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Urothelial Carcinoma with Rhabdoid Features

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Abstract **Case Report**

The histo-morphological spectrum of variant transitional cell carcinoma (TCC) types has a wide range of different impacts on both thearapeutic approaches and clinical outcomes when compared to the TCC without variant pathology. TCC with rhabdoid features is rarely encountered and has been reported in only handful of cases. Herein we report a case of urothelial carcinoma with rhabdoid features originating from the upper urinary tract.

Keywords: Rhabdoid; variant; urothelial carcinoma; transitional cell carcinoma; nephrectomy.

INTRODUCTİON

The transitional cell layer of the urinary tract, also called as the urothelium, might exhibit multifarious metaplastic transformations, moreover, neoplasms originating from the urothelium might also exhibit a variety of different morphologies (Perez-Montiel, 2006). The word "variant" represents a markedly dissimilar histo-morphological phenotype of a given neoplasm (Zhai, 2007). The histo-morphological spectrum of the variants of the transitional cell carcinoma (TCC) has a wide range of different impacts on both thearapeutic approaches and clinical outcomes when compared to the traditional TCC. Therefore, clinicians should be acquainted of this vital aspect to avoid diagnostic misapprehensions. Metastatic tumours often maintain to display a characteristic histo-pathological pattern, and awareness of the histo-pathology of the variant type promotes the affiliation of metastases to the primary cancer (Amin, 2009). Tumours with rhabdoid differentiation in various primary localizations have been described in the literature, but TCC's with rhabdoid differentiation are rarely encountered and have been reported in only handful of cases (Zhai, 2007; Parwani, 2006; Fukumura, 2009; Warren, 2014; Inagaki, 2000; Kumar, 1992; Harris, 1982). Tumours with rhabdoid cells tend to be more aggressive than tumours without rhabdoid cells, as rhabdoid cells are considered to represent phenotypic divergence in the course of dedifferentiation or tumour progression (Tajima, 2015). Herein, a case of a urothelial carcinoma with rhabdoid features originating from the upper urinary tract is presented.

CLINICAL SUMMARY

A 70 year-old male patient with upper urinary tract urothelial carcinoma with rhabdoid features is presented to our institution's outpatient clinic with his imaging studies and pathological slides. The patient was referred for the radiologically detected right renal and ureteral mass while under investigation for anemia. He had DM, HT, and CRF with an estimated GFR of 55.28. He had smoking history of 50 packs/day*years. He had no history of surgery. His physical examination revealed palpable mass in the right upper abdominal quadrant. Preoperative non-enhanced computed tomography scan revealed grade IV calyceal dilatation with severely thinned right renal parenchyma and nodular irregularly shaped soft tissue formations in pelvicalyceal system and various locations in the right ureteral lumen (Figure 1). Preoperative FDG PET/CT imaging study revealed high uptake in these soft tissue formations with SUVmax of 17.4 in kidney and 7 in the ureter, also pararenal areas in the proximity of diaphragm had high uptake with SUVmax of 16.5 and the lymph nodes with a diameter of 1 cm in the paraaortic area close to renal hilus had high uptake with

SUVmax of 20.6. No metastases were present other than lymph nodes. The patient underwent laparoscopic surgery consisting of radical nephroureterectomy with cuff excision and paraaortic lymphadenectomy. Gross appearence of the specimen is shown in the Figure 2. Pathological diagnosis was urothelial carcinoma with rhabdoid features. Histopathological examination is shown in the Figure 3. One month after the surgery, the patient was hospitalized because of respiratory distress due to Covid-19 infection. Imaging studies revealed diffuse metastases in the liver up to 4 cm in diameter. The patient died because of ARDS due to SARS-CoV-2 infection in the ICU 6 weeks after the surgery. Although the cause of death of this case was SARS-CoV-2 infection, the prognosis of the locally advanced urothelial carcinoma with rhabdoid features is poor as indicated with too early diffuse liver metastases.

