

Metastatic lesions: A diagnostic dilemma-retrospective study, Srinagar, Jammu and Kashmir, India

Summyia Farooq, Afreen Nadaf¹, Ambreen Beigh, Mehnaaz Khuroo, Nazia Bhat, Naila Nazir

Department of Pathology, GMC, ¹Department of Oral Pathology, GDC and H, Srinagar, Jammu and Kashmir, India

Abstract

Background: Renal clear cell carcinoma (RCC) accounts for about 3% of adult malignancies and about 90% of neoplasms of the kidney. It is most common in men aged 50 to 60 years old. RCC has different manifestations, including metastasis in uncommon sites and paraneoplastic syndromes.

Aims: To evaluate the clinicopathological pattern of RCC.

Materials and Methods: This study was conducted in the Department of Pathology, Government Medical College, Srinagar. It was a retrospective study done over a period of 5 years, November 2009 to November 2014.

Results: The study was done to evaluate the clinicopathological pattern of 6 cases of RCC diagnosed at a tertiary care hospital. All patients were males, presenting with submandibular swellings without any other symptom. Radiological and histopathological examination proved the lesion as metastasis of renal cell carcinoma to the mandible.

Conclusion: Being a rare presentation in the head and neck region, metastatic renal cell carcinoma needs to be considered in the differential diagnosis of submandibular swellings even in patients younger than 40 years.

Key Words: Mandible, metastasis, renal cell carcinoma

Address for correspondence:

Dr. Afreen Nadaf, Department of Oral Pathology, GDC and H, Srinagar, Jammu and Kashmir, India. E-mail: aanadaf@gmail.com

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INTRODUCTION

Renal clear cell carcinoma (RCC) accounts for about 3% of adult malignancies and about 90% of neoplasms of the kidney.^[1] It is the most common malignancy of the kidney. In 2007, 58,000 people in the United States developed RCC and 12,980 died from the disease.^[2] The incidence of RCC has been increasing by about 3% per year in North Americans, with the highest rates now seen among African Americans.^[3] It is most common in men aged 50–60 years.^[4] Only 10% of the patients exhibit the classic Grawitz triad (flank pain, palpable mass and

hematuria).^[5-7] RCC has different manifestations, including metastasis in uncommon sites and paraneoplastic syndromes.^[8]

Almost 30% of patients with RCC present with metastatic disease and furthermore, about 40% of patients who undergo resection of their primary lesion with curative intent will relapse with disseminated disease.^[9] RCC is well known for its potential to metastasize to nearly every organ system in the body. The tumor is highly vascular and thought to metastasize via both hematogenous (via the Batson's plexus) and lymphatic

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routes.^[10] The most common sites for metastasis are the lung, bone, adrenal, liver, brain and the contra-lateral kidney.^[11] Although not as frequent, metastasis to the head and neck has been identified in the thyroid, salivary glands, skull base, sinuses, pharynx, tonsils, jaw bone, tongue, lip and skin.^[12] It is the third most frequent neoplasm to metastasize to the head and neck region preceded only by breast and lung cancer. Only in 1% of patients with advanced RCC metastases are limited exclusively to head and neck.^[13] The most common sites of bone involvement are the pelvis and ribs (48%), followed by the spine (42%), then the long bones and skull.^[14]

The mechanisms responsible for tumor growth in bone are complex and involve tumor-driven stimulation of the osteoclasts, osteoblasts and other components of the bone microenvironment. Contrary to the pattern in some other tumor types such as prostate cancer, bone metastases from RCC are predominantly osteolytic and associated with bone destruction. In the aforementioned series, 71% of bone lesions evaluable by radiologic assessment were osteolytic with the remainder being either osteoblastic or mixed.^[14]

MATERIALS AND METHODS

This study was conducted in the Department of Pathology. It was a retrospective study done over a period of 5 years November 2009 to November 2014. Of 35,000 surgical biopsy cases excluding the gynecological specimens, 40 cases were diagnosed as RCC, of which 6 cases were included in our study which showed metastasis to submandibular region presenting as a swelling without any other symptom. All the cases were retrieved with the help of medical records. Preliminary data such as age, sex, clinical and radiologic findings were recorded from each patient. All the patients had come for fine needle aspiration cytology (FNAC). Surgical excision of the lesion was performed. Slides were reviewed by two pathologists and metastatic RCC was diagnosed on histopathology and immunohistochemical markers (cytokeratins 8 and 18, vimentin and PAX 5 and 8). All patients received postoperative chemotherapy. All patients are alive till date and are on regular follow-up.

