component is one of the factors responsible for the poor prognosis in RCC patients 7. After confirming the pathological diagnosis of cutaneous metastatic RCC, the patient underwent re-excision and chemotherapy, and at the last follow-up he was alive and in good condition.

Case Report

A 74-year-old man noticed a painless papula in the submandibular region six months prior to his medical examination. As the papula progressed to a growing tumor, he visited our hospital for further examination and treatment. The submandibular cutaneous mass was a reddish, pedunculated lesion, measuring 8 × 9 × 7 mm in diameter (Fig. 1a), and was clinically diagnosed as a pyogenic granuloma, which was then removed by excisional biopsy. After skin biopsy, examination of the patient’s history revealed that six years before the biopsy he had undergone nephrectomy for right renal cancer, classified as stage 1 ccRCC (pT1a, N0, M0). On further clinical and radiological examinations, left lung metastases were detected; therefore, both re-excision and chemotherapy were performed because of positive excisional skin margins and lung metastases. Now the patient is free from malignancy nine months after the biopsy and six years after the nephrectomy.
solid mass in the dermis not related to the epidermis. The mass was mainly composed of clear neoplastic proliferating cells with a medium-sized alveolar arrangement (Fig. 1b, c). The tumor parenchyma was separated by irregularly distributed fibrovascular and/or fibromyxoid stroma with hemorrhage. Periodic acid—Schiff staining of the clear neoplastic cells showed glycogen deposition in the cytoplasm (Fig. 1d). On immunohistochemical examination, these clear neoplastic cells were positive for both CD10 and vimentin (Fig. 1e, f).

Since the patient underwent nephrectomy for
right renal cancer six years earlier, we conducted a pathological re-evaluation of the resected right kidney. The resected kidney was macroscopically affected by a relatively well-circumscribed yellowish mass measuring 3 × 2 × 2 cm. Histopathologically, the tumor was found to be a ccRCC composed of clear neoplastic cells with small, round, and uniform nuclei. Interestingly, although the majority of the tumor was composed of clear neoplastic cells (Fig. 2a, b), neoplastic cells with eosinophilic cytoplasm were observed in some parts of the nephrectomy specimen (Fig. 2c).

Fig. 2  Histological features of the previous nephrectomy specimen.

The nephrectomy specimen is a clear cell renal cell carcinoma (ccRCC), similar to the submandibular skin lesion (a ×10, hematoxylin-eosin; b ×40, hematoxylin-eosin). (c) Some carcinoma cells with eosinophilic cytoplasm are detectable. (d) The clear cell component of ccRCC is positive for CD10 in the cytoplasm (×40). (e) The eosinophilic cell component of ccRCC is positive for vimentin (×40). (f) The eosinophilic cell component of ccRCC is negative for E-cadherin (×40).
Immunohistochemically, carcinoma cells with clear and eosinophilic cytoplasm were positive for both vimentin and CD10 (Fig. 2d, e) and were negative for E-cadherin (Fig. 2f). There were no significant differences in Ki-67 labeling index between the eosinophilic component and clear cell component: the index was <2% of tumor cells for both components (data not shown). There was no neoplastic cell infiltration to the lymph ducts and vessels, and the surgical margins were neoplasm-free.

The histopathological and immunohistochemical features of the cutaneous excisional biopsy specimen were similar to those of the nephrectomy specimen; therefore, we considered the cutaneous mass to be consistent with metastatic ccRCC, although the eosinophilic cell component was not observed in the skin biopsy specimen.

Discussion

Cutaneous RCC metastasis, especially to the neck, has rarely been reported. It is known that RCC metastasizes to the head and neck region through the Batson’s venous plexus or by lymphatic spread through the thoracic duct. With regard to rare RCC metastases, metastatic routes to the submandibular cutaneous tissue and tumor-related growth factors play important roles in guiding submandibular cutaneous RCC metastases.

The initial clinical diagnosis of the skin mass was pyogenic granuloma through a differential diagnosis including hemangioma, external dental fistula, and Kaposi’s sarcoma. On histopathological analysis, the mass showed proliferation of clear neoplastic cells with fibrovascular and/or myxoid stroma. For a neoplasm arising in the submandibular region, these histopathological features would usually indicate lipoma, acinic cell carcinoma, calcifying epithelial odontogenic tumor, granular cell tumor, or mucoepidermoid carcinoma. Furthermore, in cases of a metastatic tumor, we should consider not only RCC, but also breast cancer and hepatocellular carcinoma as the primary source. Regarding the immunohistochemical features of RCC, CD10 is a useful marker to distinguish RCC from other clear cell tumors because it is present in most RCC cases. In addition, PAX-2 and/or PAX-8, vimentin, and alpha-methylacyl-CoA racemase are also useful RCC markers. In the present case, in addition to the patient's history of nephrectomy for RCC, the submandibular cutaneous tumor was found to be positive for both CD10 and vimentin. Therefore, we could confirm the pathological diagnosis of the cutaneous lesion in the submandibular region.

In general, the prognosis of patients is relatively good, with 5- and 10-year disease-specific survival rates of 76% and 70%, respectively, and 5- and 10-year progression-free survival rates of 70% and 64%, respectively. Studies focusing on RCC prognostic factors have reported that RCCs containing non-clear cell components, such as eosinophilic cell components and/or sarcomatoid components, tend to show high-grade malignancy or poor outcomes. In addition, although RCC cells are positive for vimentin in 50% of cases, vimentin immunoreactivity is a potential indicator of high-grade malignancy, as shown in breast and tongue carcinomas as well.

In the present case, the resected right renal tumor was pathologically re-evaluated as a ccRCC with a partial eosinophilic cell component. Ultrastructurally, the eosinophilic component in renal cell tumors was reported to be caused by an increase in mitochondria. Furthermore, vimentin immunopositivity was confirmed in both primary and metastatic ccRCC. To the best of our knowledge, only a few studies have described a histopathological type of RCC with skin metastasis as ccRCC without an apparent non-clear cell component; however, vimentin immunoreactivity was not analyzed in previous studies. Furthermore, the tumor sizes in the previous studies were >7 cm in diameter (pT2), whereas in our case the tumor size was <4 cm in diameter (pT1a). Cutaneous metastasis from small ccRCCs (<4 cm in diameter, pT1a) has rarely been reported. Furthermore, as described above, metastasis to the skin from vimentin-positive RCC with a non-clear cell component has not been reported yet. However, the clinico-histopathological and immunohistochemical findings in the present case suggest that small vimentin-positive ccRCC with an eosinophilic cell component may have a high-grade malignant potential.

Vimentin is an intermediate filament the mesenchymal cells, also considered as a marker of epithelial-mesenchymal transition (EMT)—an evolutionary conversed biological process whereby epithelial cells acquire mesenchymal characteristics—and known to play a role in tumor invasion and metastasis. We performed immunohistochemical staining of E-cadherin as another EMT marker. The eosinophilic component was negative for E-cadherin, suggesting that cell-cell adhesion decreased and induced metastasis. According to these findings, the eosinophilic component in this case is suggested to be involved in metastasis.

This is a case report of ccRCC metastasis to the skin of the submandibular region. Therefore, metastatic ccRCC should be considered in the differential diagnosis when cutaneous clear cell tumors are found in this region. In addition, further case studies and clinicopathological analyses are required to clarify
the biological behavior and patient prognosis for vimentin-positive, small RCC with a non-clear cell component.

References