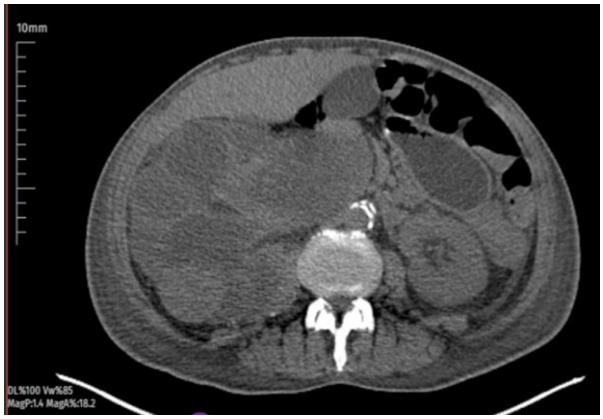

Figure 1: Preoperative non-enhanced computed tomography image with grade IV calyceal dilatation and severely thinned right renal parenchyma

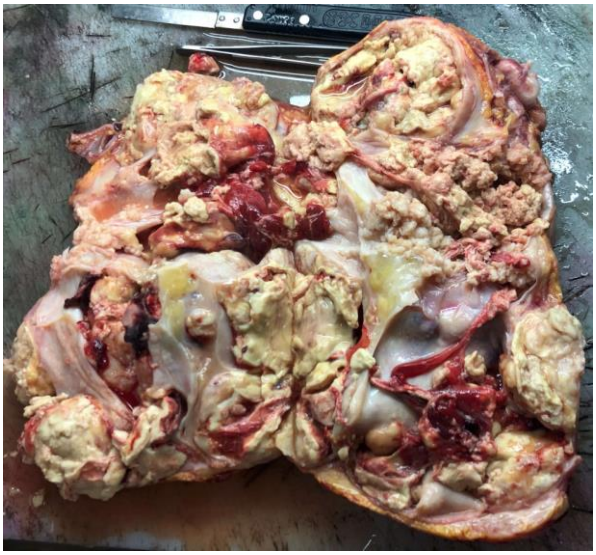

Figure 2: Gross appearance of the specimen

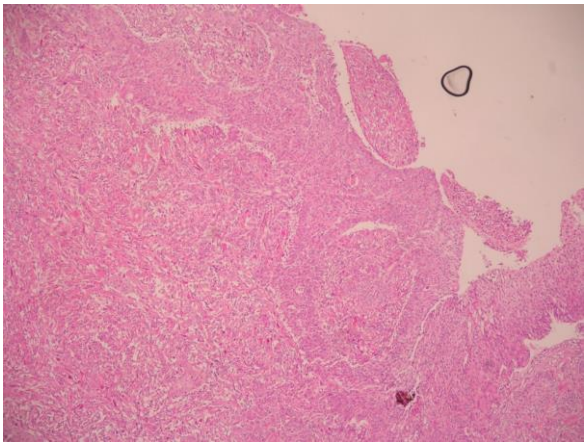

Figure 3: Rhabdoid areas are admixed with areas of conventional high-grade urothelial carcinoma (x40)

DISCUSSION

Initially Beckwith *et al*., described the first rhabdoid tumour as a variant of Wilms tumour in the year 1978 as rhabdomyosarcomatoid pattern (Beckwith, 1978). Nearly a decade later Harris *et al*., recorded a rhabdoid phenotype in bladder cancer that detected at sequential biopsies and at an autopsy examination which was the first known co-existence with transitional cell carcinoma (Harris,1987). In addition, although the tumours with rhabdoid phenotypes have been defined in many regions including liver, brain, heart, mediastinum and extremities, and even though these tumours have begun to be considered as separate entities, it still remains to be an understated condition in the urological literature due to the lack of precise data on its frequency and the demonstration of the disease owing to its rarity (Kagotani, 2015).

Gross hematuria is the most commonly reported clinical manifestation in these patients and the definitive diagnosis is made histo-pathologically by immune-staining of cytokeratin (Perez-Montiel, 2006; Kagotani, 2015). The rhabdoid phenotype has its own distinctive cytogenetic, histo-pathological and immunohistochemical findings, although the definite cell of origin is still unknown today, the characteristics of rhabdoid cells are as follows; they are large and either oval or round in shape, have ample cytoplasm and comprises of one or more prominent nucleoli, an eccentric nuclei and eosinophilic fibrillar bodies that consist of intermediate filaments (Harris, 1987). Also, these cells are found either in large sheets or in clusters. Reactivity against cytokeratin (CAM5.2, AE1/AE3), desmin and vimentin is generally seen in the immunohistochemical assays and translocation of the long arm of chromosome 22 (22q11) and the short arm of chromosome 6 (6p12) was observed in the cytogenetic analyses (Schofield, 1996). Furthermore, some of the most common genetic changes in rhabdoid tumours are the inactivation of the SMARCB1 tumour suppressor gene, bi-alleic inactivation of hSNF5-INI1 and the deletion of the INI1 gene located on the chromosome 22 (Bourdeaut, 2008; Versteege, 1998;

