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Calvarial Metastasis of a Renal Cell Carcinoma, Mimicking a Primary Alveolar Soft Part Sarcoma, in a Young Girl—a Rare Case Report

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Abstract Renal cell carcinoma (RCC) is characterized by an unpredictable clinical behavior. It has a tendency for early metastasis, which, at times is the initial presentation and therein poses a diagnostic challenge. We present a rare case of a disseminated RCC in a 15-year-old girl, who primarily presented with an occipital soft tissue mass. Computed tomography (CT) of the head revealed a soft tissue mass in the scalp, eroding the occipital bone and extending intracranially. Biopsy examination showed overlapping features of an alveolar soft part sarcoma (ASPS) and a RCC. Immunohistochemistry (IHC) showed diffuse positivity for CD10 and focal positivity for vimentin. Cytokeratin (CK) and epithelial membrane antigen (EMA) were negative. The patient was recommended a clinical 'work-up' to rule out a possible primary in the kidneys. Her CT scan abdomen unraveled a large, lobulated, heterogeneous cystic mass, involving the middle and upper pole of the left kidney. Diagnosis of a metastatic RCC was ascertained. The present case represents a rare manifestation of a RCC metastasizing at an unusual location i.e. calvarium in the youngest patient known, so far and masquerading a primary ASPS. It also highlights the value of clinico-patho-radiological correlation, including CD10 as a useful IHC marker in diagnosing a RCC in young patients, especially when histopathological features overlap with ASPS.

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Introduction

Renal cell carcinoma (RCC) accounts for 2–3% of all adult malignancies and 85% of malignant renal tumors [1]. It rarely occurs in children [2, 3]. Approximately 25% cases of RCC present with distant metastases at the initial evaluation, wherein it is challenging, but vital to guide the treating surgeon towards the exact primary [1]. Metastatic RCC has been recorded in more than 50 different, unusual locations, with lungs, liver and bones being the common sites [1]. Calvarium is an extremely unusual site for a metastatic RCC. There are only a handful of reports in the literature describing calvarial mass as the primary presentation of a disseminated RCC [4–9].

Herein, we report a rare case of a young girl, who referred with an occipital mass as the initial manifestation of a RCC that mimicked a primary alveolar soft part sarcoma.

Case History

A 15-year-old girl referred to us with a rapidly increasing, painless swelling in her occipital region of two-month duration. She also had episodes of non-projectile vomiting since the last 3–4 days. She denied any history of trauma or any neurological deficit. She underwent an excision elsewhere, which was diagnosed as an alveolar soft part sarcoma and was referred to our institute, after she developed a recurrence within a month of surgery. On clinical examination, a soft, non-tender subcutaneous soft

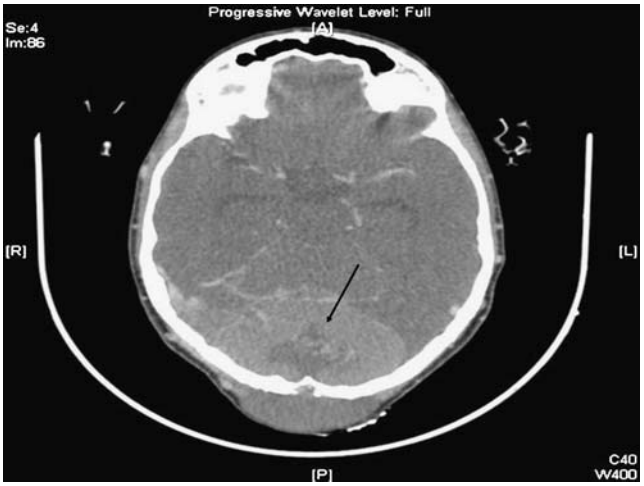

Fig. 1 Computed tomography (CT) of head revealing a vascular soft tissue mass (*arrow*) measuring 8.4×7.4×6 cm in the occipital region, showing bone destruction

tissue mass, measuring 8×6 cm was noted in her occipital region on both the sides of her scar from the previous surgery.