RESULTS

Our study period of 5 years consisted of six cases, all males in the age range of 28–50 years with mean age of 37.5 years. All cases presented with intraosseous swelling in the posterior mandible with no other symptoms. Of six patients, four patients (66.66%) were in age group of 40–49 and two patients (16.66%) were in age group of 20–29 and 30–39, respectively. Four of six patients (66.66%) were having left submandibular swellings and two (34.34%) were having right submandibular swellings [Table 1].

All the six patients were subjected to FNAC and of six, three patients (50%) were diagnosed as myoepithelioma, two (34%) as osteosarcoma and one (16%) as acinic cell carcinoma. Meanwhile, orthopantomogram (OPG) and contrast-enhanced computed tomography (CECT) of the parotid regions were ordered. OPG showed an osteolytic lesion involving ramus of left mandible in four patients and right mandible in two patients [Figure 1].

CT scan of the parotid region revealed an osteolytic lesion involving inferior middle 3rd of left ramus of the mandible in four patients and posterior body of the right mandible corresponding to the third molar in two patients [Figure 2a and b].

All the six patients were subjected to ultrasonography (USG) and CECT abdomen, 5 (84%) patients had right sided renal mass and only one patient has left sided renal mass [Figure 3a and b].

Excisional biopsy was done in all patients. On histopathological examination, hematoxylin and eosin stained sections of all the cases showed few bony trabeculae surrounded by cells with round nucleus and clear cytoplasm, all the cases were of clear cell RCC [Figure 4a and b].

DISCUSSION

RCC is a malignant pathology of difficult and many times challenging diagnosis.^[15-18] RCC also poses a particular diagnostic challenge because distant disease can present synchronous with the diagnosis of the primary renal tumor

Table 1: Distribution of cases according to age, sex and site of lesion

Number	Age/sex	Laterality of lesion
1	40/male	Left mandibular swelling
2	48/male	Left mandibular swelling
3	45/male	Right mandibular swelling
4	46/male	Right mandibular swelling
5	28/male	Left mandibular swelling
6	36/male	Left mandibular swelling

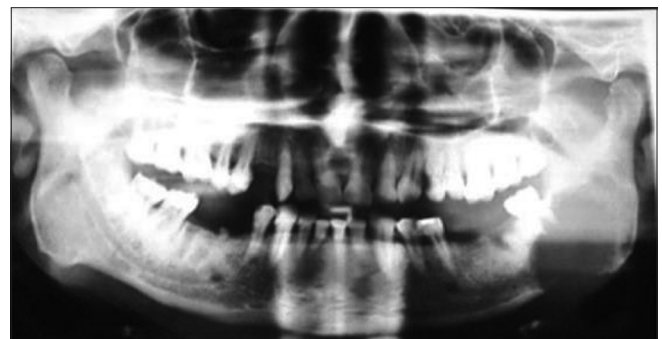


Figure 1: Orthopantomogram showing osteolytic lesion involving left angle and ramus of mandible

