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Case report

Parotid metastasis of renal cell carcinoma, mimicking primary clear cell oncocytoma: report of a case and brief review of the literature

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Key words

Parotid • Metastasis • Renal cell carcinoma • Clear cell oncocytoma

Summary

Malignancies of the parotid gland are relatively uncommon, accounting for only 3-6% of all head and neck cancers. Most of them are primary neoplasms, metastases are uncommon. Renal cell carcinoma (RCC) represents 3% of adult malignancies, the clear cell type comprises up to 70% of all RCC. RCC has an unpredictable behavior and the unique potential to metastasize to nearly every organ in the body. Though not as frequent, metastatic RCC to the head and neck has been identified in the thyroid, salivary glands, skull base, sinuses, pharynx, tonsils, tongue, lip and skin. Metastasis to the parotid gland is very rare. Here, we report the case of a clear cell type RCC metastatic to the parotid gland and mimicking a primary clear cell oncocytoma. Differential diagnoses and a brief review of the literature are added.

Introduction

Malignancies of the parotid gland are relatively uncommon, accounting for only 3-6% of all head and neck cancers [1]. Most of them are primary neoplasms, metastases are uncommon. However, cutaneous cancers, ductal carcinoma of the breast, small cell carcinoma of the lung, renal cell carcinoma (RCC) and rhabdomyosarcoma, have been described as harboring the potential for metastatic spread to the parotid [2 3]. RCC accounts for 3% of adult malignancies and is associated with approximately 13,000 deaths for year [4]. Several histologic RCC subtypes have been described, including the clear cell type, which comprises up to 70% of all RCC [5]. Nowadays more than 60% of all renal cancer cases are "screen detected" as incidental findings on imaging studies obtained for unrelated reasons [6]. Therefore, the classical teaching that renal cancer presents with signs and symptoms such as hematuria, flank pain and palpable mass is more of the exception rather than the rule [7]. RCC has an unpredictable behavior and the unique potential to metastasize to nearly every organ in the body, via both hematogenous and lymphatic routes [8]. The most common sites for metastasis are the lung, bone, adrenal glands, liver, brain, and the contralateral kidney [9]. Though not as frequent, metastatic RCC to the head and neck has been identified in the thyroid, salivary glands, skull base, sinuses, pharynx, tonsils, tongue, lip and skin [10]. Metastasis to the parotid gland is very rare. Although metastatic renal tumors comprise only approximately 1% of all salivary gland neoplasms, they are important to be recognized as clinicians could be alerted for a possible occult primary or more diffusely malignancy [11]. Here, we report the case of a clear cell type RCC, metastatic to the parotid gland and mimicking a primary clear cell oncocytoma. Differential diagnoses and a brief review of the literature are added.

Case report

A 60 year-old woman was referred to our Hospital for the management of a right parotid mass that lasted since two months. The patient denied any significant change in size of the lesion, paresthesia, or facial weakness. She had a past medical history of mono-kidney. On physical examination, there was a non-tender, soft nodule in the tail of the right parotid without associated lymphadenopathy. Both contrasted computed tomography (CT) scan and magnetic resonance imaging of the neck

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Fig. 1. Histological features of the parotid mass. Parotid lesion was composed of solid clusters of polygonal-to-round cells with abundant clear cytoplasm, large slightly basophilic nuclei and small nucleoli. Pleomorphism was limited and no mitoses were found [A-B, Haematoxylin and Eosin, Original Magnification (O.M.): A, 50x; B, 200x].