Imaging Findings of Head

Computed tomography (CT) of the head revealed a vascular soft tissue mass measuring 8.4×7.4×6 cm in the occipital region with bone destruction and intracranial extension, causing compression of the dura mater and the cerebellum. An enhancing area was also noted in the right transverse and sigmoid sinus, secondary to the tumor thrombosis. Rest of the brain parenchyma was unremarkable. Radiologically, the differential diagnoses were a malignant soft tissue sarcoma with an intracranial extension vs. a metastasis from an unknown primary. An excision biopsy of the mass was performed thereafter (Fig. 1).

The hematoxylin and eosin (H&E) stained slides and microsections from the paraffin blocks from the previous excision were submitted to us for a review. The gross findings were unavailable from the referring laboratory.

Histopathological Findings

H& E stained sections revealed a malignant tumor arranged in papillary and 'nesting' pattern with variably sized tumor cell nests separated by delicate fibrovascular septae. Cells in the larger nests were focally discohesive, giving rise to alveolar pattern. At places, the cells were arranged in papillaroid structures. The tumor cells were large, round to polygonal, containing abundant, eosinophilic, and granular to clear cytoplasm. Nuclei were round to oval, central to eccentrically placed with irregular borders, vesicular chromatin and prominent nucleoli. Mitoses were rare. Periodic acid–Schiff (PAS) staining demonstrated cytoplasmic positivity that was equivocal to diastase treatment. On immunohistochemistry (IHC) tumor cells were strongly

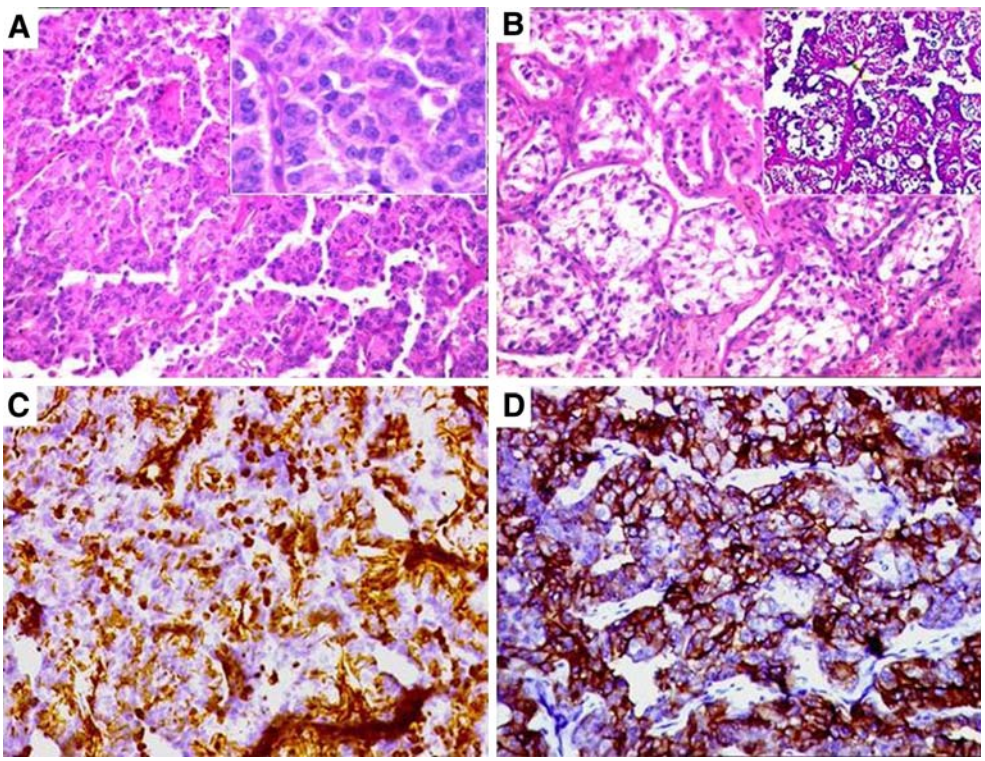

Fig. 2 **a** Tumor showing organoid, nesting and papillary pattern of eosinophilic cells separated by thin vascular septae H&E ×100. *Inset* showing high power view with large, polygonal cells with abundant, granular, eosinophilic cytoplasm and discernable nucleoli. H&E ×400. **b** Focal areas showing cytoplasmic clearing. H&E ×200. *Inset* showing equivocal PAS positivity. PAS with diastase ×200. **c** Focal positivity for vimentin. DAB ×200. **d** Diffuse positivity for CD10. DAB ×200