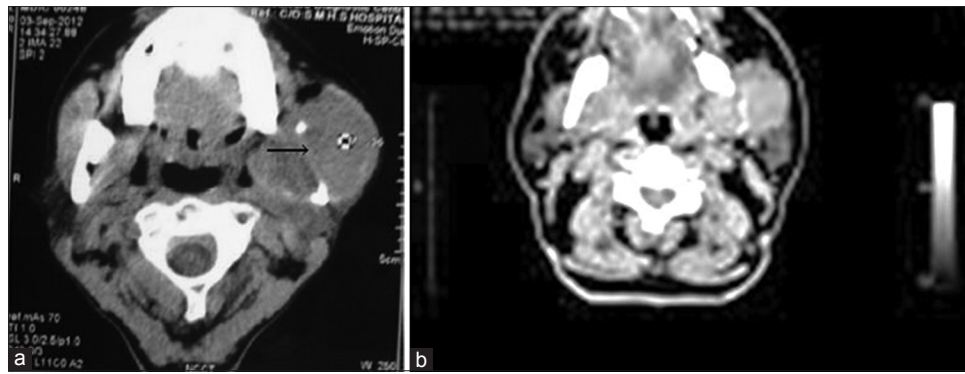


Figure 2: (a) Computed tomography of the parotid region depicting osteolytic lesion in ramus and body of mandible on left side. (b) Computed tomography images showing osteolytic lesion involving the left angle of mandible

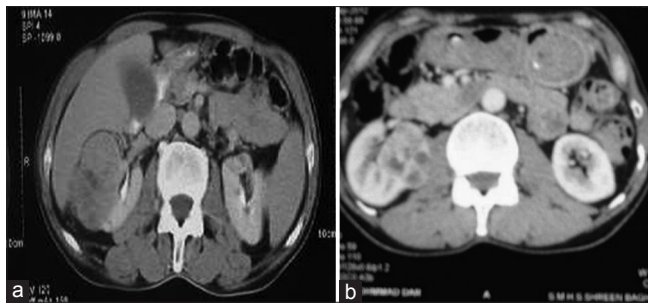


Figure 3: (a) Abdominal computed tomography scan with intravenous contrast showing a heterogeneous solid mass in the lateral side of right kidney. (b) Axial cuts showing well-circumscribed mass arising from right kidney

or a metachronous distant presentation may occur many years after therapy for the primary.^[19]

In our study, all the cases showed a male predilection which is consistent with literature.^[4] Our patients were in the age range of 28–50 years with mean age of 37.5 years. This was in accordance to the studies which have reported RCC to be more common in patients aged 50–60 years although two of our patients were aged below 40 years.^[4]

Metastatic spread in RCC is by lymphatic, hematogenous or direct invasion. Uncommon metastasis is characteristic of RCC, which may occur in any site of the body, such as the brain, contra-lateral kidney, adrenals, pancreas, peritoneum and bowel. Other areas of metastasis are endobronchial, skeletal muscle, laryngeal, dermal and spermatic cord.^[8] The rich venous anastomosis with the prevertebral, vertebral and epidural system supports a pathway for the tumor to spread. Veins, which are valveless, offer an easy way for tumor emboli to spread with less resistance. Increase in intra-abdominal or intra-thoracic pressure causes a retrograde flow from the venous channels back through the prevertebral and vertebral venous plexus. In this way, renal carcinoma apparently can travel from the kidney, bypass the pulmonary capillary filtration and metastasize in the head and neck. If there is no evidence of lung or liver disease,

it has been postulated that tumor cells can migrate through Batson's venous plexus or the lymphatics via the thoracic duct. This clearly defines the pathway for right-sided RCC going to left mandible which was seen in majority of our cases. Metastases to the oral-maxillofacial region are uncommon and account for approximately 1% of all malignant tumors in the region. However, autopsies of patients with carcinoma reveal higher level metastatic deposits in the facial bones, which do not manifest clinically.^[20] The common sites of oral soft tissues for metastases are attached gingiva followed by the tongue while in the jaws mandible is more commonly affected compared to the maxilla which is also consistent in our study.^[20-24]

Bone metastasis from renal carcinoma is purely lytic and expansile and is usually found in the axial skeleton, particularly from T12 through L5. Although metastasis to bone from RCC is common, mandibular metastasis has rarely been reported.^[20] All our cases too showed radiolucencies in the ramus area with few cases showing break in the lower border of the mandible. RCC is the primary origin in 16% of the metastatic jaw lesions. In 20% of the cases, the first presentations of neoplasm are oral symptoms such as pain, swelling, tooth mobility, bleeding and trismus which differed in all our cases as the patients presented with an asymptomatic submandibular swellings and their main concern was cosmetic appearance.^[25]