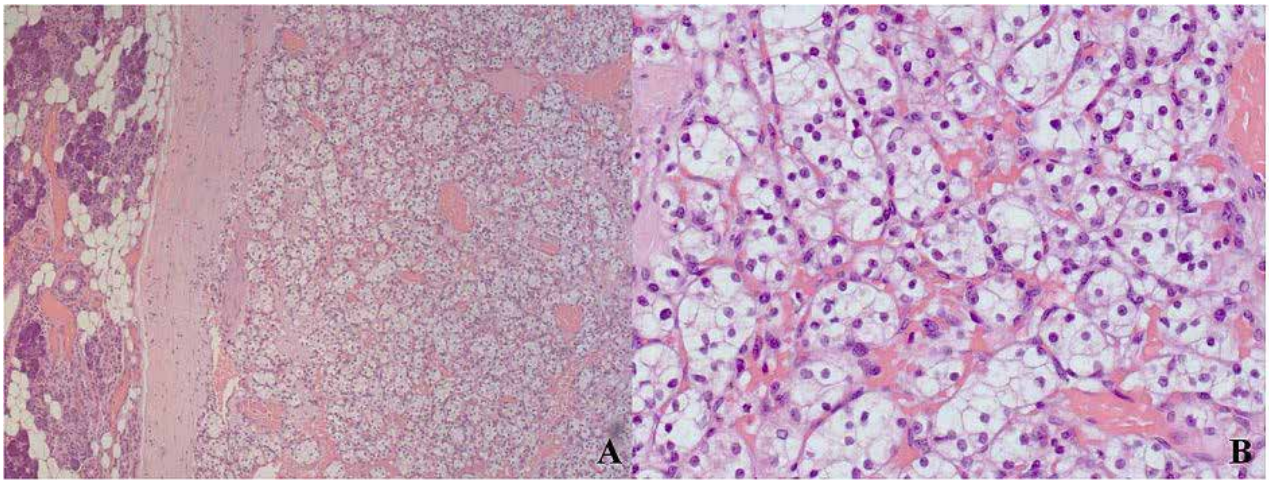
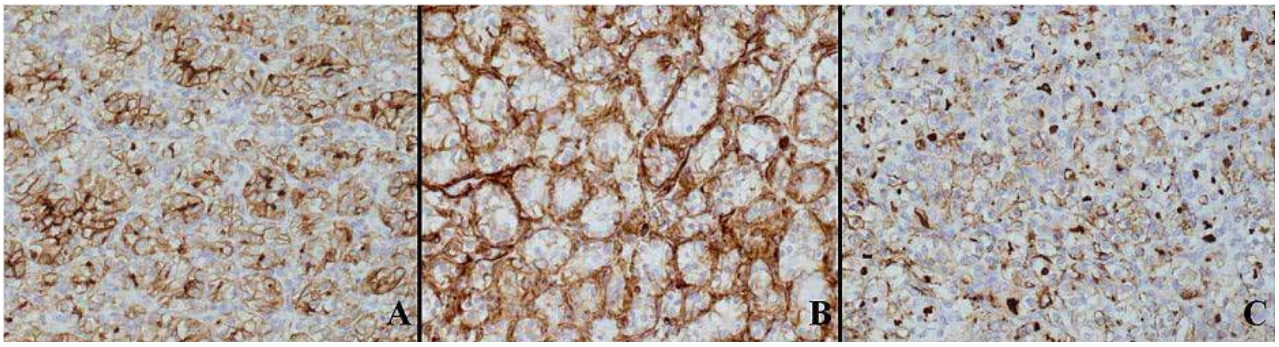
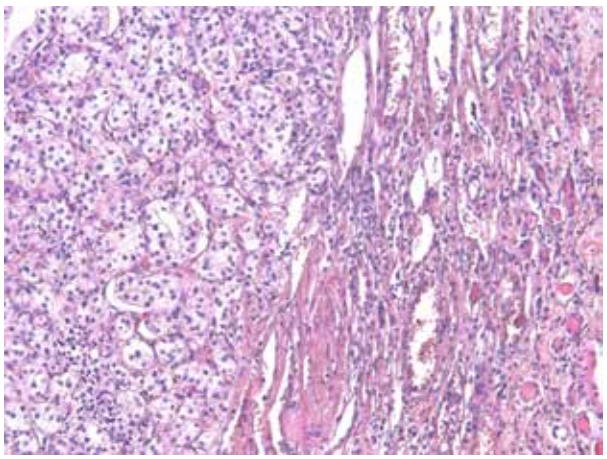


Fig. 2. Immunohistochemical findings of the parotid mass. Immunohistochemistry detected positive staining for CD10 (C), vimentin (D) and EMA (E). A-C, O.M.: 200x.



showed an isolated right-sided lobular parotid mass that measured 3.5 x 2.4 x 2.5 cm, with an intense contrast uptake. Intraoperative examination of frozen sections revealed a clear cell neoplasm. The patient underwent a total parotidectomy with facial nerve preservation. Macroscopically, the parotid harbored a soft, well-encapsulated, orange-tan, homogenous and well-circumscribed lesion. The tumor appeared to be confined within a thin capsule. The remainder of the specimen demonstrated normal parotid tissue. Histological evaluation identified a non-encapsulated tumor. The mass was totally composed of solid clusters of polygonal-to-round cells with abundant clear cytoplasm, large slightly basophilic nuclei and small nucleoli. Pleomorphism was limited and no mitoses were found (Fig. 1A-B). There was also a prominent vascularization and an expansive pattern of growth with isolated solid nests infiltrating the capsule. Differential diagnosis between clear cell oncocytoma of parotid gland and metastasis from clear cell RCC was posed. Immunohistochemistry detected positive staining for CD10, vimentin, EMA (Fig. 2A-C), and negativity of CK7 and CK20; therefore, the final diagnosis

Fig. 3. Histological features of the renal neoplasm. The renal mass consisted of nests of medium-sized polygonal cells with abundant clear cytoplasm, surrounded by a network of thin-walled blood vessels, with pleomorphic nuclei, variably vesicular chromatin and prominent nucleoli. O.M. 200x.