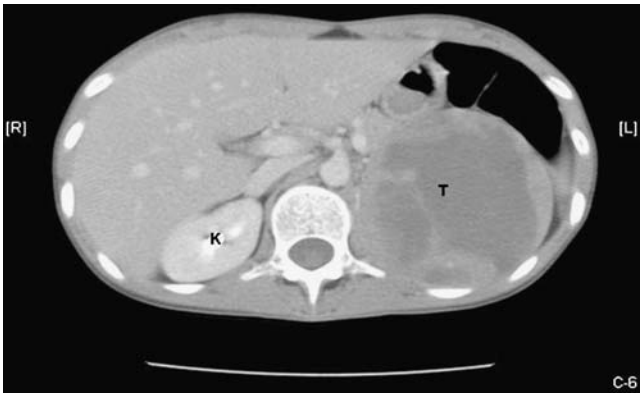

Fig. 3 CT scan abdomen revealing a large lobulated, heterogeneous, predominantly cystic tumor (*T*) mass involving middle and upper pole of left kidney measuring 12.5×9.9×7.8 cm

immunoreactive for CD10 and focally for vimentin. Pancytokeratin (CK), CK7, CK20, EMA (epithelial membrane antigen), carcinoembryogenic antigen (CEA), desmin and S100 were negative (Fig. 2).

Differential diagnoses of an alveolar soft part sarcoma (ASPS) and a metastatic RCC were offered.

Further, it was commented to perform a clinical 'work-up' for the possibility of a metastatic RCC. Her routine laboratory investigations, including renal function tests were within normal limits. The patient was subjected to detailed radiological investigations, especially abdominal imaging.

Abdominal Imaging

Abdominal ultrasound and subsequent CT scan abdomen of the patient unraveled a large lobulated, heterogeneous, predominantly cystic mass measuring 12.5×9.9×7.8 cm and involving the middle and upper pole of the left kidney. The tumor was confined to the kidney and there was no associated abdominal or pelvic lymphadenopathy (Fig. 3). A subsequent CT scan of the chest showed multiple nodules in both the lungs, suspicious for metastasis.

A final diagnosis of a metastatic renal cell carcinoma (RCC) was ascertained. The patient was subjected to palliative chemotherapy. However, unfortunately, she succumbed to the disease within 5 months of diagnosis.

Discussion

Renal cell carcinoma (RCC) is a tumor with an unpredictable clinical course and behavior [1]. Childhood RCC is a rare neoplasm which, of late, has been identified to be having a unique histologic, immunohistochemical, and cytogenetic profile [t(x; 1) (p11; q21), t(X; 17) (p11.2; q25). The incidence of childhood RCC is estimated to be from 0.1% to 0.3% of all neoplasms and 1.8% to 6.3% of all malignant renal tumors [2, 3].

The classical clinical triad of flank pain, haematuria and a palpable abdominal mass occurs in only about 10% of the patients of a RCC, and many such patients may remain asymptomatic [1, 4]. In some cases, metastasis precedes the clinical manifestations of the primary tumor as noted in our case. However, calvarium is an extremely rare site for a metastatic RCC [4–9]. Forbes et al. [10] reviewed 1,668 patients with RCC and only five patients developed skull metastasis. Out of all the cases documented with skull metastasis, in only seven cases, along with the current case, calvarial metastasis was the first presentation [4–9]. Occipital and frontal bones have been found to be commonly involved. The present case is the youngest patient to present with skull metastasis of RCC to best of our knowledge (Table 1).