Clear cell carcinoma is the most common histological presentation of RCC. The clear cells are rounded or polygonal with abundant cytoplasm, which contain cholesterol, cholesterol esters, phospholipids and glycogen. These are dissolved during routine histological processing, creating a clear cytoplasm surrounded by a distinct cell membrane. Histopathological examination commonly shows a network of small, thin-walled blood vessels interlacing between the tumor cells. Numerous tumors with clear cell features may present in the mandible. These neoplasms can be divided into primary tumors (odontogenic and nonodontogenic tumors) and metastatic tumors. The odontogenic clear cell lesions include odontogenic cysts, clear

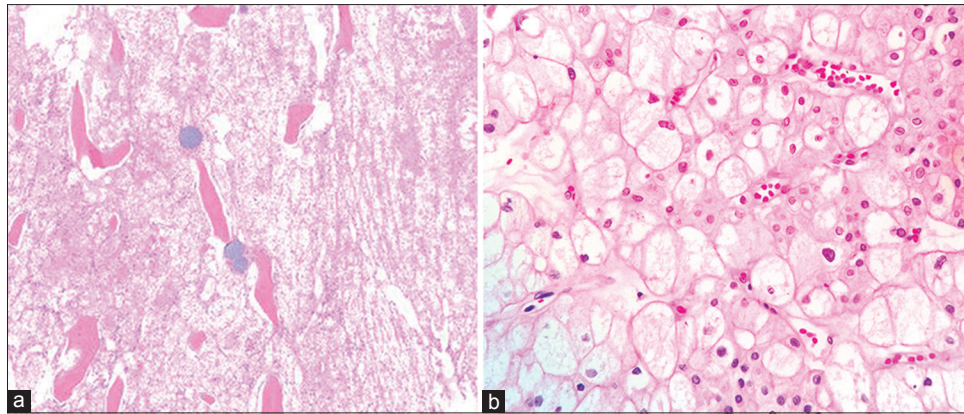


Figure 4: (a) Photomicrograph showing bony trabeculae surrounded by cells with clear cytoplasm (H&E stain, $\times 40$). (b) Image showing round to oval cells with clear cytoplasm (H&E stain, $\times 400$)

cell variants of calcifying epithelial odontogenic tumor, clear cell ameloblastoma and clear cell odontogenic carcinoma.^[26,27] Non odontogenic clear cell tumors include acinic cell carcinoma, mucoepidermoid carcinoma, squamous cell carcinoma with clear cell features, clear cell oncocytoma, glycogen-rich salivary tumors, hyalinizing clear cell carcinoma, sebaceous tumors, epithelial–myoepithelial carcinoma and clearcell variants of adenocarcinoma of salivary gland origin.^[28,29] Metastatic tumors from other organs that may present in the mandible with clear cell features include the breast (33%), lung (18%), kidney (16%), thyroid (6%), prostate (6%) and colon (6%). Of these, clear cell carcinoma of the kidney most closely resembles clear cell odontogenic carcinoma histologically.^[30] Thus in our series, none of the six patients were diagnosed as RCC on FNAC. A majority (50%) were diagnosed as myoepithelioma because of submandibular location and presence of round cells with eccentric nuclei in cytological smears. Two patients were diagnosed as osteosarcoma because of the presence of basement material which is indistinguishable from osteoid. On cytology, one patient was diagnosed as acinic cell carcinoma because of high cellularity and round cells.

In our set up, FNAC is the first investigation for swellings so all other investigations such as OPG, USG, CT scan and incisional biopsy were performed after initial diagnosis.

CONCLUSION

From our study, we conclude that metastatic RCC needs to be considered in the differential diagnosis of mandibular swellings even in patients younger than 40 years. Incisional biopsy should be performed on all patients of submandibular swellings as FNAC alone cannot differentiate metastatic RCC from primary lesions due to cytological resemblance.

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Conflicts of interest

There are no conflicts of interest.

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