was renal cell carcinoma metastatic to the parotid gland. Following this diagnosis, the patient underwent a whole body CT-scan demonstrating 3 small lesions in the right lung and a 9-cm lesion of the kidney with renal vein invasion. Although the renal lesion had a large diameter, the patient underwent only a partial nephrectomy due to her clinical condition. Grossly, the surgical specimen was entirely replaced by a 9,5 x 6 x 6 cm yellow-white mass, with focal extension through the renal capsule. Microscopically the mass consisted of nests of medium-sized polygonal cells with abundant clear cytoplasm, surrounded by a network of thin-walled blood vessels, with pleomorphic nuclei, variably vesicular chromatin and prominent nucleoli (Fig. 3). There was infiltration of surgical margins but not adipose invasion. The final diagnosis was RCC, clear cell type, grading 2 according to ISUP 2013 [5].

Discussion

Metastasis from RCC to the parotid gland is a rare finding [11 12]; however, it should be considered in the differential diagnosis of clear cell neoplasms. RCC poses a particular diagnostic challenge because metastases can present synchronous with the primary tumor; otherwise, a metachronous distant presentation may occur many years after therapy for the primary. In addition it may alert the clinician to an undiagnosed primary renal tumor as in our case, and/or more widespread metastases and, depending on the patient's symptomatology and overall clinical picture, guide the decision making for surgical resection. To date, 46 cases of RCC metastatic to the parotid gland have been described so far [8 11-13]. However, the lack of a complete radiological and immunohistochemical work-up in 14 cases, renders these diagnoses

Tab. I. Summary of case reports of RCC metastatic to the parotid gland.

Author	Age	Sex	Presenting symptom	Location	Size (cm)	Chronicity	RCC	Other simultaneous metastasis	Time to metachronous	Treatment
Patey et al.	63	F	Pulsatile mass	/	/	Syn	RCC	/	/	Radiotherapy and excision
Kucan et al.	55	M	Mass	R	/	Syn	RCC	/	/	Superficial parotidectomy
Percival et al.	71	F	Mass	R	4	Syn	L RCC	Liver, lung	/	Surgical excision
Sist et al.	62	M	Mass	L	3	Syn	R RCC	/	/	Deep parotidectomy with preservetion of facial nerve
Smits et al.	69	F	Painful mass	R	2	Meta	R RCC	Submandibular gland	9 years	Excision of mass
Hessan et al.	52	M	Mass	L	/	Syn	L RCC	Lungs, ribs, lumbar spine and brain	/	Superficial parotidectomy
Harrison et al.	60	F	Mass	R	2	Meta	RCC	None	10 years	Excision of lesion
Gunbay et al.	60	M	Painful mass and numbness of commissure of lip	L	4	Meta	L RCC	/	19 months	Total parotidectomy of mass extending into pterygomaxillary fossa
Melnick et al.	72	M	Mass	L	8	Syn	R RCC	Liver, lungs, mediastinum, adrenal	/	Palliative radiotherapy
Owens et al.	75	F	Mass	L	3	Meta	R RCC	None	8 years	Total parotidectomy with facial nerve preservation
Owens et al.	55	M	Pulsatile mass	R	4	Syn	L RCC	Chest, brain, bone	/	Superficial parotidectomy with partial excision of masseter
Coppa et al.	42	M	Pulsatile mass, tinnitus	L	4	Syn	R RCC	Perirenal lymph nodes	/	Superficial parotidectomy with facial nerve preservation
Coppa et al.	55	M	Painful mass	R	/	Meta	L RCC	Lungs, axillary lymph nodes	7 years	Multiple partial parotid resections
Pisani et al.	59	M	Mass	L	2	Syn	L RCC	Cerebellar, vertebral	/	Superficial parotidectomy with facial nerve preservation
Sarangi et al.	71	M	Mass	B	/	Syn/Meta	R RCC	/	4 months	Bilateral superficial parotidectomy
Ravi et al.	55	F	Masses	B	3	Meta	R RCC	/	7 years	Superficial parotidectomy with facial nerve preservation

Tab. I. Summary of case reports of RCC metastatic to the parotid gland (*follows*).