In view of a recurrent soft tissue mass lesion in a young girl with overlapping histological features, an ASPS was

Table 1 Literature review of documented cases of Renal cell carcinoma (RCC) primarily presenting with Calvarial Metastasis

Authors (year)	No. of cases	Age(years)/ gender	Location in the calvaria	Treatment	Follow-up
Sunita et al. [4]	1	63/F	Frontal	Not mentioned	Not mentioned
Wahner-Roedler L et al. [5]	1	72/F	Occipital	Palliative radiotherapy	LTF after 15 mo
Koutnouyan HA et al. [6]	1	33/F	Frontal	NA	DOD at 9 mo
Gaetani et al. [7]	2	66/M 60/F	Occipital Frontal	En bloc metastatectomy in both cases	Average survival 9 mo
De Vos C et al. [8]	1	NA	Temporal	Radical nephrectomy and local Radiotherapy	NA
Yeh HC et al. [9]	1	80/M	Parietal	Metastatectomy and radical nephrectomy	NED at 22 mo
Present case	1	16/F	Occipital	Excision of metastatic lesion and palliative chemotherapy	DOD at 5 mo

LTF Lost to follow up, *NED* no evidence of disease, *DOD* died of disease, *mo* months

the closest differential diagnosis. ASPS resembles a RCC morphologically, as both the tumors show nesting and alveolar growth patterns of tumor cells, which are polygonal shaped with abundant eosinophilic cytoplasm and distinct borders. In addition, the present case also showed focal papillary arrangements. Papillary tumors are quite common in younger age group RCCs that are characteristically of high-grade, high-stage tumors with several foci of dystrophic calcifications [3] However, negative immunoreactivity for epithelial markers in our case made diagnosis of a renal cell carcinoma challenging, although the same can be seen in this tumor. Lately, CD10 has been found to be a useful marker in the diagnosis of a RCC that was found to be diffusely positivity in our case [11]. Nonetheless, ASPS remained a morphological differential. Apart from morphological similarities, pediatric RCC also shares the similar cytogenetic findings with an ASPS i.e. ASPL-TFE3 gene fusion resulting from translocation, t(X; 17) (p11.2; q25) [12]. Hence, the possibility that such renal tumors might in fact be related to ASPS has been postulated. TFE3 analysis was not performed in our case. The presence of a substantial renal mass on imaging with the above described histopathological and IHC profile, including CD10 immunoreactivity led to a conclusive diagnosis of a RCC in the present case.

Other commonly occurring tumors in the calvarial location (in occipital bone) such as chordoma, germinoma, paraganglioma, hemangioblastoma, clear cell meningioma, oligodendroglioma (in view of intracranial extension) as well as other metastatic tumors which exhibit clear cell morphology were considered as in previous studies [4, 6, 7]. Clear cell sarcoma of kidney also known as “bone metastatising tumor” found in younger age group can present with skull metastasis [7]. All these differentials were excluded, based on histomorphology.

In our case, histopathologic examination of the metastatic lesion, guided the ‘work-up’ for the possible primary in kidneys.

The mode of spread of a RCC to the skull is not clearly understood. However, it has been postulated that metastatic RCC cells reach the head and neck region by normal hematogenous flow via lungs. The other possible route might be tumoral embolization via the Batson plexus, through the anastomoses between the avalvular vertebral and epidural venous system [4, 6]. We assume that the route of spread in this case was hematogenous to occipital bone and from there, it extended to scalp and brain. The presence of tumor thrombus in the sinuses and lung metastasis further supports the hematogenous spread in the present case.

Metastatic RCC has a poor prognosis, with high mortality rates (80% have a mortality within 5 years). When a RCC primarily manifests as a metastatic disease it connotes an extremely poor prognosis, as these patients have a median survival of less than a year [1, 2]. Our patient had presented at an advanced stage with skull and lung metastasis. The biologic aggressiveness of the metastatic RCC precludes a nephrectomy and metastatectomy as the treatment modality. However, in recent years, nephrectomy has acquired a new adjuvant role in the treatment of metastatic disease, because it reduces the tumor burden and spontaneous regression of RCC at metastatic site has been documented [13]. In view of this, solitary skull metastases local excision of lesion without sacrifice of vital structures seems both warranted and prudent. Unfortunately, en bloc tumor removal was not possible in the present case and patient succumbed to the disease.

To conclude, although calvarial metastasis in a young patient from a RCC is unusual, it should be considered, especially when an ASPS is a close clinicopathological differential diagnosis. CD10 can act as a useful marker in such situations in substantiating a diagnosis of a RCC. This would be helpful in guiding the treating oncosurgeons and radiodiagnosis in order to identify more such cases. Further, it would be useful to investigate the dissemination pathways and other cellular mechanisms involved in metastatic RCC, in order to achieve a better understanding and improvisation in the management of patients with advanced disease.

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