Brennan, 2013). From the viewpoint of differential diagnosis, signet-ring cell and plasmacytoid variants of urothelial carcinoma should be considered. Even though the plasmacytoid variant cells have large eosinophilic cytoplasm and eccentrically located nuclei, the neoplastic cells do not have inclusion bodies like rhabdoid cells (Perez-Montiel, 2006). This is also true for neoplastic cells of signet-ring variant of urothelial carcinoma (Perez-Montiel, 2006). For that reason, a meticulous examination of the pathological specimen sheds light on revealing the rhabdoid component.

In our case, even though the patient didn't die in consequence of urothelial carcinoma with rhabdoid features, metastatic foci up to 4 cm in the liver that developed within the first month after the surgery illustrates the severity of the situation. The prognosis of urothelial carcinoma with rhabdoid features is generally considered to be poor and as a consequence, efficacy of the conventional therapies appears to be the most striking challenge. Due to the rarity of the disease, a standard treatment modality for the rhabdoid phenotype has not yet been clearly defined.

The most comprehensive case series to date has been reported by Parwani et al. including six cases of urothelial carcinoma with rhabdoid features (Parwani, 2006). Of these patients, 2 of them were renal pelvis tumours, while 4 of them were bladder tumours. 4 of these 6 patients underwent surgery (radical nephrectomy, n:2, radical cystoprostatectomy, n:2), while 2 were followed up with observation. The rhabdoid phenotype was involved roughly 40% of the tumour components. 2 of these patients died within the first month, and the 3rd patient died in the 4th month following. The other 3 patients were alive after 9th month of the initial diagnosis. Furthermore, Kagotani *et al*., reported that in a case of a urothelial carcinoma with rhabdoid features, which was at an earlier stage and has not metastasized yet, treated with cystectomy and lymph node dissection, over 1-year recurrence-free survival was noted (Kagotani, 2015). Leite *et al*., reported in a study on neoadjuvant chemotherapy in urothelial carcinomas with variant histologies, 2 of the patients with rhabdoid phenotypes did not respond to neoadjuvant chemotherapy at all (Leite, 2022). In a study conducted by Sano *et al*., on pancreatic anaplastic carcinoma with rhabdoid histo-morphology, membrane proteins such as epithelial membrane antigen, β-catenin and E-cadherin were observed to accumulate in the rhabdoid tumour cells' cytoplasmic inclusions (Sano, 2014). Resultant mislocalization and downregulation of these molecules is thought to provide the unique eosinophilic cytoplasm of the rhabdoid phenotype (Sano, 2014). Kumar *et al*., (1992) and Warren *et al*., (2014) reported patients with pure rhabdoid features in bladder cancer without other histo-pathological constituents.

As it is seen in these studies, tumours with rhabdoid features have very aggressive potential by nature and are generally encountered at a higher stage and grade, also, the survival is poor. In the management of metastasized urothelial carcinoma, even though some immune check-point inhibitors and platinium-based chemotherapeutics have been used in the clinical practice, their efficacy on urothelial carcinomas with rhabdoid features is still obscure today. The critical role of abovementioned genes on the pathogenesis of rhabdoid phenotype may pioneer probable molecular-targeted therapeutic approaches like inducing the arrest of cell cycles in rhabdoid cell lines (Brennan, 2013).

In conclusion, the presented case affirms the aggressiveness in the clinical course of urothelial carcinoma with rhabdoid features and adds further evidence to this rare entity. Moreover, due to the limited number of studies reported on this subject, it is still unclear whether this entity is a rare urothelial carcinoma phenotype or a completely discrete entity.

Conflict of Interest: None declared.

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