Borghi et al.	63	M	Mass	R	2,5	Syn	L RCC	Liver, pancreas	/	Partial parotidectomy
Stanley et al.	71	F	/	R	/	Meta	/	/	/	/
Stanley et al.	40	M	/	R	/	Meta	/	/	/	/
Sykes et al.	59	/	Mass	L	3	Syn	L RCC	Perirenal lymph nodes	/	Superficial parotidectomy with facial nerve preservation
Gangopadhyay et al.	48	M	Mass	L	1,5	Syn	L RCC	R adrenal	/	Superficial parotidectomy
Vara et al.	55	M	Painful mass	L	2	Meta	R RCC	/	5/6 years	Total parotidectomy with facial nerve preservation
Adil et al.	52	M	Mass	R	6	Meta	L RCC	Lymph nodes	5 months	Mass excision, neck dissection
Kundu et al.	61	M	Facial weakness, post-auricular pain and mass	R	2	Syn	L RCC	R adrenal, bone, skin, lungs, cerebral	/	Radiotherapy, pain relief, hospice
Li et al.	63	M	/	B	3/2,5	Meta	/	/	10/14 years	/
Park et al.	83	F	Mass	L	2,5	Meta	L RCC	None	10 years	Superficial parotidectomy with facial nerve preservation
Gogus et al.	59	F	/	R	3	Meta	/	/	10 years	/
Seijas et al.	67	M	Mass	L	2	Syn	R RCC	B adrenal, lungs, retroperitoneal lymph nodes	/	Superficial parotidectomy with facial nerve preservation
Newton et al.	74	F	/	R	1,5	Meta	/	/	7 years	/
Mrena et al.	76	F	Mass	R	/	Meta	L RCC	Controlateral kidney, lung, bone	9 years	/
Mrena et al.	62	M	Mass	L	3	Meta	R RCC	None	5 years	Superficial parotidectomy and selective neck dissection (II-III)
Mrena et al.	58	F	Tender mass	R	0,8	Syn	R RCC	Shoulder	/	Superficial parotidectomy
Spreafico et al.	67	M	Mass	R	6	Meta	R RCC	Ipsilateral cervical lymph nodes	18 months	Total parotidectomy and selective neck dissection (I-V) with removal of large portion of masseter and inferior facial nerve
Laco et al.	75	M	/	R	3	Syn	/	/	/	/
Deeb et al.	82	M	Mass, pain	R	4	Meta	R RCC	/	19 years	Total parotidectomy
Lau et al.	79	F	/	L	2	Meta	/	/	16 years	/
Udager et al.	64	M	Mass	R	1,4	Meta	L RCC	Lungs	6 years	Sunitinib
Wayne et al.	61	F	Mass	L	/	Meta	/	Pancreas, skin	/	Superficial parotidectomy
Lawlor et al.	71	F	Mass	R	3	Meta	RCC R	Pancreas	5 years	Total parotidectomy with facial nerve preservation
Our case	60	F	Mass	R	3,5	Syn	RCC R	Lungs	/	Total parotidectomy with facial nerve preservation

M: male; F: female; R: right; L: left; B: bilateral; RCC: renal cell carcinoma; Syn: synchronous; Meta: metachronous

not confirmed (Tab. I). The mean age of onset was 63 years (range: 40-83 ys) with a male predilection. All the patients had a palpable mass on presentation, mostly right; only in three cases the lesion was bilateral. Nineteen patients were asymptomatic. The mean size of the metastatic lesion was 2.5 cm (ranging from 0.8 cm to 8 cm). Just less than half of the cases presented as synchronous metastases, while 19 cases were discovered metachronously. Fourteen patients had been diagnosed and treated for RCC prior to parotid metastasis with an interval time spanning from 5 months to 19 years. In 16 cases, staging work-up demonstrated metastatic disease beyond the parotid. The other sites of metastasis included lungs, liver and peripheral lymph nodes. The treatment consisted of surgery in about all cases, with only three cases treated with radiotherapy *plus* surgery. Interestingly, only in one case, parotid metastasis was the first sign of RCC. For all these reasons, metastatic parotid clear cell RCC can be a challenging diagnosis. Differential diagnosis includes both primary and sec-

ondary clear cell tumors (myoepithelioma, clear cell oncocytoma, clear cell acinic cell carcinoma, myoepithelial carcinoma, epithelial-myoepithelial carcinoma, mucoepidermoid carcinoma, primary clear cell carcinoma, clear cell thyroid carcinoma, RCC clear cell type and sometimes melanoma) [1]. A panel of immunohistochemical stains (according to the algorithm by Udager et al.) [11] including cytokeratin AE1/AE3, CK7, CK20, p63, vimentin, CD10, EMA, PAX8, HMB45 is mandatory to achieve the correct diagnosis. In our case, the differential diagnosis between clear cell oncocytoma of the parotid gland and metastatic RCC, clear cell type, was resolved by a limited panel of antibodies (CK7, CK20, EMA, CD10). At the last follow-up (10 months after the initial diagnosis) the patient was alive. However, prognosis as well as the appropriate management options for patients with parotid metastasis from RCC is difficult to predict due to the limited number of cases reported in the literature. A thorough metastatic work-up and a collaborative team approach is advantageous to achieve the better clinical response.

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